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SYSTEMATIC REVIEW

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Prevalence of stable and successfully treated periodontitis subjects and incidence of subsequent tooth loss within supportive periodontal care: A systematic review with meta-analyses

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Abstract

Aim: To identify (i) the prevalence of meeting the endpoints of 'stable periodontitis' (probing pocket depth [PPD] ≤ 4 mm, bleeding on probing [BoP] < 10%, no BoP at 4 mm sites), 'endpoints of therapy' (no PPD > 4 mm with BoP, no PPD ≥ 6 mm), 'controlled periodontitis' (≤4 sites with PPD ≥ 5 mm), 'PPD < 5 mm' and 'PPD < 6 mm' at the start of supportive periodontal care [SPC]) and (ii) the incidence of tooth loss in relation to not meeting these endpoints within a minimum of 5 years of SPC.

Materials and Methods: Systematic electronic and manual searches were conducted to identify studies where subjects, upon completion of active periodontal therapy, entered into SPC. Duplicate screening was performed to find relevant articles. Corresponding authors were contacted to confirm inclusion and retrieve required clinical data for further analyses to assess the prevalence of reaching endpoints and incidence of subsequent tooth loss, if available, within at least 5 years of SPC. Meta-analyses were carried out to evaluate risk ratios for tooth loss in relation to not reaching the various endpoints.

Results: Fifteen studies including 12,884 patients and 323,111 teeth were retrieved. Achievement of endpoints at baseline SPC was rare (1.35%, 11.00% and 34.62%, respectively, for 'stable periodontitis', 'endpoints of therapy' and 'controlled periodontitis'). Less than a third of the 1190 subjects with 5 years of SPC data lost teeth—a total of 3.14% of all teeth were lost. Statistically significant associations with tooth loss, at the subject-level, were found for not achieving 'controlled periodontitis' (relative risk [RR] = 2.57), PPD < 5 mm (RR = 1.59) and PPD < 6 mm (RR = 1.98).

Conclusions: An overwhelming majority of subjects and teeth do not achieve the proposed endpoints for periodontal stability, yet most periodontal patients preserve most of their teeth during an average of 10–13 years in SPC.

KEYWORDS

periodontitis, endpoints, supportive periodontal care, tooth loss, stable

Clinical Relevance

Scientific rationale for study: The risk of tooth loss is determined by clinical periodontal parameters as established in the literature. Composite measures have been established to determine when it is appropriate to end active periodontal therapy.

Principal findings: Only a small proportion of subjects reach currently defined endpoints of periodontal therapy, although tooth loss presents as a rare event in treated periodontitis.

Practical implications: The findings are novel and can have a significant impact on clinical practice, policy and research. It may be necessary to revisit the clinical endpoints of periodontal therapy to better reflect the risk of tooth loss during supportive periodontal care.

1 | INTRODUCTION

Defining periodontal health at the subject- and tooth-level is pivotal in establishing acceptable therapeutic endpoints and to evaluate individualized risk for periodontal disease progression. A successfully treated 'stable periodontitis' subject, as per the World Workshop Classification (WWC) 2017, is defined as one with probing pocket depth (PPD) ≤ 4 mm, no bleeding on probing (BoP) at 4 mm sites and BoP in <10% sites (Chapple et al., 2018). The European Federation of Periodontology (EFP) composed S3 treatment guideline—a four-step approach—to treat stages I–III periodontitis. Clinical guidelines for periodontal treatment should consider tangible outcomes—tooth survival and re-treatment (Loos & Needleman, 2020). Based on evidence for disease progression (Claffey & Egelberg, 1995; Matuliene et al., 2008), EFP's S3 treatment guideline proposed 'endpoints of therapy' for a patient to enter supportive periodontal care (SPC)—no PPD > 4 mm with BoP and no PPD ≥ 6 mm (Sanz et al., 2020). A 'treat-to-target' approach has also been proposed. 'Controlled periodontitis', defined as having ≤4 sites with PPD ≥ 5 mm, incorporates the effects of different periodontal treatments (Feres et al., 2020).

