






## SYSTEMATIC REVIEW

# Recurrence and progression of periodontitis and methods of management in long-term care: A systematic review and meta-analysis

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## Abstract

**Aim:** To systematically review the literature to evaluate the recurrence of disease of people in long-term supportive periodontal care (SPC), previously treated for periodontitis, and determine the effect of different methods of managing recurrence. The review focused on stage IV periodontitis.

**Materials and methods:** An electronic search was conducted (until May 2020) for prospective clinical trials. Tooth loss was the primary outcome.

**Results:** Twenty-four publications were retrieved to address recurrence of disease in long-term SPC. Eight studies were included in the meta-analyses for tooth loss, and three studies for disease progression/recurrence (clinical attachment level [CAL] loss  $\geq 2$  mm). For patients in SPC of 5–20 years, prevalence of losing more than one tooth was 9.6% (95% confidence interval [CI] 5%–14%), while experiencing more than one site of CAL loss  $\geq 2$  mm was 24.8% (95% CI 11%–38%). Six studies informed on the effect of different methods of managing recurrence, with no clear evidence of superiority between methods. No data was found specifically for stage IV periodontitis.

**Conclusions:** A small proportion of patients with stage III/IV periodontitis will experience tooth loss in long-term SPC (tendency for greater prevalence with time). Regular SPC appears to be important for reduction of tooth loss. No superior method to manage disease recurrence was found.

## KEYWORDS

maintenance, progression, recurrence, supportive periodontal care

## Clinical Relevance

*Scientific rationale for study:* Supportive periodontal care (SPC) is a life-long commitment for periodontitis patients as well as for dental professionals taking care of them. Prior to embarking on treatment of periodontitis, patients and dental professionals should understand the likelihood of disease recurrence/progression during SPC and the costs and harms of retreatments during SPC.

*Principal findings:* Patients in long-term routine SPC programmes should expect a low mean prevalence of tooth loss, but disease recurrence/progression may occur.

*Practical implications:* The importance of regular SPC recall visits should be emphasized to patients originally treated for stage III/IV periodontitis in order to reduce the risk of tooth loss.

## 1 | INTRODUCTION

Periodontitis is defined as a chronic, multifactorial, inflammatory disease associated with dysbiotic plaque biofilms and progressive destruction of the tooth-supporting apparatus (Papapanou et al., 2018). It is thought to be the sixth most prevalent condition in the world, with severe forms of the disease affecting 7%–11% of adults worldwide (Kassebaum et al., 2014, 2017).

Treatment of periodontitis consists of active periodontal therapy (APT), which often begins with the first step of therapy (Sanz et al., 2020) and which includes addressing modifiable risk factors such as tobacco use and glycaemic control in people with diabetes, along with building the skills and behaviours related to effective daily plaque removal (Newton & Asimakopoulou, 2018; Carra et al., 2020; Ramseier et al., 2020). Furthermore, when periodontal pockets are established, operative treatments such as non-surgical therapy (subgingival instrumentation – part of the second step of therapy) and surgical options (open flap debridement, resective and regenerative surgery – part of the third step of treatment) are required (Sanz-Sanchez et al., 2020). On completion of APT, ongoing maintenance care, known as supportive periodontal care (SPC), is thought to be essential in minimizing disease progression or recurrence (Rosling et al., 2001; Matuliene et al., 2008; Trombelli et al., 2015).

SPC is a complex intervention and may be seen as the fourth step of therapy (Sanz et al., 2020). It is a life-long phase of care, and requires ongoing commitment from the patient in order to reduce risk of disease progression and subsequently prevent tooth loss (Lee et al., 2015) and maintain oral-health-related quality of life (Armitage & Xenoudi, 2016).

Recent systematic reviews have shown that there is limited evidence to advocate the superiority of any one approach to improve tooth maintenance during SPC (Manresa et al., 2018) and that clinical attachment levels (CALs) appear to remain stable over the long term for patients in SPC (Sanz-Martin et al., 2019). Encouragingly, evidence also suggests that the mean annual tooth loss due to periodontitis during SPC of up to 14 years is low (Rosling et al., 2001; Trombelli et al., 2015); however, following the 11th European Workshop in Periodontology, it was identified that more research was required to plug gaps in the evidence, particularly regarding treatments that work best in the phase of SPC (Sanz et al., 2015), which is a conclusion strengthened by a recent Cochrane review (Manresa et al., 2018).

What is less clear from previous reviews is what patients might expect in terms of recurrence of the condition and the effect of different treatment methods of managing recurrence, which may be considered in terms of stabilizing recurrence and preventing tooth loss, associated costs, and effect on the quality of life.

Thus, in view of the gaps in the evidence and its importance both from a public health consideration as well as the perspective of the individual patient, the purpose of this systematic review was to (1) systematically review the evidence for the recurrence of periodontitis during long-term SPC and (2) identify the effect of different methods of managing recurrence.

## 1.1 | Objectives

### 1.1.1 | Focused questions

The two questions that we sought to answer were focused question 1 (FQ-1): “In people treated for periodontitis and in SPC for 5 years or more, compared with no or irregular SPC, how common is recurrence of the condition?” and, focused question 2 (FQ-2): “In people experiencing recurrence of periodontitis, what is the effect of different methods of treatment of the recurrence as assessed by measures of health, quality of life, cost and accessibility of care, and harms?”

### 1.1.2 | PICOS components

#### *Population*

Participants treated for periodontitis with no age restriction. Any definition of periodontitis was included considering there have been a number of changes in the classification of periodontal diseases over recent decades. No restriction was applied for the type of treatments carried out both in the APT or supportive periodontal care phases. The end of active treatments was clearly defined in terms of periodontal health status. The focus of the workshop for which this review was commissioned was stage IV periodontitis (advanced disease with extensive tooth loss) (Tonetti et al., 2018). However, in view of both the recent adoption of this classification and our expectation that severity of periodontitis would be incompletely described, we included all severities of periodontitis with a plan to analyse stage IV periodontitis separately if possible.

#### *Intervention*

Any kind of intervention that might be considered part of SPC. As SPC is a complex intervention, for the purposes of this review, this may have included:

- Interview: periodontal health symptoms, medical and social history, risk factors including tobacco use, stress and diabetes, and reported plaque control regime;
- Assessment: plaque and calculus deposits, periodontal health including inflammation, probing pocket depths, and bleeding pockets;
- Formulating: intervention needs, including risk factor management, oral hygiene, and retreatment;
- Practical intervention: oral hygiene coaching, instrumentation of supra- and sub-gingival plaque and calculus, treatment of sites with recurrence (finding of periodontitis at a previously healthy/stable site), or residual periodontitis (a deep periodontal pocket remaining despite active therapy) (Graziani et al., 2018);
- Planning: interval before next SPC visit.

#### *Comparison*

Studies comparing SPC with no/irregular SPC, different frequencies of SPC recall visits, different settings for SPC (specialist vs. non-specialist), and SPC using adjuncts (e.g., chemical agents, locally administered anti-septics/antibiotics, and systemically administered antibiotics).

### Outcome measures

It would be impossible to distinguish the published literature between recurrence, occurrence of disease at previously healthy (non-diseased) sites, and progression of residual disease at unstable sites. Recurrence means a finding of periodontitis at a site that was rendered periodontally healthy/stable through treatment. Occurrence refers to a site within a patient diagnosed and treated for periodontitis (periodontitis case) but which did not previously show signs of disease, and progression would be characterized by deterioration (e.g., CAL loss) at a site that had residual disease despite active treatment.

Since we could not make the distinction from the existing literature, the primary outcome measure for this systematic review was the proportion of patients who experienced tooth loss. Secondary outcomes were (1) proportion of patients who experienced at least one site of CAL loss of 2 mm or greater; (2) number of periodontal probing pocket depths (PPDs) of at least 5 mm or more with bleeding on probing; (3) number of sites that need/experienced re-treatment; (4) change in oral-health-related quality of life (OHQOL) with a validated OHQOL tool; (5) health economic outcomes; and (6) any other patient-reported outcomes (PROs).

### Study design

The search strategy included clinical studies with a prospective design (for both FQ-1 and FQ-2) in order to minimize selection bias. As FQ-2 was an intervention research question, studies were limited to randomized controlled trials (RCTs), controlled trials, and prospective cohorts.

## 2 | METHODS

### 2.1 | Protocol development and registration

This protocol was evaluated and approved by the Scientific Committee of the XVII European Workshop on Periodontology and was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Moher et al., 2009). Details of the protocol for this systematic review were registered on PROSPERO (Unique ID: CRD42020176451).

### 2.2 | Patient involvement

This review was co-produced with a member of the British Society of Periodontology Patient Forum, who contributed to the design, interpretation, and publication.

### 2.3 | Eligibility criteria

To conduct this systematic review, we searched for all studies that had included treatment for periodontitis and had a minimum of 5 years following the end of APT.

### 2.4 | Literature search

#### 2.4.1 | Electronic search

A sensitive search strategy was formulated with an experienced librarian (DM) with consideration of previous systematic reviews related to this topic (Trombelli et al., 2015; Manresa et al., 2018; Sanz-Martin et al., 2019) using a string of medical subject headings and free-text terms (see Appendices S1–S6). The search strategies were modelled on that devised for the MEDLINE database and subsequently modified for other databases as was needed. The search was restricted to the English language (to harmonize methods across all reviews being conducted for the European Workshop and due to time constraints) and results were downloaded to EndNote X9 (2013).

Electronic databases searched included:

Ovid MEDLINE (1946 – 1 May 2020) (Appendix S1);  
Ovid EMBASE Classic and EMBASE (1947 – 1 May 2020) (Appendix S2);  
LILACS VHL Regional Portal (to 2 May 2020) (Appendix S3);  
Cochrane Central Register of Controlled Trials (CENTRAL) (to 2 May 2020) (Appendix S4);  
Dentistry and Oral Sciences Source EBSCOHost (to 2 May 2020) (Appendix S5);  
CINAHL Plus EBSCOHost (1937 – 2 May 2020) (Appendix S6).

OpenGrey was searched for grey literature and the register of clinical studies at the US National Institutes of Health ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) in order to identify unpublished studies that may be relevant.

### 2.5 | Study selection

#### 2.5.1 | Inclusion criteria

In regard to FQ-1, the following inclusion criteria were applied:

- Prospective studies (to minimize the risk of selection bias).
- Minimum follow-up of 5 years in SPC (to consider outcome of disease progression/recurrence).
- End point of APT and the start of SPC clearly defined.

For FQ-2, the following inclusion criteria were applied:

- Prospective studies.
- Minimum follow-up of 12 months.

#### 2.5.2 | Exclusion criteria

The following exclusion criteria were applied:

- Cross-sectional studies.
- Retrospective studies.
- Case series.

To distinguish between case-series and cohort studies (particularly with low numbers of participants), a key characteristic for exclusion was the lack of information on the method of enrolment/participant selection (e.g., consecutive cases).

