

## Effects of smoking on tooth loss among individuals under periodontal maintenance therapy: a systematic review and meta-analysis

Os efeitos do tabagismo sobre a perda dentária em indivíduos em terapia periodontal de suporte: uma revisão sistemática e meta-análise

Los efectos del consumo de tabaco en la pérdida de dientes entre personas con una terapia de mantenimiento periodontal: un revisión sistemática y metaanálisis

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### Abstract

Dental mortality has been reported by longitudinal studies on periodontal maintenance therapy (PMT), but the independent effect of smoking on tooth loss (TL), adjusted for important confounding variables, has been poorly evaluated. This systematic review aimed to assess and analyze the isolated effect of smoking TL among individuals undergoing PMT. Electronic, manual, grey literature, and recent articles (from April 2018) were searched, with no restriction regarding language; respective dates of publication were included. Epidemiological clinical studies reporting TL data among smokers undergoing PMT in comparison to nonsmoker control groups were selected. Methodological quality was assessed using the Newcastle-Ottawa Scale. Meta-analysis was performed, as well as  $I^2$  heterogeneity and sensitivity tests. Evidence quality was assessed using GRADE (Grading of Recommendations, Assessment, Development and Evaluation). Eleven papers were included in the systematic review: four case-control and seven cohort studies. Ten out of the 11 studies concluded that smoking was an important risk factor for the occurrence of TL. Meta-analysis of four of the cohort studies found that smokers had 3.24 times the chance of occurrence of TL than nonsmokers undergoing PMT (95%CI: 1.33-7.90). Overall, studies' risk of bias was low. The quality of the scientific evidence moderately supports that smokers undergoing PMT have a greater chance of TL than nonsmokers.

Tooth Loss; Smoking; Periodontitis; Meta-analysis

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## Introduction

Periodontal maintenance therapy (PMT) can be considered a critical factor for success in controlling periodontitis and in the long-term maintenance of teeth <sup>1</sup>. In addition, neglecting a regular PMT program has been associated with increased risk of reinfection and progression of periodontitis, as well as increased tooth loss (TL) <sup>2,3</sup>.

During periodontal clinical reevaluation in PMT, it is important to analyze the biological, behavioral, and social risk variables associated with periodontal disease, especially smoking, dental plaque scores, and diabetes mellitus <sup>4,5,6</sup>. Moreover, many other factors can affect clinical outcomes during PMT: degree of compliance and adherence to the proposed recommendations, oral hygiene practice, age, smoking status, systemic diseases that can compromise the immune response, initial tooth prognosis, tooth location, residual periodontal pockets, and bleeding on probing (BOP). These factors have been cited as critical for periodontal condition stability <sup>7,8</sup>.

Identification of risk variables for TL in PMT programs can help clinicians and periodontists establish the frequency of recall visits, as well as improve the adherence to maintenance programs, with greater compliance from individuals <sup>9</sup>. Several studies have demonstrated the effectiveness of periodontal therapy in reducing TL rates, as well as the importance of PMT compliance <sup>10,11,12,13</sup>.

Smoking is an important risk factor for periodontitis. Various studies have shown that this deleterious habit is strongly associated with increased susceptibility to periodontitis, increased periodontitis severity and progression, as well as higher TL <sup>14,15,16,17</sup>.

Although TL has already been reported by longitudinal studies among individuals undergoing PMT <sup>1,7,8,18,19,20,21,22,23,24,25,26</sup>, the independent effect of smoking on TL, adjusted for important confounding variables (i.e. age, gender, diabetes, and socioeconomic level) in individuals undergoing PMT, has not yet been evaluated through systematic review and meta-analysis. Therefore, this paper aimed to evaluate scientific evidence of the independent effect of smoking on TL among individuals undergoing PMT.

## Material and methods

This systematic review was registered in PROSPERO (n. CRD42016026083) and was conducted in agreement with the guidelines of *Transparent Reporting of Systematic Reviews and Meta-Analyses* (PRISMA Statement) <sup>27</sup>.

### Focal question

Our clinical question (PICO) was: “what is the effect of smoking on tooth loss, for individuals undergoing periodontal maintenance therapy?” (P = individuals undergoing PMT; I = smoking; C = non-smoker individuals undergoing PMT; O = tooth loss).

### Inclusion criteria

Epidemiological clinical studies (observational studies and clinical trials), containing data on TL among smokers and nonsmokers undergoing PMT, were included. There was no restriction regarding age, language, date of publication or follow-up period.

### Exclusion criteria

Papers with absence of nonsmokers (control group), case reports or case series, letters to the editor, and literature reviews were excluded.

## **Search strategy**

The databases included MEDLINE via PubMed (<https://pubmed.gov>), Web of Science (<https://isiknowledge.com>), Cochrane Library (<https://cochrane.org/index.htm>), and Scopus (<https://scopus.com>).

No restrictions were imposed with regard to language or year of publication. MeSH terms, keywords, and other selected terms were searched. Boolean operators (OR, AND) were used to combine searches. The following search strategy was used in MEDLINE, Web of Science, Cochrane and Scopus: ((periodontal disease [Mesh] OR periodontitis [Mesh] OR periodontitis OR maintenance periodontal therapy OR periodontal maintenance OR supportive periodontal therapy OR maintenance care OR long-term care [Mesh] OR long-term maintenance) AND (smoke [Mesh] OR smoke OR smoker\* OR tobacco OR tobacco smoker\*) AND (tooth loss [Mesh] OR tooth loss OR tooth mortality OR dental mortality)).