Guidance may present us with an ideal scenario where unless the endpoints are met, a subject should not enter into SPC. Yet, the evidence is unclear whether this is the reality within clinical practice. The aim of this systematic review is to assess the prevalence of treated periodontitis subjects who have met the following definitions:

- 'Stable periodontitis' (Chapple et al., 2018)
- 'Endpoints of therapy' (Sanz et al., 2020)
- 'Controlled periodontitis' (Feres et al., 2020)
- PPD < 5 mm
- PPD < 6 mm

With tooth loss being the final sequela of periodontitis, the proposed endpoints should be based on whether their unachievement results in increased tooth loss. Therefore, the relationships between the aforementioned endpoints and subsequent tooth loss during a minimum of 5 years of SPC were also assessed, leading to the following focused questions:

- *Focused question 1 (FQ-1)*: What is the prevalence of periodontitis in subjects who, at the start of SPC, meet the aforementioned endpoints?
- *Focused question 2 (FQ-2)*: What is the incidence of periodontitis-related (when reported) or non-specific tooth loss among treated adult periodontitis subjects, using each of the above definitions, who have been in SPC for a minimum of 5 years?

2 | MATERIALS AND METHODS

2.1 | Protocol development and registration

A systematic review protocol was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Moher et al., 2009). Details of the protocol were registered on PROSPERO on 16 February 2022 (ID: CRD42022310238). Amendments were made to the original protocol to expand the number of endpoints assessed.

2.2 | Eligibility criteria

2.2.1 | PICOS components

Population: Adult human subjects with periodontitis (excluding as a manifestation of systemic or necrotizing disease), who have completed active periodontal therapy (APT). Studies with inclusion/exclusion criteria that would affect the outcome of this systematic review (i.e., prevalence of reaching endpoints) were excluded.

Intervention: APT encompasses many interventions ranging from behavioural changes to surgical interventions (Sanz et al., 2020). Studies including a minimum of subgingival non-surgical periodontal therapy (NSPT) as part of their APT were selected (FQ-1).

Comparison: Not applicable.

Outcome measures: The primary outcomes were defined as follows:

- FQ-1 assesses the prevalence of subjects who achieved the aforementioned endpoints at the end of APT/start of SPC.
- FQ-2 was the incidence of tooth loss (periodontitis-related when available) for treated subjects who had been in SPC for a minimum of 5 years and its association with various endpoints.

Study design: Randomized controlled trials (RCTs), cohort (prospective/retrospective), case–control and cross-sectional studies published from 2017 were included. Cross-sectional studies were included if the original retrospective data from the study could be obtained. Studies selected for FQ-1 with a minimum SPC follow-up of 5 years were used to answer FQ-2.

2.3 | Literature search

A search strategy was formulated with an experienced librarian using a combination of MeSH and free-text terms (Supplemental Material S1), with no language restrictions. Electronic database searches included Ovid MEDLINE, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and OpenGrey from 2017 to 18 February 2022. This was complemented by a manual search of the *Journal of Dental Research*, the *Journal of Clinical Periodontology*, the *Journal of Periodontology* and the *Journal of Periodontal Research* from 2017 to 18 February 2022. Reference lists of the included articles and relevant reviews were manually searched. Editors of the above-named journals were contacted about any articles in press that fit the inclusion criteria.

2.4 | Screening and study inclusion

Study selection was based on a two-step approach: (i) screening of titles and abstracts and (ii) full-text analysis, with reasons for exclusion (Supplemental Material S2). Full texts were obtained for those studies selected by at least one reviewer. Both steps were performed in duplicate by two independent reviewers (V.R. and D.R.). Disagreements were resolved by consensus. An arbitrator (L.N.) was consulted if the disagreement could not be resolved. Where studies showed duplication of the subject sample or database, the first published study with all the required data or relevant multi-centre study were selected. Inter-observer agreement at both stages was assessed via the Cohen's kappa statistic. The corresponding authors were contacted to confirm inclusion, as individual patient data (IPD) are rarely reported.