- Studies that investigated solely specific systemic disease or risk factors (e.g., smoking, diabetes), or recruited participants only for periodontitis treatment, or previously treated for periodontitis.

### 2.5.3 | Screening

Titles and abstracts (if available) retrieved from the searches were screened by a combination of two review authors (NL, FM, and SH), in duplicate and independently. Based on titles and abstracts, irrelevant studies were discarded. Full texts were obtained for the remaining studies and included those that had insufficient information in the title and abstract and if at least one reviewer included the study for the next phase of screening. Reference lists of all studies that were included for full text screening, and previous reviews were screened for missing records.

Two reviewers (NL and FM) assessed the full text reports according to the inclusion criteria, in duplicate and independently. Disagreements were resolved by discussion, and a third author was consulted (IN) when agreement could not be resolved. Where there were several publications from the same original study, we included the study with the longest follow-up period for the relevant outcome measure. Studies that did not meet the eligibility criteria were excluded, with specified reasons for exclusion (Appendix S7).

## 2.6 | Data collection

### 2.6.1 | Data extraction

Data were extracted by two review authors (NL and FM), in duplicate and independently, using a data extraction form on Microsoft® Excel. Disagreements were resolved by discussion, and when resolution was not possible, a third reviewer was consulted (IN). In order to clarify missing or unclear data, the authors were contacted (where possible).

### 2.6.2 | Risk of bias

Quality assessment was carried out by two review authors (NL and SH), in duplicate and independently. Regarding FQ-1, studies were assessed for risk of bias in relation to the phase of SPC. The included studies were assessed as prospective cohorts using a modified version of the Newcastle–Ottawa Scale (NOS) (Wells et al., 2011) to account

for single-arm cohorts. The modified version of the NOS removed questions concerning control groups, and therefore two domains, selection and outcome, were assessed with a maximum possible score of 6. FQ-2 included studies were assessed for risk of bias using the Cochrane RoB 2.0 tool (J. A. C. Sterne et al., 2019) for interventional RCTs, ROBINS-I tool (J. A. Sterne et al., 2016) for interventional non-randomized controlled trials (CCTs), and cohorts.

## 2.7 | Data synthesis

Data were entered into tables stratified by study design, and decisions on which studies to include in a meta-analysis were made depending on the similarity of chief study characteristics related to each research question (i.e., incidence of recurrence or methods of managing recurrence).

Evaluation of the included studies displayed substantial heterogeneity between publications in regard to design and reporting of outcomes in the SPC phase and in trials addressing treatment methods for disease recurrence. A qualitative report of the data was planned for those studies that could not be included in the meta-analyses.

## 2.8 | Data analysis

The number of events on the total number observed at the final assessment was used for the meta-analyses. To avoid underestimating both tooth loss and CAL loss  $\geq 2$  mm, we decided to use the “per protocol” number of participants. Numerous studies reported tooth loss per participant at the end of the study. An intention-to-treat (ITT) approach would not be able to account for tooth loss associated with subjects during follow-up, and thus risk under-estimating average tooth loss. In order to check this, an ITT analysis was carried out for the primary outcome of tooth loss.

Data were grouped with respect to (a) frequency of SPC, 3-monthly (3M) or unmonitored/irregular (IRREG), and (b) length of follow-up (FU), 5–10 years follow-up (5–10 FU) or greater than 10 years follow-up ( $>10$  FU). Meta-analyses were subsequently performed to determine an overall prevalence of tooth loss (primary outcome) and CAL loss ( $\geq 2$  mm) (secondary outcome) at the patient level. The number of events on the total number observed (per protocol) was entered into the statistical software. In regard to tooth loss, this was the number of patients who lost at least one tooth, on the total number of patients available at follow-up. For CAL loss, this was the number of patients experiencing CAL loss  $\geq 2$  mm at a minimum of one site, on the total number of patients available at follow-up. In the meta-analyses, “clusters” were formed in each subgroup (Salvi et al., 2018). One cluster was representative of one treatment arm in APT. Therefore, studies with multiple treatment arms contributed more than one cluster. The open source software OpenMeta[Analyst] (Wallace et al., 2012) was used for meta-analysis, and a binary random-effects model was chosen. Weighted mean values and 95% confidence intervals

(CI) are presented via Forest plots. A  $p$ -value of  $<.05$  was considered statistically significant.

The degree of statistical heterogeneity between studies was assessed using the Chi-square test and quantified utilizing the  $I^2$  statistical test. Subgroup and meta-regression analyses were performed to determine the effect of (a) the type of treatment in APT either regenerative (reg) or non-regenerative (non-reg), (b) frequency of SPC, 3-monthly or IRREG, and (c) length of follow-up, 5–10 years or greater than 10 years on tooth loss and CAL loss  $\geq 2$  mm and expressed as coefficients (COEF) and 95% CIs. Meta-analysis was stratified into subgroups of reg and non-reg surgery to allow evaluation of potential differences in outcomes. The summary estimate includes both types of therapy combined.

Interpretation of the  $I^2$  test was according to the guidance of the *Cochrane Handbook* (Deeks et al., 2019), as follows:

- 0%–40%: might not be important.
- 30%–60%: moderate heterogeneity.
- 50%–90%: substantial heterogeneity.
- 75%–100%: considerable heterogeneity.

Studies that could not be included in the meta-analysis were described in a narrative form, and an attempt to triangulate qualitative

results with that of the meta-analysis was made to assess consistency of data.

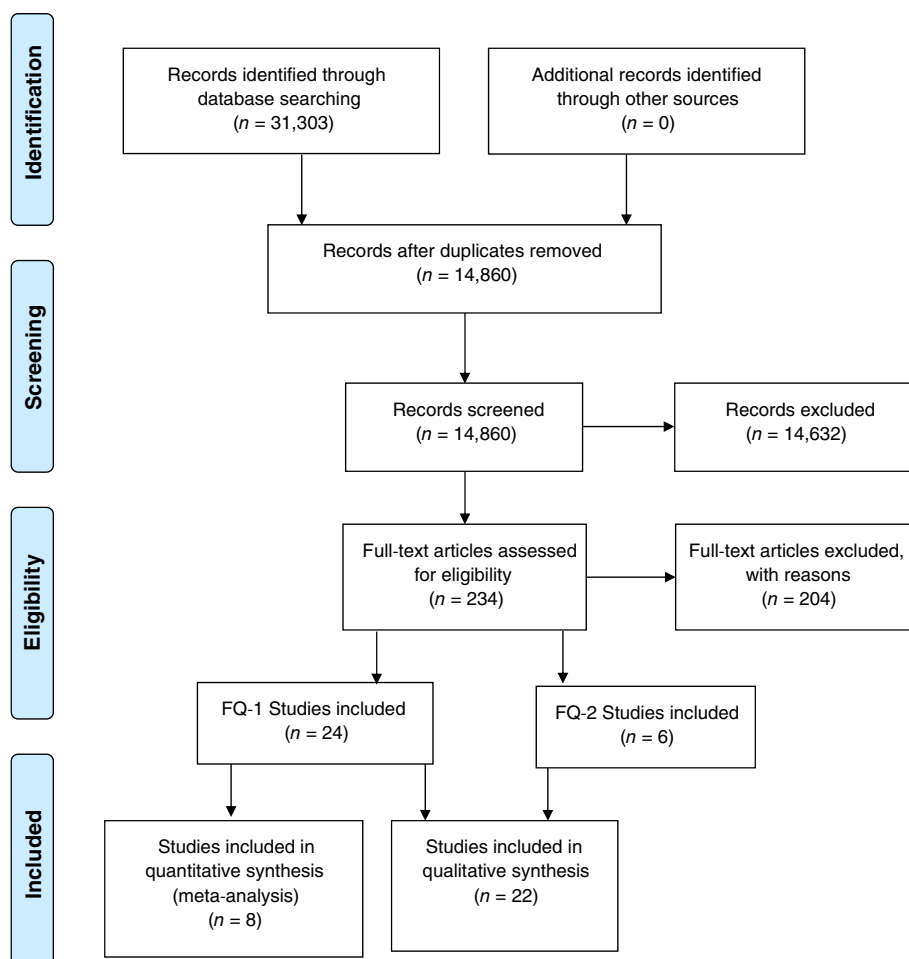
Kappa statistic was used to assess the reviewer agreement based on full-text screening, and the score was interpreted using values suggested by Cohen (1960). The reviewers were calibrated with the first 10 full-text publications.

### 3 | RESULTS

#### 3.1 | Study selection

The search yielded a large number of records, confirming high sensitivity and low specificity, which reflected the search strategy. Based on the definition of stage III versus stage IV periodontitis (Tonetti et al., 2018), we were unable to restrict the studies to solely stage IV periodontitis cases. Studies screened gave no detail of reasons for previous extraction(s), and most used previous classifications for defining included cases. Additionally, there was a lack of studies that specifically addressed recurrence in SPC.

A total of 31,303 records were found through the electronic searches, and following removal of duplicates, 14,860 remained (Figure 1). Following screening of titles and abstracts, 234 titles



**FIGURE 1** Flow diagram of the systematic review [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13553)]

TABLE 1 Focused question 1: Characteristics of included studies

Publication	Country	Setting	Funding	Diagnosis	APT
Axelsson & Lindhe, 1981	Sweden	University	NR	Adv. periodontal disease	Surgery: MWF in all four quadrants
Becker et al., 2001	United States	University	NR	Mod-Adv. adult periodontitis	Split mouth (RCT) a: SRP with LA b: Surgery: osseous recontouring c: Surgery: MWF
Buchmann et al., 2002	Germany	University	NR	Aggressive periodontitis	Surgery: MWF in all four quadrants
Cieplik et al., 2018	Germany	University	Partly supported by Robert Matheys Foundation (Bettlach Switzerland)	Aggressive/chronic periodontitis	Split mouth (RCT) a: GTR + $\beta$ -TCP granules (soaked in blood) b: GTR + $\beta$ -TCP granules (soaked in APC)
Cortellini et al., 2017	Italy	Private practice	Partly supported by Accademia Toscana di Ricerca Odontostomatologica, Italy; European Research Group on Periodontology, Genova, Italy	NR (angular defects)	RCT a: Surgery: MWF b: Surgery: MPPT with e-PTFE c: Surgery: Flap with e-PTFE
Cortellini et al., 2020	Italy	Private practice	Partly supported by the European Research Group on Periodontology (ERGOPerio), Berne, Switzerland	Stage III/IV periodontitis (generalized)	RCT (only one arm assessed for this review) Surgery: PPF (Membrane or EMD/membrane + xenograft/EMD + alloplast or EMD + membrane)
Crespi et al., 2011	Italy	Private practice	NR	Mod-Adv. adult periodontitis	Split mouth a: Surgery: MWF (quadrant) b: Surgery: CAF + CO <sub>2</sub> laser root conditioning
Dori et al., 2013	Hungary	University	NR	Adv. chronic periodontitis	RCT a: Surgery: EMD + xenograft b: Surgery: EMD + $\beta$ -TCP granules
Hou et al., 1997	Taiwan	University	NR	Mod-Adv. adult periodontitis	SRP with LA
Kaldahl et al., 1996a	United States	University	NIH-NIDR grant DE06103	Mod-Adv. adult periodontitis	Split mouth (RCT) a: coronal scaling b: SRP with LA c: Surgery: MWF d: Surgery: osseous recontouring
Kaldahl et al., 1996b	United States	University	NIH-NIDR grant DE06103	Mod-Adv. adult periodontitis	As above (same population)
Knowles et al., 1979	United States	University	Partly supported by US Public Health Service Grant DE 02731	Mod-Adv. adult periodontitis	Split mouth (RCT), half mouth a: Surgery: Pocket elimination, curettage b: Surgery: MWF, curettage c: Surgery: MWF, pocket elimination
Loesche et al., 2002	United States	University	US Public Health Service Grant DE-06030 from the National Institute of Dental and Craniofacial Research	Adv. periodontal disease (chronic/adult/aggressive/early onset)	RCT a: NST + placebo (systemic) b: NST + Metronidazole (systemic) c: NST + doxycycline (systemic)