A manual and grey literature search was performed through the ISRCTN Registry (<http://isrctn.com>) and Clinical Trials (<https://clinicaltrials.gov>) databases. Manual searches in the reference lists of included articles were also performed. The reference list retrieved by the electronic databases search was organized by EndNote software, version 17.0 (<https://www.endnote.com/>).

Initially, 780 articles were found. After the removal of 138 duplicates, 642 articles were available for selection. The selection of articles was based on abstracts and titles and carried out independently by three trained and calibrated researchers (A.M.O.A., R.M.C., and T.R.V.). An initial reading of a 10% sample of the list was performed and the kappa agreement was of 0.84. Thus, the three researchers continued reading the remaining articles. Disagreements were resolved by discussion and consensus. After this phase, 44 studies were selected for full text analysis. This analysis was performed independently by each of the three researchers and disagreements were again resolved by discussion and consensus (Figure 1). When a study had missing data or additional information was needed, the corresponding author was contacted.

## **Data extraction and methodological quality assessment**

Data extraction followed a form in which the following information was extracted: study design, sample size, interval time, dental care protocols and procedures, smoking status, and number and/or mean of teeth lost during PMT (Tables 1 and 2, for cohort studies and case-control studies, respectively).

The methodological quality of the included studies was assessed via the *Newcastle-Ottawa Scale* (NOS), by two independent reviewers (A.M.O.A. and T.R.V.). Case-control and cohort studies were evaluated by the NOS for case-control studies and the NOS for cohort studies, respectively. Criteria was comprised of three main items: sample selection, comparability, and exposure (Tables 3 and 4).

**Selection:** whether the study had data on smoking status during PMT, to determine cases and/or exposed individuals.

**Comparability:** whether smoking was adjusted for two or more factors, e.g. diabetes, age, gender, or other risk variables. In this case, a maximum of two points could be assigned (one for each confounder).

**Outcome of interest or Exposure:** whether TL was clinically assessed using clinical examination, radiographic examination, through existing recorded data, or through self-report.

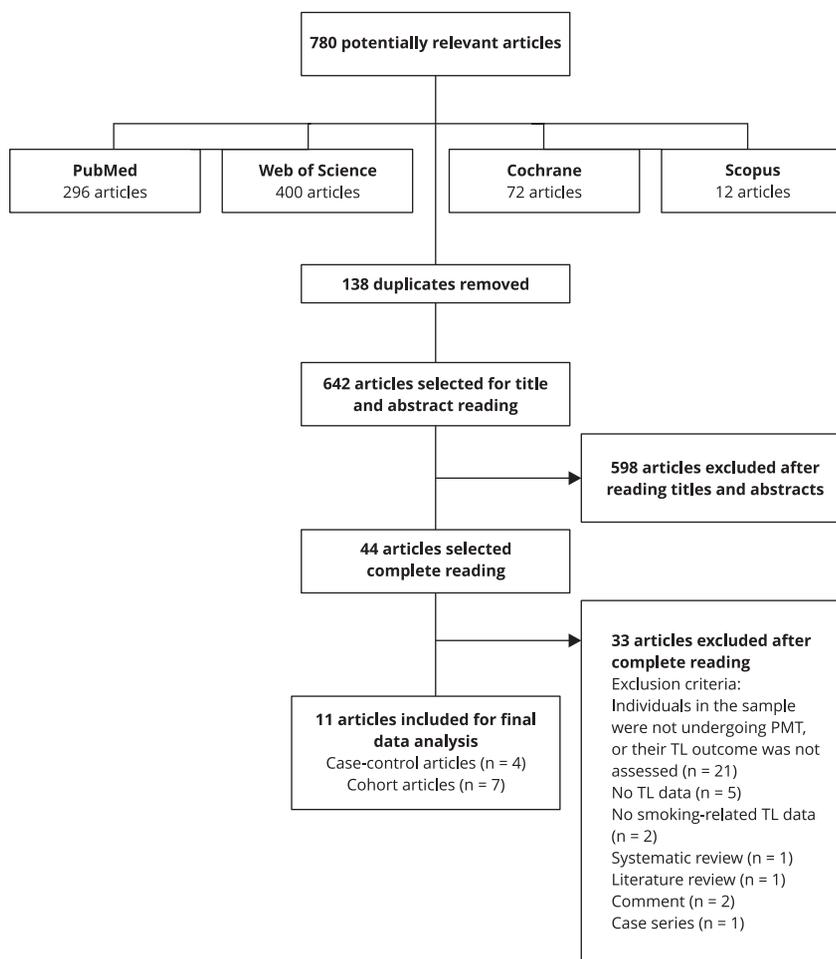
For case-control studies, the NOS scale ranges from 0 (lower methodological quality) to 9 (higher methodological quality). For cohort studies, it ranges from 0 to 10.

## **Meta-analysis**

Comprehensive Meta-Analysis Software, version 2 (<https://www.meta-analysis.com/>), was used for meta-analysis. Odds ratio (OR) and 95% confidence interval (95%CI) for TL in smokers and nonsmokers were extracted as reported in the studies. I<sup>2</sup> heterogeneity and sensitivity tests were performed<sup>28</sup>. For medium to moderate heterogeneity and for low heterogeneity (< 25%), the random effect (≥ 25%) and the fixed effect were used, respectively. Funnel plot analysis was not performed due to the absence of sufficient study numbers<sup>29</sup>. Instead, publication bias was analyzed qualitatively.

**Figure 1**

Flowchart: search strategy and screening process.



PMT: periodontal maintenance therapy; TL: tooth loss.

### **Quality of evidence**

Two reviewers (C.C.M. and F.O.C.) evaluated evidence quality using GRADE (*Grading of Recommendations, Assessment, Development and Evaluation*)<sup>30</sup>. Disagreements were resolved by discussion and consensus. GRADE evaluates evidence quality as high, moderate, low, or very low. Evidence quality assessment was performed through the GRADE PRO software (<https://www.gradepro.org>) (Box 1).

### **Results**

#### **Selection of studies**

Eleven papers were included in this systematic review (Figure 1): seven cohort studies<sup>5,9,20,23,24,31,32</sup>, and four case-control studies<sup>3,33,34,35</sup>. The final selection included no controlled clinical trials.

**Table 1**

Cohort studies characteristics.

Study	Study design	Participants	Maintenance interventions	Smoking status	Primary outcome
Graetz et al. <sup>32</sup>	This longitudinal study investigated the risk of tooth loss under a nonregenerative treatment regimen and aimed to identify prognostic factors for tooth loss.	315	Nine years. Patients with chronic periodontitis who had been treated between 1982 and 1998 (according to a database) and received PMT ( $\geq 1$ visit/year), including annual documentation of PD, as well as complete radiographic documentation at T0 and at the last documented PMT visit (T2).	Smoking status was assessed categorically as nonsmoker/ex-smoker (quit > 5 years ago) or current smoker. Statistical analyses only used smoking status at T0; note that this ignores possible changes of smoking status during SPT.	Current smokers had HR = 2.62 (95%CI: 1.34-5.14) for TL. Former smokers or individuals who never smoked had HR = 1.02 (95%CI: 0.59-1.76) for TL.
Costa et al. <sup>9</sup>	This 5-year study evaluated the incidence, underlying reasons and influence of risk predictors for the occurrence of TL in individuals undergoing a PMT program.	212	Five years. All individuals had undergone APT. In the PMT program, there were 96 RC individuals with maintenance intervals of 6 months, and 116 IC individuals with a maximum interval of 18 months between recalls.	This study included nonsmokers/ex-smokers and smokers (10-19 and > 19 cigarettes per day).	IC smoker individuals lost significantly more teeth. OR = 4.22 (95%CI: 2.01-8.78).
Ravald & Johanson <sup>31</sup>	Assessed the numbers of lost teeth and causes for TL for a time period of 11-14 years after APT (during PMT).	64	11-14 years. Individuals were submitted to PMT with 1-4 times per year maintenance intervals. Evaluated parameters were: BOP, PI, PD and bone level (measured radiographically).	Subjects were divided into 3 groups: smokers with consumption of 1-9 cigarettes/day, smokers with consumption of more than 10 cigarettes/day, and nonsmokers.	TL was significantly more prevalent among smokers than nonsmokers. Smoking contributed to explain TL with OR = 8.0 (95%CI: 1.6-39.0).
Fisher et al. <sup>5</sup>	Assessed disease progression longitudinally in smokers and nonsmokers with chronic periodontitis, undergoing PMT every 3-4 months.	108	3 years. Individuals undergoing PMT underwent evaluation of the following parameters: PI, BOP, PD and CAL, with 3-4 intervals months for each recall.	Smoking status was determined according to self-report, while analysis of expired carbon monoxide concentration identified and quantified this condition. A concentration $\leq 8$ ppm defined nonsmokers, and > 8ppm defined smokers.	No significant difference in the mean number of teeth lost between smokers and nonsmokers at baseline or after 3 years PMT ( $p > 0.05$ ).
Chambrone & Chambrone <sup>23</sup>	Assessed reasons for TL in individuals undergoing APT and PMT.	120	Above 10 years. All subjects followed a PMT protocol: oral hygiene instructions; scaling and root planning; crown polishing; reassessment and surgical periodontal therapy, when indicated. Intervals ranged from 6-12 months.	Individuals grouped into smokers or nonsmokers; number of cigarettes smoked per day not included.	Smokers had the highest TL rates. OR = 4.76 (95%CI: 1.42-15.89).

(continues)

**Table 1 (continued)**

Study	Study design	Participants	Maintenance interventions	Smoking status	Primary outcome
Leung et al. <sup>24</sup>	Identified risk indicators associated with TL and periodontitis in individuals undergoing PMT.	97	5-12 years. Subjects were instructed to perform their own PMT. At each first callback visit, they completed a questionnaire with a trained interviewer, to record TL reasons.	11 of the previously treated patients were current smokers, with a self-reported cumulative consumption of 0.5-56.9 packs/year.	TL due to periodontal reasons was 2.5 times higher for smokers in comparison to nonsmokers.
König et al. <sup>20</sup>	Determined the treatment outcomes of compliant periodontal patients, which were observed for at least 8 years. All patients had been treated for moderate to advanced periodontitis and regularly received PMT.	142	8-13 years. During PMT, dental prophylaxis and/or subgingival debridement were performed when the operator found necessary. Periodontal conditions were documented annually with PD charts and IP values. 12-month recall interval.	Article mentions smokers and nonsmokers but does not describe the criteria for smoking status.	Smoking significantly associated with TL ( $r^2 = 0.12$ ).