(Continues)



TABLE 1 (Continued)

Publication	Country	Setting	Funding	Diagnosis	APT
Loesche et al., 2005	United States	University	US Public Health Service Grant DE-06030 from the National Institute of Dental and Craniofacial Research	Adv. periodontal disease (chronic/adult/ aggressive/early onset)	As above (same population)
Moder et al., 2012	Germany	University	Robert Matheys Stiftung (RMS Foundation, Bettlach, CH)	Aggressive/chronic periodontitis	Split mouth (RCT) a: GTR + $\beta$ -TCP granules (soaked in blood) b: GTR + $\beta$ -TCP granules (soaked in APC)
Nygaard-Ostby et al., 2010	Norway	Private practice	Supported by grant from Atrix Laboratories Inc., Fort Collins, CO, USA	Chronic periodontitis (+ angular defect)	RCT a: Surgery: Autogenous bone graft b: Surgery: Autogenous bone graft + GTR
Orsini et al., 2008	Italy	Unclear	National Research Council (CNR), Finalized Project Materials Tailored for Advanced Technologies PF MSTA II, Ministry of University, Research, Science and Technology (MURST) Italy	NR (angular defect)	Split mouth (RCT) a: Surgery: Autogenous bone graft + resorbable membrane b: Surgery: Autogenous bone graft + calcium sulfate graft
Petso et al., 2019	Germany	University	Partly by Moessner Stiftung research grant (Frankfurt am Main, Germany) to the Centre for Dentistry and Oral Medicine (Carolinum)	Severe chronic periodontitis (+ angular defect)	RCT a: Surgery: OFD b: Surgery: OFD + resorbable membrane
Pihlstrom et al., 1983	United States	University	NR	Mod-Adv. adult periodontitis	Split mouth (RCT) a: SRP with LA b: Surgery: MWF
Pihlstrom et al., 1984	United States	University	NR	Mod-Adv. adult periodontitis	As above (same population)
Ramberg et al., 2001	Sweden	University	Grants from NIDCR (DE-12861) and Colgate Technology Centre, NJ, USA	Adv. periodontitis	a: SRP b: SRP + tetracycline (systemic)
Rosling et al., 2001	Sweden	University and 12 community dental clinics	Supported by grants from NIDCR (DE-12861) and Colgate Technology Centre, NJ, USA	Adv. periodontitis or normal prevalence of periodontal disease	NST
Serino, Rosling, Ramberg, Hellstrom, et al., 2001	Sweden	University	Colgate Technology Centre, NJ, USA and NIDCR (DE-12861) Bethesda, Maryland, USA	Adv. periodontal disease	NST + metronidazole (systemic) + amoxycillin (systemic)
Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001	Sweden	University	NIDCR (DE-12861) and Colgate Technology Centre, NJ, USA	Adv. periodontal disease	RCT a: SRP b: Surgery: MWF

Abbreviations: Adv., advanced; APC, autogenous platelet concentrate; CAF, coronally advanced flap; CO<sub>2</sub>, carbon dioxide; EMD, enamel matrix derivative; e-PTFE, expanded-polytetrafluoroethylene membrane; GTR, guided tissue regeneration; LA, local anaesthetic; Mod-Adv., moderate to advanced; MPPT, modified papilla preservation technique; MWF, modified Widman flap; NR, not reported; NST, non-surgical therapy; OFD, open flap debridement; PPF, papilla preservation flap; RCT, randomized controlled trial; SRP, scaling and root planing  $\beta$ -TCP,  $\beta$ -tricalcium phosphate.

remained for full-text evaluation. Subsequently, 204 studies were excluded (Appendix S7) for often more than one reason; however, the main reason was generally recorded.

#### *Focused question 1*

Twenty-four studies (Knowles et al., 1979; Axelsson & Lindhe, 1981; Pihlstrom et al., 1983; Pihlstrom et al., 1984; Kaldahl et al., 1996a, 1996b; Hou et al., 1997; Becker et al., 2001; Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001; Buchmann et al., 2002; Loesche et al., 2002; Loesche et al., 2005; Orsini et al., 2008; Nygaard-Ostby et al., 2010; Crespi et al., 2011; Moder et al., 2012; Dori et al., 2013; Cortellini et al., 2017, 2020; Cieplik et al., 2018; Petsos et al., 2019) were included in the qualitative and quantitative analysis (Tables 1 and 2).

Studies reporting on the same population were included if each paper reported on a different but relevant outcome important for this systematic review (Pihlstrom et al., 1984; Kaldahl et al., 1996b) (Table 2). The kappa score for FQ-1 was calculated to be 0.81 for full-text screening agreement, indicating almost perfect agreement (Cohen, 1960).

#### *Focused question 2*

Six studies were included (Jenkins et al., 2000; Bogren et al., 2008; Lulic et al., 2009; Tonetti et al., 2012; Costa et al., 2015; Killeen et al., 2018) (Tables 3 and 4). These were qualitatively analysed owing to heterogeneity, particularly in types of intervention. The kappa score for full-text screening for FQ-2 was calculated to be 0.62, indicating substantial agreement (Cohen, 1960).

## 3.2 | Population

We were unable to find data on stage IV periodontitis or that could be analysed as such. Studies reported an initial diagnosis of periodontitis, with some further describing as moderate and severe disease. Types of diagnosis reported in the articles included “advanced periodontal disease”, “moderate to advanced adult periodontitis”, “aggressive periodontitis”, “chronic periodontitis”, “advanced chronic periodontitis”, and “severe chronic periodontitis”. One recently published study (Cortellini et al., 2020) referred to the population as “stage III or IV periodontitis” in a retrospective manner, as recruitment was prior to the publication of the most recent classification (Table 1).

## 3.3 | Supportive periodontal care

### 3.3.1 | Description of SPC

When assessing the elements carried out in the phase of SPC, the majority of studies included brief description of oral hygiene review and re-enforcement in conjunction with focused supra- and subgingival instrumentation (Axelsson & Lindhe, 1981; Pihlstrom et al., 1983; Pihlstrom et al., 1984; Kaldahl et al., 1996a, 1996b; Hou

et al., 1997; Becker et al., 2001; Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001; Buchmann et al., 2002; Loesche et al., 2002, 2005; Orsini et al., 2008; Nygaard-Ostby et al., 2010; Crespi et al., 2011; Dori et al., 2013; Cortellini et al., 2017). Five publications did not describe any detail about recall visits (Knowles et al., 1979; Moder et al., 2012; Cieplik et al., 2018; Petsos et al., 2019; Cortellini et al., 2020).

Nine studies provided some description of the operator(s) who carried out the SPC visits (Knowles et al., 1979; Axelsson & Lindhe, 1981; Pihlstrom et al., 1984; Rosling et al., 2001; Loesche et al., 2002, 2005; Nygaard-Ostby et al., 2010; Cortellini et al., 2017; Cieplik et al., 2018) although the level of experience was not advised.

No studies specifically addressed risk factor control in regard to smoking cessation or glycaemic control advice. Details of the factors that influenced recall interval length were not given in any study.

### 3.3.2 | Recall intervals

All studies reported on the frequency of recall intervals, with the majority of studies applying 3 monthly visits. However, there was some variability between studies, with the shortest interval being 1–3 months (Hou et al., 1997) and the longest up to 12 months (Rosling et al., 2001), based on a perceived disease risk by the attending dentist (details not specified). Some studies reported a more frequent recall plan in the first 1–2 years after APT (Axelsson & Lindhe, 1981; Buchmann et al., 2002; Moder et al., 2012; Cieplik et al., 2018), thereafter reducing the frequency with tailored SPC intervals.

### 3.3.3 | Length of follow-up

The minimum follow-up period in SPC to be included in this review was 5 years. Seventeen studies had a follow-up of 5–10 years (Knowles et al., 1979; Axelsson & Lindhe, 1981; Pihlstrom et al., 1983, 1984; Kaldahl et al., 1996a, 1996b; Hou et al., 1997; Becker et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Buchmann et al., 2002; Loesche et al., 2002, 2005; Orsini et al., 2008; Nygaard-Ostby et al., 2010; Moder et al., 2012; Dori et al., 2013; Cortellini et al., 2020). Seven studies (Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001; Crespi et al., 2011; Cortellini et al., 2017; Cieplik et al., 2018; Petsos et al., 2019) had SPC follow-up periods greater than 10 years. Two studies reported on 20 years of follow-up (Cortellini et al., 2017; Petsos et al., 2019).