95%CI: 95% confidence interval; APT: active periodontal therapy; BOP: bleeding on probing; CAL: clinical attachment level; HR: hazard ratio; IC: irregular compliance; OR: odds ratio; PD: probing depth; PI: plaque index; PMT: periodontal maintenance therapy; RC: regular compliance; SPT: supportive periodontal therapy; TL: tooth loss.

**Table 2**

Case-control studies characteristics.

Study	Study design	Participants	Maintenance interventions	Smoking status	Primary outcome
Costa et al. <sup>35</sup>	Investigated the influence of glycemic control in the progression of periodontitis and TL during PMT.	92	5 years. Subjects were monitored at a private dental clinic. PMT was performed with 4-6 months recall intervals for all participants.	Included smokers/ex-smokers (reported having smoked > 100 cigarettes during their lifetime) and nonsmokers.	Smoking status had OR = 4.1 (95%CI: 1.98-11.6) for TL.
Costa et al. <sup>3</sup>	Investigated the association of periodontal risk assessment model with recurrence of periodontitis and TL during PMT.	164	Data obtained after APT were determined at baseline (T1) and compared to data obtained after 3 years of follow-up (T2). T2 was performed after 9 recall visits (RC individuals) and 4 visits (IC individuals). Periodontal clinical examinations during monitoring visits assessed: PD, CAL, furcation involvement, BOP, suppuration, radiographic evidence of bone loss (collected after T1 and T2).	Included nonsmokers/ex-smokers and smokers: 10-19 or > 19 cigarettes per day.	Smoking status had OR = 3.41 (95%CI: 1.26-11.41) for TL.

(continues)

Table 2 (continued)

Study	Study design	Participants	Maintenance interventions	Smoking status	Primary outcome
Costa et al. <sup>34</sup>	Evaluated and compared periodontal status, periodontitis progression, TL and influence of predictable risk variables of two PMT programs over a 12-month period.	288	Minimal follow-up time of 12 months. At each recall visit (T1, T2, T3 and T4), the following procedures were performed: interviews to determine possible changes in the variables of interest (demographic, biological, and behavioral); periodontal assessment through clinical parameters; disclosure of oral hygiene instructions using the Bass technique, interproximal brushes and dental floss; and, where appropriate, mechanical debridement, including prophylaxis, coronary polishing, and topical application of fluoride.	Included smokers/ex-smokers (reported having smoked > 100 cigarettes during their lives) and nonsmokers.	For the private group, final multivariate logistic regression models showed that smoking had OR = 3.1 (95%CI: 1.98-11.6) for TL. For the private group, OR for TL associated with smoking was not reported.
Costa et al. <sup>33</sup>	Determined and compared periodontal status, especially progression of periodontitis and TL, among RC and IC smokers and nonsmokers during PMT.	116	3 years. At each recall visit (T1, T2, T3 and T4), the following procedures were performed: interviews to determine possible changes in the variables of interest (demographic, biological and behavioral); periodontal assessment through clinical parameters; disclosure of oral hygiene instructions using the Bass technique, interproximal brushes and dental floss; and, where appropriate, mechanical debridement, including prophylaxis, coronary polishing, and topical application of fluoride.	Included smokers/ex-smokers (reported having smoked > 100 cigarettes during their lives) and nonsmokers.	Smokers in the IC group had OR = 7.3 (95%CI: 1.17-14.9) for TL. RC smokers presented OR = 4.2 (95%CI: 1.42-9.89) for TL.

95%CI: 95% confidence interval; APT: active periodontal therapy; BOP: bleeding on probing; CAL: clinical attachment level; IC: irregular compliance; OR: odds ratio; PD: probing depth; PMT: periodontal maintenance therapy; RC: regular compliance; TL: tooth loss.

### Quality assessment

Results of the quality assessment are summarized in Tables 3 and 4, for case-control and cohort studies, respectively. Studies were evaluated using the NOS, with scores varying from 7 to 9 for cohort studies, and 7 to 8 for case-control studies. Among cohort studies, one did not specify TL rate of the sample <sup>20</sup>, while four studies adjusted smoking only for one confounding factor <sup>20,23,24,31,32</sup>. Among case-control studies, TL rate of samples was not specified <sup>34,35</sup>, and only one confounding factor was adjusted <sup>3,33,34,35</sup>.