## 3.4 | Meta-analyses

### 3.4.1 | Tooth loss

Eight studies addressing FQ-1 contributed data for estimating tooth loss at the patient level (Orsini et al., 2008; Nygaard-Ostby



TABLE 2 Focused question 1: Characteristics of study that are related to supportive periodontal care (SPC)

Publication	Participants entering SPC (n)	Recall intervals (m = months)	Follow up in SPC (months)	Description	Outcomes
Axelsson & Lindhe, 1981	77	0–2 yrs to 2 m 3–6 yrs to 3 m	72	<ul style="list-style-type: none"> <li>Oral hygiene reviewed. Bass method of brushing, floss, toothpicks advocated</li> <li>Supra- and sub-gingival scaling as required</li> </ul>	Tooth loss (mean) CAL loss (%) PPD (mean) FMBS
Becker et al., 2001	16	0–5 yrs to 3 m	60	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>SRP (1 h) and polish with fluoride paste</li> </ul>	Tooth loss CAL (mean, %) PPD (mean) GI (mean)
Buchmann et al., 2002	13	0–5 yrs to 3–6 m	60	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Subgingival instrumentation if PPD &gt; 4 mm + BOP</li> </ul>	CAL (mean, no. of sites) PPD (mean) BOP (%) GI (mean)
Cieplik et al., 2018	22	3 m	144	Not reported	Tooth loss CAL (median) PPD (median)
Cortellini et al., 2017	45	3 m	240	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Increased PPD <math>\geq</math> 2 mm (BOP) and CAL loss <math>\geq</math> 2 mm, adjunctive periodontal therapy consisting of non-surgical root planing, flap surgery, or regenerative surgery as indicated</li> </ul>	Tooth loss CAL (mean) PPD (mean) FMBS (%) Sites requiring re-tx Health economics
Cortellini et al., 2020	25	3 m	108	Not reported	Tooth loss CAL (mean) PPD (mean) OHIP Health economics Other PROs
Crespi et al., 2011	25	6 m	114	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Coronal scaling, polishing and subgingival instrumentation as needed</li> </ul>	PPD (mean) GI
Dori et al., 2013	22	3–6 m	108	<ul style="list-style-type: none"> <li>Occlusal adjustment as needed</li> <li>Oral hygiene reviewed</li> <li>Supra- and sub-gingival scaling and polishing (tailored)</li> </ul>	CAL (mean) PPD (mean) BOP (per tooth)
Hou et al., 1997	51	1–3 m	66	<ul style="list-style-type: none"> <li>Oral hygiene reviewed;</li> <li>Repeated instruments where required</li> </ul>	CAL (mean) PPD (mean) GI

(Continues)

TABLE 2 (Continued)

Publication	Participants entering SPC (n)	Recall intervals (m = months)	Follow up in SPC (months)	Description	Outcomes
Kaldahl et al., 1996a	82	3 m	84	<ul style="list-style-type: none"> <li>Sites of <math>\geq 3</math> mm CAL loss received SRP</li> </ul>	Tooth loss CAL (mean) PPD (mean) FMBS Other PROs
Kaldahl et al., 1996b	82	3 m	84	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Supra- and sub-gingival instrumentation as needed</li> </ul>	CAL (yearly incidence %) CAL (mean)
Knowles et al., 1979	78	3 m	96	Not reported	CAL (mean)
Loesche et al., 2002	90	3 m	61.2 (median)	<ul style="list-style-type: none"> <li>Oral hygiene reviewed. Bass method of brushing, floss, toothpicks advocated</li> <li>Full-mouth instrumentation</li> <li>Recurrent sites, 1 week of unsupervised systemic metronidazole or placebo</li> </ul>	Tooth loss (range per patient and total number) Patients requiring surgery (mean per patient)
Loesche et al., 2005	90	3 m	76.8 (median)	<ul style="list-style-type: none"> <li>Oral hygiene reviewed. Bass method of brushing, floss, toothpicks advocated</li> <li>Full-mouth instrumentation</li> <li>Recurrent sites, 1 week of unsupervised systemic metronidazole or placebo</li> </ul>	Pts requiring surgery (mean per patient)
Moder et al., 2012	25	0–1 yr to 3 m (Univ.) 2–7 yrs to (1) 6 m (Univ.) or (2) private practice (not recorded)	72	Not reported	Tooth loss CAL (median) PPD (median) PBI
Nygaard-Ostby et al., 2010	40	3, 4 or 6 m	111	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>SRP and polished as needed. Fluoride application, and pts advised to use daily 0.05% NaF mouth rinse</li> </ul>	Tooth loss CAL (mean) PPD (mean) PBI
Orsini et al., 2008	12	3 m	66	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Instrumentation as needed</li> </ul>	Tooth Loss CAL (mean) PPD (mean) FMBS
Petsos et al., 2019	14	Unmonitored	228	Not reported	Tooth Loss CAL (mean) PPD (mean) GBI
Pihlstrom et al., 1983	17	3–4 m	72	<ul style="list-style-type: none"> <li>Oral hygiene reviewed</li> <li>Supra- and sub-gingival instrumentation</li> </ul>	CAL (mean) PPD (mean)

(Continues)

TABLE 2 (Continued)

Publication	Participants entering SPC (n)	Recall intervals (m = months)	Follow up in SPC (months)	Description	Outcomes
Pihlstrom et al., 1984	17	3–4 m	72	<ul style="list-style-type: none"> <li>• Oral hygiene reviewed</li> <li>• Supra- and sub-gingival instrumentation</li> </ul>	Tooth loss CAL (mean) PPD (mean)
Ramberg et al., 2001	115 (34 periodontitis patients)	3–4 m	144	<ul style="list-style-type: none"> <li>• Oral hygiene reviewed</li> <li>• Sites of PPD <math>\geq 5</math> mm + BOP received subgingival instrumentation under local anaesthetic</li> </ul>	Tooth loss (mean) CAL PPD (mean) FMBS
Rosling et al., 2001	334 (highly susceptible group, HSG = 109/normal group, NG = 225)	3–4 m (HSG) 6–12 m (NG)	156	HSG: <ul style="list-style-type: none"> <li>• Oral hygiene reviewed</li> <li>• Sites of PPD <math>\geq 5</math> mm + BOP received subgingival instrumentation under local anaesthetic</li> <li>• Teeth that at any recall had advanced mobility or abscess were extracted</li> </ul>	Tooth loss (mean) CAL (mean) Sites with increase of PPD $\geq 2$ mm (%) No. of pts with increase of CAL $\geq 2$ mm
Serino, Rosling, Ramberg, Hellstrom, et al., 2001	20	3–4 m	60	<ul style="list-style-type: none"> <li>• Oral hygiene reviewed</li> <li>• Sites of PPD <math>\geq 5</math> mm + BOP received subgingival instrumentation under local anaesthetic</li> <li>• Teeth that at any recall, had advanced mobility or abscess were extracted</li> </ul>	Tooth loss (mean) CAL (mean) PPD (mean) FMBS
Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001	64	3–4 m	144	<ul style="list-style-type: none"> <li>• Oral hygiene reviewed</li> <li>• Sites of PPD <math>\geq 5</math> mm + BOP received subgingival instrumentation under local anaesthetic</li> <li>• Teeth that at any recall had advanced mobility or abscess were extracted</li> </ul>	Tooth loss (mean) CAL (mean) PPD (mean) FMBS

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; FMBS, full-mouth bleeding score; GI, gingival index; NaF, sodium fluoride; OHIP, Oral Health Impact Profile questionnaire; PBI, papillary bleeding index; PPD, periodontal probing pocket depth; PRO, patient-reported outcome; re-tx, re-treatment; SRP, scaling and root planing Univ., university setting; yrs, years.

et al., 2010; Moder et al., 2012; Dori et al., 2013; Cortellini et al., 2017, 2020; Cieplik et al., 2018; Petsos et al., 2019). Data were sub-grouped according to treatment arms in APT, culminating in (a) six clusters for patients in the 3M subgroup and seven clusters in the IRREG subgroup, and (b) seven clusters for patients in the 5–10 FU subgroup and six clusters in the >10 FU subgroup. The per protocol meta-analysis at the patient level for tooth loss observed 192 participants (Figure 2).

The 3M subgroup included 98 participants, while the IRREG subgroup observed 94. The proportion of patients experiencing tooth loss overall yielded a weighted value of 9.6% (95% CI 5%–14%), with low heterogeneity  $I^2 = 28\%$  ( $p = .161$ ). Subgroup analysis showed a weighted mean value for the 3M group as 8% (95% CI 2%–14%), with low to moderate heterogeneity  $I^2 = 32\%$  ( $p = .195$ ), while the IRREG group displayed a 11.9% (95% CI 5%–19%) prevalence and low to moderate heterogeneity  $I^2 = 30.2\%$  ( $p = .198$ ).

The ITT meta-analysis included a total of 218 participants (Appendix S8). The 3M subgroup had 107 patients, and the IRREG subgroup included 111. As anticipated, the percentages were less than in the per protocol analysis. Overall, the proportion of patients experiencing tooth loss was 8.3% (95% CI 4.3%–12.3%) and had low heterogeneity ( $I^2 = 24\%$ ,  $p = .197$ ). The subgroup analysis found that the 3M group displayed a prevalence of 7.3% (95% CI 1.8%–12.8%) and low heterogeneity,  $I^2 = 28\%$  ( $p = .223$ ), while the IRREG group showed 9.9% (95% CI 3.6%–15.1%), with low heterogeneity once again,  $I^2 = 29\%$  ( $p = .207$ ).

Length of follow-up time was also considered at the patient level for tooth loss (Figure 3). One hundred and six participants were observed in the 5–10 FU subgroup and 86 in the >10 FU subgroup. The weighted value for tooth loss was 8.2% (95% CI 3%–13%) for the 5–10 FU group and 12.7% (95% CI 4%–22%) for the >10 FU group, with substantial heterogeneity  $I^2$  test 70% ( $p = .374$ ) and 51% ( $p = .070$ ), respectively.

The ITT analysis according to follow-up time at the patient level (Appendix S9) observed 124 participants in the 5–10 FU subgroup and 94 in the >10 FU subgroup. The proportion of patients experiencing tooth loss for the 5–10 FU group was 7.3% (95% CI 2.9%–11.7%) and for the >10 FU group 11.5% (95% CI 3.2%–19.9%), with no heterogeneity detected  $I^2 = 0\%$  ( $p = .453$ ) and substantial heterogeneity  $I^2$  test 50% ( $p = .073$ ), respectively.

Meta-regression analyses were performed to investigate the influence of the type of treatment in APT (regenerative or non-regenerative), frequency of SPC (3M or IRREG), and length of follow-up (5–10 FU or > 10 FU) on tooth loss. There was no evidence of any association between the type of treatment (COEF 0.1; 95% CI –0.07 to 0.3,  $p = .249$ ), frequency of SPC (COEF 0.05; 95% CI –0.05 to 0.1,  $p = .341$ ), or length of follow-up (COEF 0.02; 95% CI –0.08 to 0.1,  $p = .704$ ) and tooth loss was found.

### 3.4.2 | Clinical attachment level loss ( $\geq 2$ mm)

Three studies for FQ-1 contributed data for estimating the number of patients experiencing CAL loss  $\geq 2$  mm (Dori et al., 2013; Cortellini

et al., 2017; Petsos et al., 2019). Data were sub-grouped according to treatment arms in APT, culminating in (a) three clusters for patients in the 3M subgroup and four clusters in the IRREG subgroup, and (b) two clusters for patients in the 5–10 FU subgroup and five clusters in the >10 FU subgroup. The meta-analysis for patients experiencing CAL loss  $\geq 2$  mm observed 86 participants (Figure 4).

The 3M subgroup observed 41 participants, while the IRREG subgroup observed 45. The proportion of patients experiencing at least one site of CAL loss  $\geq 2$  mm overall yielded a weighted mean value of 24.8% (95% CI 11%–38%), with substantial heterogeneity  $I^2 = 63\%$  ( $p = .013$ ). Subgroup analysis showed a weighted mean value for the 3M group as 30.2% (95% CI –2% to 63%),  $I^2 = 87\%$  ( $p < .0001$ ), while the IRREG group displayed a 21.4% (95% CI 10%–33%) prevalence,  $I^2 = 0\%$  ( $p = .884$ ). The difference between the groups was not statistically significant ( $p = .332$ ).