**Table 3**Quality assessment of included cohort studies based on the *Newcastle-Ottawa Scale*.

	König et al. 20	Leung et al. 24	Chambrone & Chambrone 23	Fisher et al. 5	Ravald & Johansson 31	Costa et al. 9	Graetz et al. 32
<b>Sample selection criteria #</b>							
1) Representativeness of the exposed cohort (subjects undergoing PMT)	★	★	★	★	★	★	★
a) Truly representative of the average no. of individuals undergoing PMT (20%) in the community ★							
b) Partially representative of the average no. of individuals under PMT (20%) in the community ★							
c) Selected group of affected individuals							
d) No description of the derivation of cohort							
2) Selection of the nonexposed cohort	★	★	★	★	★	★	★
a) Selected from the same community as the exposed group ★							
b) Selected from a different source							
c) No description of the derivation of the nonexposed group							
3) Ascertainment of exposure (smokers undergoing PMT)	★	★	★	★	★	★	★★
a) Secure record (pocket probing depth + bone loss + tooth loss) ★							
b) Clinical or radiographic exams ★							
c) Written self-reports or data described in the clinical records							
d) No description							
4) Demonstration that outcome of interest (TL) was not presented at start of study	★	★	★	★	★	★	★
a) Yes ★							
b) No							
<b>Comparability of cohorts ##</b>							
1) Control of confounding factors	★	★	★	★★	★	★★	★★
a) Exposure of interest (smoking) is adjusted for one confounding variable (eg.: diabetes) ★							
b) Exposure of interest (smoking) is adjusted for two or more factors (eg.: diabetes, gender, age, ...) ★★							
<b>Outcome assessment (TL) #</b>							
1) TL diagnostic	★	★	★	★	★	★	★
a) Secure assessment using clinical and radiographic parameters ★							
b) Clinical examination without radiographic assessment, or only partially met the criteria (a/b)							
c) Based on self-report or assessment of clinical data							
2) Adequate follow-up time for the outcome (TL) to occur	★	★	★	★	★	★	★
a) Yes (more than 12 months PMT) ★							
b) No							
3) Nonresponse rate	d	★	★	★	★	★	c
a) Complete follow-up: all subjects accounted for ★							
b) Nonresponse rate ≤ 20% ★							
c) Nonresponse rate > 20%							
d) Not described							
<b>Sum of scores ###</b>	7/10 (high)	8/10 (high)	8/10 (high)	9/10 (high)	8/10 (high)	9/10 (high)	9/10 (high)

c: non response rate; d: not described; PMT: periodontal maintenance therapy; TL: tooth loss.

★ 1 point;

# Maximum of 1 point for each item;

## Maximum of 2 points for each item;

### Maximum of 9 points.

**Table 4**Quality assessment of included case-control studies based on the *Newcastle-Ottawa Scale*.

	Costa et al. 33	Costa et al. 3	Costa et al. 34	Costa et al. 35
<b>Sample selection criteria #</b>				
1) Adequate tooth loss diagnostic for smokers undergoing PMT (cases)?	★	★	★	★
a) Clinical and radiographic examination ★				
b) Clinical examination without radiographic examination				
c) Record linkage or based on self-reports				
2) Representativeness and selection of smokers under PMT (cases)	★	★	★	★
a) Cases selected from private or public clinic, random sample, sample calculation ★				
b) Selection biases or "a" criteria not satisfied				
3) Selection of nonsmokers undergoing PMT (controls)	★	★	★	★
a) Controls selected from private or public clinics, random sample, sample calculation ★				
b) Selection biases or "a" criteria not satisfied				
c) No description				
4) Definition of controls	★	★	★	★
a) Nonsmokers undergoing PMT ★				
b) No description				
<b>Comparability of cases and controls ##</b>				
1) Control of confounding factors	★	★	★	★
a) Exposure of interest (smoking) adjusted for one confounding variable (diabetes) ★				
b) Exposure of interest (smoking) adjusted for two or more factors (diabetes, gender, age and other variables) ★★				
c) No description				
<b>Assessment of outcome (TL) #</b>				
1) Tooth loss diagnostic	★	★	★	★
a) Secure assessment using clinical and radiographic parameters ★				
b) Based on self-report or assessment of clinical data				
c) No description				
2) Same method of assessment for cases and controls	★	★	★	★
a) Yes ★				
b) No				
3) Nonresponse rate	★	★	c	c
a) Nonresponse rate ≤ 20%, for both groups (cases and controls) ★				
b) Nonresponse rate > 20%				
c) Not described				
<b>Sum of scores ###</b>	8/9 (high)	8/9 (high)	7/9 (high)	7/9 (high)

c: non response rate; PMT: periodontal maintenance therapy; TL: tooth loss.

★ 1 point;

# Maximum of 1 point for each item;

## Maximum of 2 points for each item;

### Maximum of 9 points.

**Box 1**

Quality of evidence evaluated through GRADE (*Grading of Recommendations, Assessment, Development and Evaluation*).

<b>Certainty assessment</b>	
Studies	4
Design	Observational studies
Risk of bias	Not serious *
Inconsistency	Not serious **
Indirectness	Not serious ***
Imprecision	Serious #
Other considerations	Publication bias strongly suspected
	Very strong association
	All plausible residual confounding factors would reduce demonstrated effect
<b>Effect</b>	
Relative (95%CI)	OR = 3.24 (1.33-7.90)
Absolute (95%CI)	3 fewer per 1.000 (1-8 fewer)
<b>Certainty</b>	⊕ ⊕ ⊕ ○ MODERATE

95%CI: 95% confidence interval; OR: odds ratio; PMT: periodontal maintenance therapy.