Length of follow-up time was assessed at the patient level for CAL loss  $\geq 2$  mm (Figure 5), with 22 participants observed in the 5–10 FU subgroup and 64 in the >10 FU subgroup. The proportion of patients experiencing at least one site of CAL loss  $\geq 2$  mm was 22.1% (95% CI 5%–39%) for the 5–10 FU group and 26.3% (95% CI 8%–45%) for >10 FU group  $I^2 = 0\%$  ( $p = .609$ ) and 75% ( $p = .003$ ), respectively.

The random-effects meta-regression analyses found no association between the frequency of SPC (COEF 0.13; 95% CI –0.1 to 0.4,  $p = .332$ ) and the length of follow-up (COEF –0.16; 95% CI –0.5 to 0.2,  $p = .311$ ) with percentage of patients experiencing CAL loss  $\geq 2$  mm; however, the type of treatment carried out in APT (regenerative or non-regenerative) was significantly associated (COEF 0.26; 95% CI 0.01–0.5,  $p = .043$ ), whereby a non-regenerative intervention was more likely to experience greater proportion of patients with CAL loss  $\geq 2$  mm. Therefore, the estimate of the prevalence of patients with CAL loss  $\geq 2$  mm would be expected to increase by 0.26 when non-regenerative treatment was carried out in APT according to this random-effects meta-regression model.

## 3.5 | Qualitative analyses

### 3.5.1 | Tooth loss

#### *Focused question 1*

Tooth loss was reported in 17 studies. However, due to substantial heterogeneity in reporting of this outcome, nine studies could not be included in the meta-analyses (Axelsson & Lindhe, 1981; Pihlstrom et al., 1984; Kaldahl et al., 1996a; Becker et al., 2001; Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001; Loesche et al., 2002) and are described in a narrative form (Appendix S10).

One study (Loesche et al., 2002), with regular 3-monthly SPC and a follow-up of a median of 61.2 months, reported the proportion of patients with tooth loss as being 56.8%. This is substantially higher than that estimated for the 3M subgroup analyses (8.0%, 95% CI

**TABLE 3** Focused question 2: Characteristics of included studies

Publication	Country	Setting	Funding	<ul style="list-style-type: none"> <li>• <b>Diagnosis</b></li> <li>• <b>Inclusion criteria</b></li> </ul>	Study design	Intervention
Bogren et al., 2008	Multi-centre (Sweden, United States)	Specialist private practice and university	Part funded by National Institute of Dental and Craniofacial Research (Bethesda, Maryland)	<ul style="list-style-type: none"> <li>• Moderate to advanced periodontitis</li> <li>• Minimum of four teeth with PPD <math>\geq 5</math> mm</li> </ul>	RCT	Test: Instrumentation + 8.8% doxycycline gel in PPD $\geq 5$ mm at BL, 1 and 2 years Control: Instrumentation alone (PPD $\geq 5$ mm)
Costa et al., 2015	Brazil	Private practice	Grants from Minas Gerais State Foundation & National Counsel of Technological and Scientific Development	<ul style="list-style-type: none"> <li>• Moderate to advanced chronic periodontitis</li> <li>• Minimum four sites with PPD <math>\geq 5</math> mm and CAL <math>\geq 3</math> mm, BOP and/suppurative</li> </ul>	Prospective cohort	RC: 96 subjects IC: 116 subjects Instrumentation (NST or ST, when appropriate) ST when PPD $\geq 5$ mm + BOP (45–60 days after NST) Compared treatment of recurrence via NST or ST in RC and IC groups
Jenkins et al., 2000	UK	University	NR	<ul style="list-style-type: none"> <li>• NR</li> <li>• Minimum of four sites with PPD <math>\geq 4</math> mm and persistent BOP</li> </ul>	CCT	Test: Subgingival scaling at 3, 6, and 9 months Control: Coronal scaling only (and for any sites with CAL $\geq 2$ mm, but excluded from analysis) at 3, 6, and 9 months
Killeen et al., 2018	United States	University	Dr. D. H. Reinhardt Scholar Program Dr. Mick Dragoo and wife Mary and the Nebraska Dental Association Foundation	<ul style="list-style-type: none"> <li>• One posterior interproximal PPD <math>\geq 5</math> mm with history of BOP</li> </ul>	RCT	Test: NST + 1 mg of minocycline microspheres (local application) at 0, 6, 12, and 18 months Control: NST alone
Lulic et al., 2009	Switzerland	University	Part supported by HEL-Bos Photodynamic Systems GmbH, Austria and by the Clinical Research Foundation (CRF) for the Promotion of Oral Health, Switzerland	<ul style="list-style-type: none"> <li>• Single PPD <math>\geq 5</math> mm with/out concomitant BOP</li> </ul>	RCT	Test: NST + photosensitizer dye (phenothiazine chloride) + PDT (diode laser, wavelength 670 nm and power density 75 mW/cm <sup>2</sup> ) Control: NST + photosensitizer dye (phenothiazine chloride)
Tonetti et al., 2012	Multi-centre (Italy, Germany, Greece, Netherlands, Switzerland)	Private practice and university	European Research Group on Periodontology (ERGOPero) with an unrestricted grant from IVOCCLAR Vivadent (Liechtenstein) Doxycycline gel provided by IVOCCLAR	<ul style="list-style-type: none"> <li>• Moderate to severe periodontitis</li> <li>• Minimum 4 teeth with residual PPD <math>\geq 5</math> mm and BOP</li> </ul>	RCT	Test: Instrumentation + 14% doxycycline gel in PPD $\geq 4$ mm at BL Control: Instrumentation alone (PPD $\geq 4$ mm)

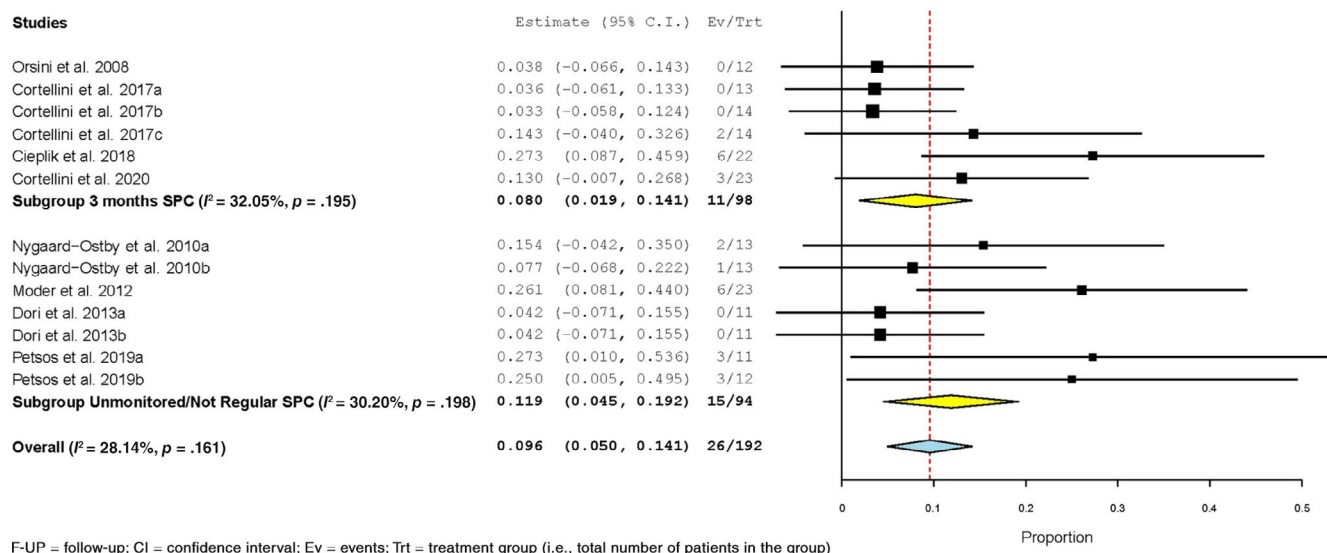
Abbreviations: BL, baseline; BOP, bleeding on probing; CAL, clinical attachment level; CCT, controlled clinical trial; IC, irregular compliers; mg, milligram; mW/cm<sup>2</sup>, milliwatt per square centimetre; nm, nanometre; NR, not reported; NST, non-surgical therapy; PDT, photodynamic therapy; PPD, periodontal probing pocket depth; RC, regular compliers; RCT, randomized controlled trial; ST, surgical therapy.

TABLE 4 Focused question 2: Characteristics of studies related to intervention(s)