\* Some risk of bias due to: adjusting for just one confounder; not reporting missing data. Authors could have adjusted for number of cigarettes per day, but the overall risk of bias was judged as low risk. For this reason, it was considered "not serious";

\*\* Inconsistency: confidence intervals have some overlap, and the statistical test for heterogeneity is not significant ( $p = 0.055$ ).  $I^2$  is moderate and two studies have different effect estimates (Ravald & Johansson <sup>31</sup>; Graetz et al. <sup>32</sup>). However, sensitivity test including and excluding those studies did not change the effect estimate. Also, testing the model by random or fixed effect did not change the effect estimate. For these reasons, these two premises did not affect the final effect estimate and inconsistency was considered "not serious";

\*\*\* Indirectness: consider the PICO question. According to Table 1 factors that could influence the estimate for the population (patients under PMT) were not found;

# Imprecision: the lower and upper boundary of 95%CI might lead to different recommendations.

**Studies description**

Overall, follow-up time of individuals undergoing PMT ranged from 1 <sup>34</sup> to 36 years <sup>23</sup>. The study sample included a minimum of 288 and a maximum of 6,431 individuals <sup>34</sup>. Three studies were case-control studies nested in cohort studies, including 238 individuals <sup>3,33,35</sup>. Some studies <sup>3,33</sup> evaluated the number of teeth lost and TL percentage in comparisons between regular complier (RC) and irregular complier (IC) individuals. One study <sup>35</sup> evaluated the number of teeth lost and TL percentage in individuals with diabetes and good glycemic control compared to individuals with diabetes and poor glycemic control, and to individuals without diabetes.

The 11 selected studies recruited and treated individuals at different clinics. Participants of five studies were treated in private clinics <sup>3,9,23,33,35</sup> and participants of six studies were treated in university clinics <sup>5,20,24,31,32,34</sup>. One study had a mixed sample, with individuals from private and university clinics <sup>34</sup>.

Recall visits during PMT were performed with different time intervals, taking into consideration individuals' degree of compliance: 3 months <sup>5,33,34</sup>, 4 months <sup>3</sup>, 4-6 months <sup>35</sup>, 6 months <sup>9</sup>, 3-12 months <sup>31</sup>, 12 months <sup>20,24,32</sup>, and 18 months <sup>9</sup>.

Besides their different recall time intervals, studies also diverged in relation to dental care protocols and procedures performed during PMT. In one study <sup>20</sup>, dental prophylaxis and subgingival debridement were performed when the operator deemed necessary, and periodontal conditions were documented annually with probing depth (PD) and plaque index (PI) values. In another study <sup>24</sup>, all

subjects were instructed to perform their own PMT. At each initial return visit, they underwent a questionnaire by a trained interviewer, to record reasons for TL. In other studies<sup>23,32</sup>, all subjects underwent the following PMT protocol: oral hygiene instructions, scaling and root planning, crown polishing, and surgical periodontal therapy (when indicated). Studies evaluated different periodontal parameters: BOP, PI, PD, and clinical attachment level (CAL)<sup>5</sup>, as well as PI, PD, BOP, and bone level radiographic measurements (Table 1). During the monitoring visits, complete periodontal clinical examinations, nonsurgical and surgical procedures were also performed<sup>3,34</sup> (Table 2).

### **Smoking status characterization**

Different definition criteria for smoking status were adopted. Some studies<sup>33,34,35</sup> classified smokers and former smokers (individuals who reported having smoked more than 100 cigarettes during their lifetime) and nonsmokers according to the criteria by Tomar & Asma<sup>36</sup>. Other studies<sup>3,9,32</sup> classified nonsmokers and former smokers (individuals who smoked 10-19 cigarettes per day) and smokers (individuals who smoked more than 19 cigarettes per day) according to a previous study<sup>37</sup>. In a study by Raval & Johansson<sup>31</sup>, subjects were divided into three categories: smokers who consume 1-9 cigarettes per day, smokers who consume more than 10 cigarettes per day, and nonsmokers. In a study by Leung et al.<sup>24</sup>, 11.3% of the individuals were classified as current smokers, with self-reported consumption of 0.5-56.9 packets/year. In a study by Chambrone & Chambrone<sup>23</sup>, individuals were classified as smokers or nonsmokers, but the number of cigarettes smoked per day was not reported. In a study by Fisher et al.<sup>5</sup>, smoking status was determined by self-report, while an analysis of expired carbon monoxide concentration identified and quantified the smoking status. A concentration of  $\leq 8$ ppm (parts per million) defined nonsmokers, and a concentration of  $> 8$ ppm defined smokers, according to the criteria by Scott et al.<sup>38</sup>. A study by König et al.<sup>20</sup> classified smokers and nonsmokers but did not describe smoking status.

### **Summarization of findings**

Ten out of 11 selected studies in this systematic review concluded that smoking was an important factor, significantly associated with TL. Smokers had a greater chance of TL in comparison to nonsmokers [(crude OR = 8.0; 95%CI: 1.6-39.0)<sup>31</sup>; (adjusted OR = 4.76; 95%CI: 1.42-15.89)<sup>23</sup>; (adjusted OR = 4.1; 95%CI: 1.98-11.6)<sup>35</sup>; (adjusted OR = 3.41; 95%CI: 1.26-11.41)<sup>3</sup>].

TL occurrence due to periodontal reasons was 2.5 times higher in smokers than in nonsmokers<sup>24</sup>. According to one study<sup>20</sup>, smoking was significantly associated with TL ( $r^2 = 0.12$ ). The same association was also observed among individuals in a private clinic, where smoking was significantly associated with TL (adjusted OR = 3.1; 95%CI: 1.98-11.6)<sup>34</sup>.

Smokers among IC individuals (OR = 7.3; 95%CI: 1.17-14.9) presented a greater chance of TL when compared to smokers among RC individuals (OR = 4.2; 95%CI: 1.42-9.89)<sup>32</sup>. In another study from the same research group<sup>9</sup>, IC smokers lost significantly more teeth (adjusted OR = 4.22; 95%CI: 2.01-8.78).

Only one study did not find a statistically significant difference in the mean number of teeth lost between smokers and nonsmokers (at baseline and after three years of PMT) ( $p > 0.05$ )<sup>5</sup>.

Four studies were included in the meta-analysis<sup>9,23,31,32</sup> (Figure 2). There was a statistically significant association of TL and smoking habits (OR = 3.24; 95%CI: 1.33-7.90). The quality of evidence was determined to be moderate for smokers undergoing PMT and for odds of TL (Box 1).

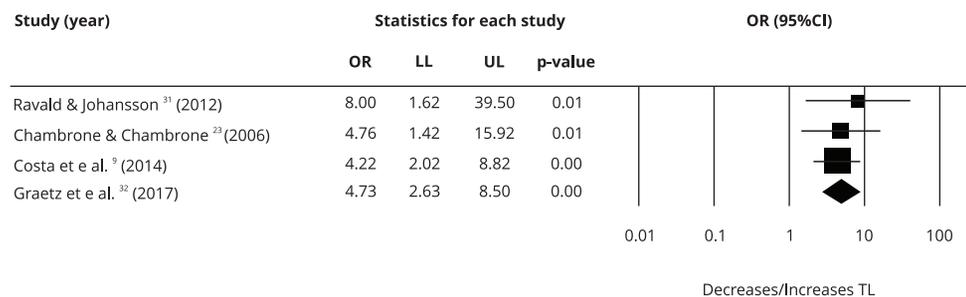
## **Discussion**

In this systematic review and meta-analysis, smokers undergoing PMT presented a greater chance of TL when compared to nonsmokers in 10 out of 11 selected studies, and also in the meta-analysis. However, several factors seem to have impacted these findings.

Although the meta-analysis presented a relative statistical homogeneity, it was limited due to the inclusion of only four studies. Seven studies were excluded from the meta-analysis due to insufficient data for extraction.

**Figure 2**

Meta-analysis.



95%CI: 95% confidence interval; LL: lower limit; OR: odds ratio; TL: tooth loss; UL: upper limit.

Other limitations can also be pointed out, such as clinical and methodological heterogeneity among included studies. The quality of the evidence was determined to be moderate, since there was “serious” imprecision due to the wide confidence interval. Moreover, publication bias was observed <sup>39</sup>. These issues can limit the validation of the findings, indicating the need for additional, more robustly designed studies, including a greater number of individuals.

There were differences in time intervals for recall visits during PMT, varying from 3 <sup>5,33,34</sup> to 18 months <sup>9</sup>. In addition to the differences in reevaluation intervals, the studies also diverged in relation to maintenance protocols and periodontal procedures performed during PMT, including the evaluation of different clinical parameters. Additionally, different criteria to establish regular or irregular PMT compliance may have had a high impact on studies’ different periodontal and TL outcomes.

Regarding smoking status characterization, different criteria were considered. In some studies <sup>3,9,23,24,32,35</sup>, individuals were grouped into smokers or nonsmokers according to self-report. Analysis of expired carbon monoxide concentration was also employed <sup>5</sup>. One study <sup>20</sup> classified smokers and nonsmokers but did not describe its criteria for definition of smoking status. It should be noted that, even though there is a relative agreement on TL rates reported in these studies, there is also a lack of information on methodological issues, which can lead to difficulty in establishing comparisons between studies.

When evaluating study quality, the follow-up interval then adopted was considered sufficient to deal with the occurrence of TL, since eligible studies showed a great variation in the follow-up period: from a minimum of 1 year <sup>34</sup> to a maximum of 36 years <sup>23</sup>. The mean time required for the occurrence of TL is subjected to many factors and is difficult to establish from the literature. A minimum follow-up interval of 12 months was considered adequate, and all studies fulfilled this quality requirement. However, clinical responses to periodontal treatment over time are unpredictable, involving many variables, such as periodontal diseases (and its related prognostic factors, e.g. severity of periodontal disease, degree of compliance during APT and PMT), endodontic pathologies, extensive caries lesions, gender, age, individual tooth prognosis, global prognosis, systemic conditions (e.g. diabetes, smoking), socioeconomic conditions, clinical training and operator experience, quality of dental care, and “philosophical” differences in the treatment <sup>9</sup> (particularly issues related to the maintenance or extraction of periodontally compromised teeth and replacement by dental implants) <sup>40,41</sup>.

One systematic review <sup>8</sup> included 13 retrospective cohort studies that evaluated prognostic risk factors in individuals undergoing PMT. Results showed that only 6.8% of all teeth were extracted for periodontal reasons, allowing us to speculate that teeth can be preserved for as long as possible. However, other than extraction due to periodontal reasons, other reasons were also considered, such as endodontic complications, root fractures, caries lesions, prosthetic reasons (i.e. loss of crown retention), unknown reasons, or due to differences in treatment philosophies.

Another systematic review analyzed the effect of individuals' PMT compliance on TL and investigated the potential factors affecting the association between compliance and TL. The final analysis included eight studies: seven retrospective cohort studies and one prospective cohort study<sup>9</sup>. In the retrospective studies, it was difficult to determine clear reasons for tooth extraction, so the differentiation of the reasons underlying extractions are usually divided only into periodontal and other reasons. This fact was observed in this systematic review, as well as in the retrospective studies<sup>11,20</sup>.