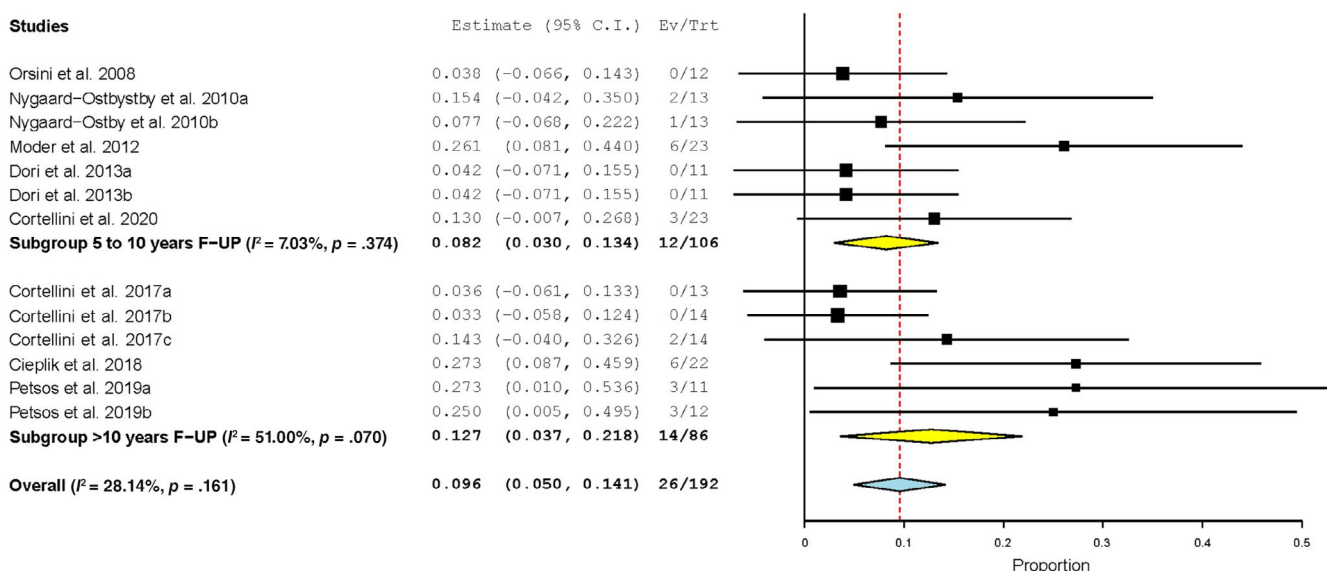
Publication	Participants (n)	Recall intervals (months)	Follow-up (months)	Description	Outcomes
Bogren et al., 2008	BL = 128 F = 124	6	36	Parallel group, multi-centre (2 × private practices, 1 × university), RCT Moderate/advanced periodontitis Test: NST + 8.8% doxycycline gel in PPD ≥ 5 mm at BL, 1 and 2 years Control: NST alone (PPD ≥ 5 mm)	Tooth loss (mean) CAL (mean) PPD (mean) BOP (mean) No. sites PPD ≥ 5 mm (mean)
Costa et al., 2015	BL = 212 F = 212	Regular: ≤ 6 Irregular: ≤ 18	60	Prospective cohort, private practice Moderate/advanced periodontitis RC: 96 subjects, IC: 116 subjects Instrumentation (NST or ST, when appropriate). ST when PPD ≥ 5 mm + BOP (45–60 days after NST) Compared treatment of recurrence via NST or ST in RC and IC groups	Tooth loss (mean) Sites experiencing CAL loss ≥ 2 mm PPD (mean % affected sites) CAL (mean) BOP (mean)
Jenkins et al., 2000	BL = 39 F = 31	3	12	Controlled clinical trial Severity of periodontitis not reported Test: Subgingival scaling at 3, 6 and 9 months Control: Coronal scaling only (and for any sites with CAL ≥ 2 mm, but excluded from analysis) at 3, 6, and 9 months	No. sites CAL loss ≥ 2 mm CAL (mean) PPD (mean) BOP (mean)
Killeen et al., 2018	BL = 60 F = 48	6	24	Parallel group, RCT Moderate to severe periodontitis Test: NST + 1 mg minocycline microspheres, applied every 6 months (four doses) Control: NST alone	PPD (mean) CAL (mean)
Lulic et al., 2009	BL = 10 F = 10	Unclear	12	Parallel group, RCT Chronic periodontitis Test: NST + photosensitizer dye + PDT Control: NST + photosensitizer dye	PPD (mean) CAL (mean) BOP (mean)
Tonetti et al., 2012	BL = 202 F = 181	3	12	Parallel group, multi-centre, RCT Moderate to severe periodontitis Test: NST + 14% doxycycline gel in PPD ≥ 4 mm at BL Control: NST alone (PPD ≥ 4 mm)	PPD (mean) CAL (mean) BOP (mean) No. sites PPD ≥ 5 mm (mean) No. sites CAL loss ≥ 2 mm Adverse events

Abbreviations: BL, baseline; BOP, bleeding on probing; CAL, clinical attachment level; F, final; IC, irregular compliers; No., number; NST, non-surgical therapy; PDT, photodynamic therapy; PPD, periodontal probing pocket depth; RC, regular compliers; RCT, randomized controlled trial; ST, surgical therapy.





**FIGURE 2** Forest plot of the proportion of patients who experienced tooth loss according to frequency of supportive periodontal care (SPC) - per protocol [Colour figure can be viewed at [wileyonlinelibrary.com](#)]



**FIGURE 3** Forest plot of the proportion of patients who experienced tooth loss according to length of follow-up (per protocol) [Colour figure can be viewed at [wileyonlinelibrary.com](#)]

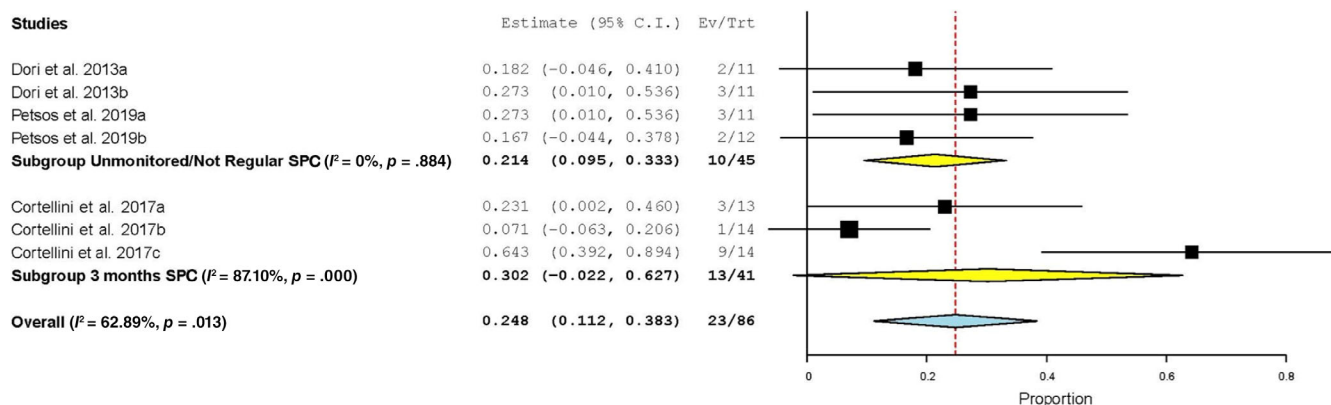
1.9%–14.1%) and the 5–10 FU subgroup (8.2%, 95% CI 3.0%–13.4%). Additionally, the authors reported a substantial drop-out rate of 46 participants from the original 90 subjects who entered the maintenance phase. On the other hand, one other small split-mouth study (Becker et al., 2001) reported the prevalence as 0% over the course of 5 years.

A number of studies reported mean tooth loss over the course of SPC (Axelsson & Lindhe, 1981; Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001). Some studies did not report the reasons for extraction and, so as to prevent underestimation of tooth loss, were included in the summary (Appendix S10).

Other studies reported absolute numbers of teeth lost (Pihlstrom et al., 1984; Kaldahl et al., 1996a).

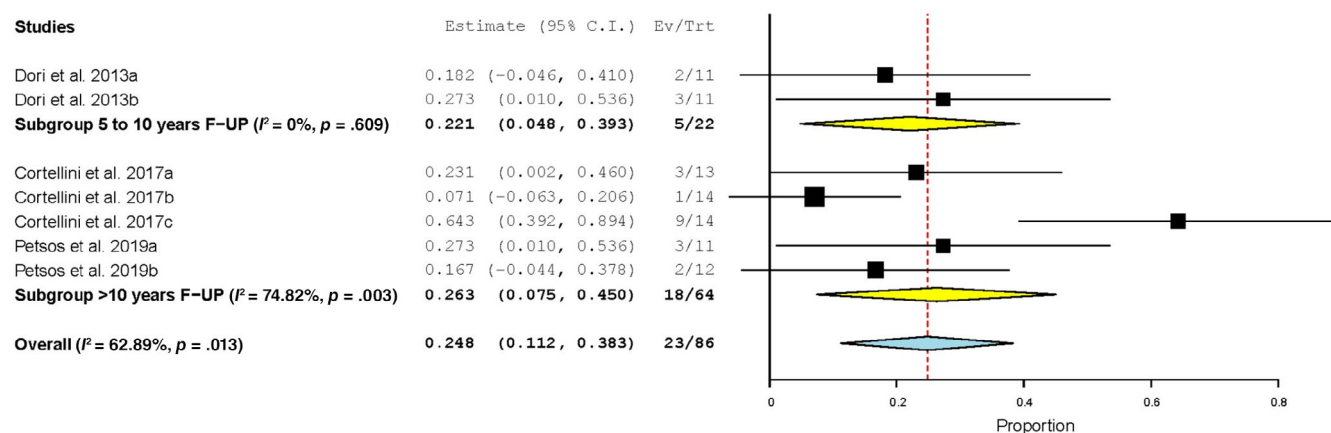
For studies with 5–10 FU (Axelsson & Lindhe, 1981; Pihlstrom et al., 1983; Pihlstrom et al., 1984; Kaldahl et al., 1996b; Becker et al., 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Buchmann et al., 2002; Loesche et al., 2002, 2005), the average tooth loss per patient ranged from 0 to 2.6 teeth, while for studies with >10 FU (Ramberg et al., 2001; Rosling et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001), this ranged from 0.6 ( $\pm 1.1$ ) to 2.7 ( $\pm 3.7$ ) teeth per patient.

Studies that performed regular 3–4-monthly SPC (Axelsson & Lindhe, 1981; Pihlstrom et al., 1983, 1984; Kaldahl et al., 1996a,



F-UP = follow-up; CI = confidence interval; Ev = events; Trt = treatment group (i.e., total number of patients in the group)

**FIGURE 4** Forest plot of proportion of patients with at least one site of clinical attachment loss  $\geq 2$  mm according to frequency of supportive periodontal care (SPC) – per protocol [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13553)]



F-UP = follow-up; CI = confidence interval; Ev = events; Trt = treatment group (i.e., total number of patients in the group)

**FIGURE 5** Forest plot of the proportion of patients with at least one site of clinical attachment loss  $\geq 2$  mm at patient level according to length of follow-up (per protocol) [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1111/jcpe.13553)]

1996b; Becker et al. 2001; Ramberg et al. 2001; Rosling et al. 2001; Serino, Rosling, Ramberg, Hellstrom, et al., 2001; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001; Loesche et al., 2002, 2005) reported mean tooth loss ranging from 0 to 2.7 or absolute numbers of teeth lost (from the cohort) in the range 8–46 (+2 roots) over the course of SPC.

#### Focused question 2

One RCT (Bogren et al., 2008) and one prospective cohort (Costa et al., 2015) reported on tooth loss in patients previously treated for moderate to advanced periodontitis in SPC with unstable disease (Appendix S11).

Bogren et al. (2008) compared locally delivered 8.8% doxycycline gel applications (every 3 months) with scaling and root planing (SRP) in 63 participants (test) in sites of PPD  $\geq 5$  mm to SRP alone (control) in 65 participants. The study reported 25 lost sites due to tooth extraction (mean of 0.4 sites/participant) in the test group compared with 45 lost sites (mean 0.7 sites/participant) in the

control group over a 3-year follow-up period with routine 6-monthly SPC. The difference was not statistically significant ( $p > .05$ ) between treatment groups.

A prospective cohort study (Costa et al., 2015) analysed a population of 212 individuals over a 5-year period and retrospectively divided the cohort into two groups according to SPC visit compliance. Ninety-six regular compliers (RC) and 116 IRREG compliers (IC) were subject to non-surgical therapy (NST) and, if deemed necessary, surgical therapy (ST) (if persistent PPD  $\geq 5$  mm were detected). Mean tooth loss was reported to be 0.6 and 0.8 for RC and IC, respectively. The difference was found to be statistically significant ( $p < .05$ ). Tooth loss was also assessed according to treatment modality within each compliance group. The RC group demonstrated a mean tooth loss of 0.3 (NST) and 0.8 (ST), compared with the IC group, which was 2.2 and 2.8 for NST and ST, respectively. The differences between groups for both NST and ST were statistically significant. Interestingly, in both RC and IC groups, ST influenced greater tooth loss after 5 years.