Certain studies<sup>1,8</sup> suggest a lower risk of TL in individuals with greater PMT compliance. In the present systematic review, we attempted to isolate the independent effect of smoking on TL. All possible efforts were made, employing literature electronic research, manual search, and grey literature, with no date of publication or language restrictions. Although it was not possible to generate a funnel plot, there was a predominance of studies with positive results for TL and smoking, indicating a possible publication bias. Citation bias was also identifiable, since many studies belonged to the same research group.

Thus, regardless of the presence of different risk factors for TL in individuals undergoing PMT, the simple presence of smoking should be a factor to classify individuals undergoing PMT as high risk, determining a short time interval for the recall visits. Additionally, these findings can be used by public health services to create strategies for avoiding smoking initiation and promoting smoking cessation, in order to improve systemic and oral health. However, it is important to highlight the scarcity and the need for well-designed prospective cohort studies, since the GRADE evaluation considered the quality of the scientific evidence moderate.

For future studies, a methodological standardization for the following issues is imperative: (1) characterization of smoking status in terms of both frequency and dose-exposure, and (2) identification of unique dental care protocols and periodontal procedures performed during PMT. Moreover, to minimize heterogeneity, studies with larger samples and longer follow-up periods are necessary.

In conclusion, there is moderate scientific evidence that the independent effect of smoking is associated with the occurrence of TL in individuals undergoing PMT. More prospective longitudinal studies are needed to confirm these findings.

## Contributors

T. R. Vieira contributed to conception, design and acquisition of the study, analysis and interpretation of data, and draft of the manuscript. C. C. Martins contributed to acquisition, analysis of data, and manuscript review. R. M. Cyrino contributed to analysis and interpretation of data, and manuscript review. A. M. O. Azevedo contributed to study design, analysis of data, and manuscript review. L. O. M. Cota contributed to the conception of the study, interpretation of data, and manuscript review. F. O. Costa contributed to conception and design of the study, analysis and interpretation of data, and manuscript review.

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## Resumo

A perda dentária tem sido relatada em estudos longitudinais sobre terapia periodontal de suporte (TPS), mas houve menos investigação sobre o efeito independente do tabagismo sobre a perda dentária, ajustado por importantes variáveis de confusão. Esta revisão sistemática teve como objetivo avaliar e analisar o efeito isolado do tabagismo sobre perda dentária em indivíduos em TPS. A estratégia incluiu fontes eletrônicas, busca manual, literatura cinzenta e artigos recentes (publicados a partir de abril de 2018), sem restrição quanto ao idioma; as datas de publicação foram incluídas. Foram selecionados estudos clínico-epidemiológicos com dados sobre perda dentária entre tabagistas em TPS, comparado com grupos-controle de não-tabagistas. A qualidade metodológica foi avaliada com a Escala de Newcastle-Ottawa. Foi realizada uma meta-análise, assim como, I<sup>2</sup> testes de heterogeneidade e de sensibilidade. A qualidade das evidências foi avaliada com a escala GRADE (Grading of Recommendations, Assessment, Development, and Evaluation). Onze artigos foram incluídos na revisão sistemática, sendo quatro estudos de casos e controles e sete estudos de coorte. Dez dos 11 estudos concluíram que o tabagismo é importante fator de risco para a ocorrência de perda dentária. De acordo com a meta-análise de quatro dos estudos de coorte, os tabagistas em TPS apresentavam risco 3,24 vezes maior de ocorrência de perda dentária quando comparados aos não tabagistas (IC95%: 1,33-7,90). O risco global de viés nos estudos foi baixo. A revisão mostrou qualidade moderada das evidências científicas de que os tabagistas em TPS apresentam risco maior de perda dentária do que os não-tabagistas.

Perda de Dente; Fumar; Periodontite; Metaanálise

## Resumen

La mortalidad dental ha sido estudiada en estudios longitudinales acerca de la terapia de mantenimiento periodontal (TMP), pero el efecto independiente de fumar en la pérdida de dientes (PD), ajustado a variables de confusión importantes, se ha evaluado muy poco. Esta revisión sistemática tuvo como objetivo evaluar y analizar el efecto aislado de fumar en la PD con personas bajo TMP. Se investigó en medios electrónicos, manuales, literatura gris, y artículos recientes (desde abril 2018), sin restricciones respecto a la lengua; incluyendo sus respectivas fechas de publicación. Además, se seleccionaron estudios clínicos epidemiológicos que trabajaban sobre datos de PD entre fumadores que estaban bajo TMP, en comparación con grupos de control de no fumadores. La calidad metodológica se evaluó usando la Escala de Newcastle-Ottawa. Se realizó un metaanálisis, así como tests de heterogeneidad I<sup>2</sup> y sensibilidad. La evidencia de calidad fue evaluada usando GRADE (Grading of Recommendations, Assessment, Development and Evaluation). Se incluyeron once trabajos en la revisión sistemática (cuatro de caso-control y siete estudios de cohortes). Diez de los once estudios concluyeron que fumar era un factor de riesgo importante para la ocurrencia de PD. Los metaanálisis de cuatro de los estudios de cohorte descubrieron que los fumadores tenían 3,24 veces más la oportunidad de sufrir PD, en comparación con los no fumadores TMP (IC95%: 1,33-7,90). En general, el riesgo de sesgo en los estudios fue bajo. La calidad de la evidencia científica respaldó moderadamente que los fumadores bajo TMP contaban con más oportunidad de PD que los no fumadores.

Pérdida de Diente; Fumar; Periodontitis; Metaanálisis

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