### 3.5.2 | Sites with CAL loss $\geq 2$ mm

#### *Focused question 1*

The majority of studies reported mean or median CAL over the duration of SPC. Some studies reported sites experiencing mean CAL loss  $\geq 2$  mm as frequency distributions at various timepoints in SPC or in relation to initial PPD (prior to APT).

One study (Buchmann) of 13 participants reported the prevalence of disease progression over a 5-year follow-up at various time points. This study reported a total of 64 sites which experienced disease progression, and it was not clear whether these sites were recurrent or newly occurring. The greatest number of sites experiencing disease progression occurred at 60 months, where 17 sites (18.3%) experienced CAL loss  $\geq 2$  mm, followed by 12 sites (16.3%) in which it occurred at 36 months.

Another study (Kaldahl et al., 1996b) reported “breakdown” sites, where the attachment loss was  $\geq 3$  mm. This group found a mean incidence per year of 1.24% over the course of 84 months of routine 3-monthly SPC. Of interest, a small proportion of participants (10%) accounted for a mean of more than 3.0% incidence per year, and these were all smokers.

Moder et al. (2012) conducted a split-mouth study over 72 months of SPC and reported a total of 14 sites lost less than or equal to 2 mm of attachment. It should be noted that some sites may have lost less than 2 mm of attachment, but we were unable to extract this information.

Finally, one study with 64 participants with a follow-up of 144 months in SPC reported mean annual proportions of sites showing 2 mm attachment loss with respect to baseline PPD (Table 2) (Ramberg et al., 2001). The greatest mean proportion was consistently seen in the PPD  $\geq 6$  mm category for the SRP group, which was 7.5% ( $\pm 6.4$ ) between 12 and 36 months, 7.8% ( $\pm 8.7$ ) between 36 and 60 months, and 2.9% ( $\pm 8.2$ ) between 60 and 156 months of SPC.

#### *Focused question 2*

Two studies reported on the sites with CAL loss  $\geq 2$  mm (Jenkins et al., 2000; Tonetti et al., 2012), and both trials reported no statistically significant difference between test and control groups (Appendix S11).

One controlled clinical trial (CCT) (Jenkins et al., 2000) assessed 17 patients (146 sites) in a coronal scaling (CS) group versus 14 patients (130 sites) in a subgingival scaling (SS) group over a 12-month period. Participants who previously had been treated for periodontitis and entered SPC presented with at least four pockets of PPD  $\geq 4$  mm. The appropriate intervention was delivered at baseline and at 3, 6, and 9 months. The authors reported 21 of these “loser” sites (defined as CAL loss  $\geq 2$  mm) in each group but found no statistically difference between the groups. Initial PPD  $\geq 6$  mm demonstrated a greater proportion of sites that were “loser” sites (28.6%) compared to 11.6% of those with initial PPD 4–5.9 mm for the SS group. The corresponding proportions for the CS group were 20.5% (initial PPD  $\geq 6$  mm) and 11.8% (initial PPD 4–5.9 mm). The authors concluded that the risk of attachment loss was greater if the initial PPD was 6 mm or above; however, this was only statistically significant for the SS group.

Tonetti et al. (2012) reported on 202 subjects in a multi-centre RCT, comparing SRP and a single adjunctive 14% doxycycline gel application to SRP alone with a follow-up of 12 months. Participants had previously been treated for periodontitis and presented with at least four teeth with residual PPD  $\geq 5$  mm and a positive BOP. SPC was performed every 3 months for 1 year. A total of 15 participants (7.5%) experienced CAL loss  $\geq 2$  mm (8 test, 7 controls). No statistically significant difference between the groups was reported for any parameters at 12 months.

### 3.5.3 | Pockets of 5 mm or more with bleeding on probing

No studies reported specifically on the number of pockets of  $\geq 5$  mm with bleeding on probing during the SPC phase, but some reported on the proportion of sites within specific PPD categories. Additionally, for treatment of recurrence in SPC, the mean number of sites with PPD  $\geq 5$  mm was reported without any mention of bleeding on probing (Bogren et al., 2008; Tonetti et al., 2012).

### 3.5.4 | Sites that need/experience re-treatment

Kaldahl et al. (1996b) reported at total of 685 breakdown sites (461 from the SRP, modified Widman flap [MWF], and osseous recontouring groups) during the course of SPC that required re-treatment. From this, 5%–12% of breakdown sites experienced  $\geq 3$  mm attachment loss, which were subsequently re-treated, and experienced further loss of attachment.

### 3.5.5 | Oral-health-related quality of life

The only study that reported on OHQOL was Cortellini et al. (2020). This study used the Italian translation of the Oral Health Impact Profile (OHIP)-14 questionnaire at baseline, and at 1, 5, and 10 years after treatment. One year after regenerative treatment (the first reassessment after APT), the mean OHIP-14 score was 6.6 ( $\pm 2.4$ ), and this was compared with a rehabilitated group (not relevant to this review). No data were reported at 10 years.

One study (Cortellini et al., 2017) reported recurrences that required retreatment. These recurrences occurred in all three treatment groups, MWF, modified papilla preservation technique (MPPT) with expanded-polytetrafluoroethylene membrane (e-PTFE), and flap with e-PTFE. A total of 26 recurrences occurred in 20 years, where sites of PPD  $\geq 5$  mm at the 1-year reassessment showed the highest frequency of recurrence that required re-intervention.

### 3.5.6 | Health economic outcomes

Two studies (Cortellini et al., 2017, 2020) reported the total cumulative costs for operative interventions. This cost calculation included

the actual cost of the procedures (using average fees from nine practices in Italy) and all complications that required re-treatment, and included tooth loss. Cortellini et al. (2020) reported (in graphical form) that the cumulative costs for a regenerative procedure over 10 years amounted to a mean of just over €2500; however, SPC appointments were not included in this calculation. The cumulative costs over a 20-year period (including 3-monthly SPC) ranged from a mean of €3090.98 ( $\pm 210.66$ ) to €3382 ( $\pm 88.95$ ), depending on the initial surgical therapy (Cortellini et al., 2017).

### 3.5.7 | Other patient-reported outcomes

One study (Kaldahl et al., 1996a) reported on the occurrence of periodontal abscesses in the context of the therapy type in APT over the 84 months of follow-up. Twenty-seven abscesses were reported, with 23 episodes (85%) occurring in the group originally treated by coronal scaling alone. Deep probing depths ( $\geq 7$  mm) at the initial examination was associated with 17 abscesses (63%).

Masticatory function and aesthetics were assessed by Cortellini and co-workers (Cortellini et al., 2020). A 5-point Likert scale was utilized to assess changes from baseline to 10 years. The authors reported that between the 1- and 10-year follow-up period, the proportion of participants with “no concern” in regard to masticatory function remained stable. Those reporting “some concern” appeared to increase over the 9 years of SPC (graphical information only available). A similar scale was used for assessing aesthetics, and once again, while those reporting “no concern” appeared to remain stable between the 1- and 10-year follow-up, those reporting “some concern” appeared to increase over the follow-up.

Two studies reported on adverse events in the context of experimental treatment groups (Jenkins et al., 2000; Tonetti et al., 2012). Jenkins et al. (2000) reported no adverse events in relation to coronal and subgingival scaling. In contrast, Tonetti et al. (2012) reported at 12 months 49 patients (75 adverse events) in the control group and 34 patients (56 adverse events) in the test group. The authors reported no difference in the incidence of adverse events between the groups (a test of significance was not carried out).

### 3.6 | Risk of bias

#### *Focused question 1*

All studies were assessed as prospective cohorts (SPC being the exposure) using the modified version of the NOS. Overall, most studies had a low risk of bias (Appendix S12), assessed as having five out of a possible six stars in regard to the selection and outcome domains. Two studies were found to have a moderate risk of bias, with four stars (Hou et al., 1997; Loesche et al., 2002), with one of these studies having a low score in the exposure/outcome domain (Hou et al., 1997). When assessed by means according to the domains of the NOS, it was found that “selection” had an average score of 2.9

(SD  $\pm 0.3$ ), while “outcome/exposure” showed an average of 2.5 (SD  $\pm 0.6$ ).

#### *Focused question 2*

Four RCTs were assessed using the Cochrane Risk of Bias Tool 2.0 (Appendix S13). Three studies were judged as being of “some concern” (Bogren et al., 2008; Lulic et al., 2009; Tonetti et al., 2012), while one study was deemed to be “high” risk (Killeen et al., 2018).

The Robins-I tool was used to assess the quality of one interventional non-RCT (Jenkins et al., 2000) and one prospective cohort (Costa et al., 2015). Both studies were judged to suffer from “serious” overall risk of bias (Appendix S14).

## 4 | DISCUSSION

### 4.1 | Key findings

Findings of the meta-analyses indicated that the proportion of patients who experienced tooth loss was 9.6% (95% CI 5%–14%), that is, 10% of patients can expect to lose at least one tooth during SPC of at least 5 years duration. Subgroup analysis showed that the proportion of patients with regular 3-monthly SPC recall visits who experienced tooth loss was 8.0% (95% CI 2%–14%), compared with 11.9% (95% CI 5%–19%) for the IRRREG SPC group ( $p = .161$ ). A shorter length of follow-up (5–10 years) corresponded to an average of 8.2% (95% CI 3%–13%), and as this time period increased ( $>10$  years), the proportion also increased to 12.7% (95% CI 4%–22%). Studies that could not be included in the meta-analyses reported a mean tooth loss per patient of 0–2.7 ( $\pm 3.7$ ), which was not greatly affected by the length of follow-up in SPC.

Patients who experienced at least one site of CAL loss  $\geq 2$  mm was estimated to be 24.8% (95% CI 11%–38%), that is 25% of patients can expect to have at least one site with progression of periodontitis by at least 2 mm during SPC of at least 5 years duration. According to the subgroup analyses, more patients who underwent 3-monthly SPC experienced CAL loss  $\geq 2$  mm, which amounted to 30.2% (95% CI –2% to 63%), while the proportion of those in IRRREG group SPC was 21.4% (95% CI 10%–33%). The longer length of follow up of  $>10$  years led to a slightly higher proportion of patients with attachment loss of 26.3% (95% CI 8%–45%) as compared to 22.1% (95% CI 5%–39%) for the 5–10-year group.

### 4.2 | Agreements and disagreements with other reviews

To our knowledge, this is the first systematic review assessing disease progression with the primary outcome of tooth loss in the phase of SPC in the long term ( $>5$  years).

The results of our review agree with those of a recent Cochrane review (Manresa et al., 2018), which reported on RCTs with a minimum of 12 months follow-up to determine the effects of maintenance

care in the management of periodontitis. The authors found the quality of evidence to be low or very low and could not make conclusions on the merit of SPC versus monitoring alone/irregular SPC. Furthermore, no conclusion could be drawn regarding the optimum frequency of SPC.

One recent systematic review (Sanz-Martin et al., 2019), similar to the present review, reported mean CAL loss ranging from  $\leq 0.5$  to  $>1$  mm and proportion of sites showing CAL loss  $\geq 2$  mm ranging from 3% to 20% in their qualitative review. We were unable to compare the outcomes, as reporting of CAL loss in the current review was different and on a patient level. Tooth loss was reported at 1% based on one study only. One explanation for the differing results could be that Sanz-Martin et al. (2019) excluded regeneration studies, which formed a key part of the current review. Additionally, the present review only included studies with minimum 5 years specifically in the phase of SPC, rather than 5 years of follow-up (which was often calculated before APT). Quality assessment also differed. The present review employed the modified version of the NOS to assess the SPC phase only, whereas the previous authors assessed studies based on the APT phase (thereby using the Cochrane Collaboration tool for RCT and NOS for prospective cohorts). Their judgement was thus that most studies were at a high risk of bias, compared with this review which found that most studies were at low risk of bias.

#### 4.2.1 | Overall completeness and applicability of the evidence

This review was intended to focus on patients diagnosed with stage IV periodontitis; however, the majority of studies were published prior to the most recent classification, with the exception of one (Cortellini et al., 2020), whereby the authors retrospectively classified patients as stage III–IV. No data could be extracted on what would specifically be considered stage IV periodontitis. In light of the fact that we have a lack of data on complexity factors such as numbers of teeth previously lost to periodontitis, masticatory dysfunction, bite collapse, and/or remaining teeth, it would be reasonable to assume that the majority of studies in this review probably represent stage III periodontitis patients. It is unclear to what extent complexity factors might influence disease recurrence in SPC, and thus our results might be generalized to include stage IV cases.

The limited number of studies included in this systematic review might seem surprising; however prospective long-term studies ( $>5$  years) in the periodontal literature are rare, with the majority having a clear focus on the outcomes of APT with  $\leq 12$  months follow-up.

It is unclear if the data presented are representative of disease occurrence, recurrence, or progression; furthermore, it is unclear if tooth loss was due to periodontitis alone. A number of studies did not present any information on reasons for tooth loss, and thus the results presented in this review could be overestimated. Although our subgroup analysis showed that the proportion of patients who experienced CAL loss  $\geq 2$  mm was greater for those in the 3M subgroup

than the IRREG SPC subgroup, this difference was not statistically significant. Additionally, the disparity may be explained by a single outlier (Cortellini et al., 2017), where participants in this group presented with a greater number of residual PPD at the start of SPC and subsequently greater disease recurrence.

The studies in this systematic review were largely conducted in the university setting, with only a few conducted in private practice, some of which were from the same practice. Additionally, the meta-analyses included studies where regenerative procedures were part of APT, which limits the applicability of the evidence to all periodontal patients in general practice. The variability of SPC recall intervals and possible variety of operators, however, may be more realistic of that which occurs in practice. This systematic review was also unable to inform on specialist versus non-specialist SPC in regard to disease progression/recurrence. A previous systematic review (Gaunt et al., 2008) reported that SPC delivered in specialist care represented greater financial cost, but this was accompanied by greater periodontal stability (CAL) over a minimum follow-up period of 12 months.

There was an obvious lack of detail in regard to the description of SPC, and the majority of studies provided no information on who carried out the recall appointments. Use of the CONSORT–NPS extension (Leow et al., 2016) might help guide authors to describe the SPC intervention more completely even for non-randomized trials.

Studies that included PRO and health economic data were clearly lacking; therefore, no conclusions could be made on the impact of disease recurrence in regard to these important outcomes from this review. However, health economic modelling of SPC has demonstrated that it is cost effective in developed economies when considering tooth loss or progression of CAL (Pennington et al., 2011). Furthermore, prevention of tooth loss in an ageing population is a priority for long-term health and well-being (Tonetti et al., 2017). In relation to OHQOL, a recent pilot study has shown that after 32 years of SPC, OHQOL impacts are low. Interestingly, there were higher OHQOL impacts associated with “insufficient” adherence to SPC compared with those with “sufficient” adherence (Graetz et al., 2020).

Four studies specifically investigated treatment of recurrence in SPC, with only two being RCTs. Owing to heterogeneity in terms of methodology and outcome reporting, we were unable to answer FQ-2. Some of the included studies that addressed FQ-1 indicated that management of recurrence was left to the discretion of the operators but usually managed by further subgingival debridement. Success of this treatment modality in regard to resolution or halting progression of disease was not reported, although one study mentioned that “most” recurrent sites responded favourably to NST (Costa et al., 2015).

#### 4.2.2 | Overall quality, strength, and consistency of the evidence

The quality assessment judged that the majority of included studies had a low risk of bias in regard to the SPC phase (FQ-1), with two studies found as having moderate risk. The meta-analysis highlighted



heterogeneity for both tooth loss and CAL loss  $\geq 2$  mm, which reflects the limited number of studies fulfilling the inclusion criteria for this systematic review. Type of initial therapy (regenerative or non-regenerative) was one factor that could explain some heterogeneity; however, residual unexplained heterogeneity should be assumed, and results should be interpreted with caution. Studies included in the meta-analysis were predominantly of a regenerative nature. Split mouth studies were included in this review, and it should be acknowledged that there is an uncertain risk of contamination from one side/quadrant to another. This, however, would be most relevant for studies assessing APT. The strength of the evidence to answer FQ-2 was weak, with two studies having a “serious” risk of bias (Robins-I tool), three studies of “some concern”, and one study determined as having a “high” risk of bias (Cochrane Risk of Bias Tool 2.0). There was no clarity on which treatment modality (if any) was superior in the management of disease recurrence/progression in SPC.

Finally, it should be recognized that studies included in this review were not originally designed for assessment of disease progression/recurrence and/or treatment of recurrence in SPC, thus the strength of conclusions from these studies is weak.

### 4.3 | Strengths and limitations of the review

In order to minimize the risk of bias in the review process, this protocol was submitted a priori to PROSPERO. Furthermore, screening, study eligibility, data extraction, and quality assessment were all conducted in duplicate and independently.

This systematic review is the first to comprehensively look at disease progression/recurrence in SPC, incorporating all forms of treatment in APT, over a minimum of 5 years in maintenance. Additionally, it is the first to assess methods of managing disease progression/recurrence of patients in an established SPC programme. We incorporated a sensitive search strategy in multiple electronic databases to detect a broad range of studies. Other strengths were the quality assurance including duplicate, independent study screening and data extraction.

Several studies described a significant number of drop-outs over the follow-up period, and in order not to underestimate the prevalence of tooth loss and CAL loss  $\geq 2$  mm, we chose to carry out a per protocol meta-analyses. However, for comparison and thoroughness, an ITT analysis was also included for tooth loss.

A number of limitations could be identified that might bias the outcomes of this systematic review.

Publication bias is an important problem in evidence-based medicine, and this may lead to selection bias in systematic reviews. In the present review, some publications following the screening of titles and abstracts could not be obtained in full-text form, and clarification on studies from authors could not be followed up. We also limited ourselves to publications in the English language, which means that many relevant studies could have been missed.

Some post hoc changes were made to the original protocol. We added case series to the exclusion criteria, and a distinction was also

made as to what we defined as a case series versus prospective cohort. Additionally, a modified version of the NOS needed to be implemented to adjust for the studies included in the review.

One post hoc analysis was included based on the data collected. This was subgrouping according to SPC recall intervals and was conducted as it became clear that a number of studies had quite variable or unmonitored SPC visits.

### 4.4 | Implications for practice and policy

Most patients enrolled in SPC following successful treatment of periodontitis should not expect to experience tooth loss, which, considering the severity of disease (stage III or IV periodontitis), is highly encouraging. However, 25% of patients are likely to experience further CAL loss. It is unclear from the data whether the CAL loss represents periodontitis progression or gingival recession in shallow pockets. However, in some studies (Bogren et al., 2008; Costa et al., 2015; Cortellini et al., 2017), CAL loss was noted as an increase in PPD at some sites, suggesting disease progression. These findings, together with other evidence discussed in this review, highlight that SPC is an important element in the long-term management of stage III and IV periodontitis.

Evidence external to this review indicates that SPC is cost effective in developed economies (Pennington et al., 2011; Schwendicke et al., 2020) and that prevention of tooth loss is important in ageing populations (Tonetti et al., 2017).

Although SPC is poorly described in the literature, the common elements in studies suggest that it should include repeated risk assessment, health behaviour motivation, tailored oral hygiene coaching, professional mechanical plaque removal, and targeted subgingival debridement appropriate for each patient (Rosling et al., 2001). The recently published “Clinical Practice Guideline” from the European Federation of Periodontology (Sanz et al., 2020) supports inclusion of these elements also. Individual needs of each patient should be considered when deciding on the frequency of SPC, and until the influence of risk factors is better understood, this is likely to be no longer than 3–6 months interval for stage III–IV periodontitis patients. While there was no evidence of a difference in tooth loss between groups receiving 3-monthly and less regular SPC, it is important to remember that these were not RCTs and were therefore at higher risk of bias. A lack of randomized evidence was also found in another systematic review (Manresa et al., 2018).

### 4.5 | Implications for further research

There is a clear need for high-quality trials focused on SPC, with particular attention to SPC recall intervals, and documenting and treating disease progression/recurrence. SPC should be carefully described in detail, including who delivered it and the components of care using the CONSORT-NPE as a guide, even for non-randomized studies. The demographics of the population entering SPC should be clearly



described, particularly with reference to risk factors of smoking and diabetes. Information on tailoring procedures in each SPC visit and recall intervals would be highly valued.

In order to increase the clinical relevance of studies, it would be ideal to report outcomes such as tooth loss or CAL loss at a patient level, in addition to mean values. Patient-reported outcomes and costs of treatment would also be important and essential aspects of a clinical trial.

## 5 | CONCLUSIONS

Within the limitations of this study, we have found that the mean prevalence of tooth loss in patients in SPC for 5 years or more is less than 10%, with a tendency for greater prevalence with time. Regular SPC appointments (3-monthly) appear to be important for reduction of the prevalence of tooth loss.

## CONFLICT OF INTEREST

The authors declare no conflict of interest. No external funding was received for this study. University College London paid salaries to Natalie M. Leow, Federico Moreno, Debora Marletta, Jacopo Buti, and Ian Needleman.

## AUTHOR CONTRIBUTIONS

All authors met criteria for authorship and were given the opportunity to critically revise the manuscript and gave final approval of the version to be published. Additionally, all authors agreed to be accountable for all aspects of the work, ensuring integrity and accuracy.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

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