2.5 | Data collection

2.5.1 | Data extraction

Data were extracted from journal articles based on the general study and population characteristics (Table 1). Subject-, tooth- and site-level data for periodontal parameters (PPD ± BoP) were extracted from individual 6-point pocket charts or datasets, sent by the journal article authors, by one reviewer (V.R.). Alternatively, the authors completed a summary data collection form if they opted to do their own re-analysis (Supplemental Material S3). Depending on availability, data were for subjects accounted for in the sample size of the selected journal article or the whole database on which the journal article was based. Data were entered into tables stratified by study design on Microsoft Excel. Data consistency, completeness and sequence generation were reviewed by the second reviewer (D.R.). Any disagreements were resolved by consensus. An arbitrator (L.N.) was consulted if the disagreement could not be resolved.

2.5.2 | RoB assessment

Quality assessment was carried out by one reviewer (D.R.) and reviewed independently by V.R. Included studies were assessed using Cochrane Risk of Bias (RoB) 2 Tool for RCTs (Sterne et al., 2019), the Newcastle–Ottawa Scale (NOS) for cohort and case–control studies (Wells et al., 2011) and the AXIS tool for cross-sectional studies (Downes et al., 2016). Disagreements were resolved by consensus. An arbitrator (L.N.) was consulted if it could not be resolved.

2.6 | Data analyses

The data were used to assess the prevalence of achieving the aforementioned endpoints at the subject-level and, when possible, tooth level. Although 'stable periodontitis' defines a case at the subject-level, the composite measures defining the endpoint (PPD ≤ 4 mm and PPD = 4 mm + BoP) were used at the tooth level to identify the teeth responsible for not meeting the endpoint. The number of diseased teeth per patient, as per WWC 2017, was calculated using the total number of 'unstable' teeth divided by the total number of (i) subjects and (ii) 'unstable' subjects.

Incidence of tooth loss within a minimum duration of 5 years of SPC was recorded at the subject- and tooth-level in relation to the various endpoints. The number of teeth lost per patient per SPC year was calculated using the total number of teeth lost divided by the total number of subjects with tooth loss data divided by the weighted average SPC years.

Authors of journal articles were contacted if any queries arose from the data. Where data were unavailable for a subject, the corresponding subject was eliminated from the analyses.

Meta-analyses were performed using 'RStudio' application and R core software to determine the association between the incidence of tooth loss during SPC, as a summary risk ratio, and the unsuccessful achievement of various endpoints. Studies answering FQ-2 with zero subjects or teeth within one of the arms (successful or unsuccessful in meeting endpoints) were not included in the meta-analyses, as two arms were required for the calculation of relative risk (RR). The zero count was inflated to 0.5 to avoid computational errors for studies where no events (tooth loss) were observed in one or both arms. Subanalyses of studies following conventional APT, as per EFP's S3 treatment guideline, or those reporting periodontitis-related tooth loss were performed to explore possible causes of heterogeneity among study results. RRs, their ratios and the corresponding 95% confidence intervals (CIs) were calculated as effect sizes. With treatment outcome affected by subject-, tooth- and treatment-related factors, a random effects model was deemed appropriate to calculate the average distribution of mean effects, based on clinical and statistical reasoning (Papageorgiou, 2014). The Paule–Mandel method was chosen to

TABLE 1 Study characteristics of included studies.

Author, year of publication	Funding	Study design	Country	Setting	Patient sample size in: (a) journal article, (b) raw data received, (c) raw data received from subjects in SPC for ≥5 years	Demographics	Medical history of sample	Smoking history of sample	Definition and severity of periodontitis	Types of APT carried out	SPC regime	Duration of SPC for studies/ subjects answering FQ-2 (years)	Diagnostic method employed in study
Aimetti et al. (2020)[a,b]	1	4	Italy	1	a. 21 b. 21 c. 21	Mean age: 52.6 ± 5.9 years (range: 44–68 years) Gender F/M: 16/5	Good general health	Current smokers: 3 (smoked 4–6 cigarettes/day)	WWC 2017—Stage IV (requiring orthodontics for pathological tooth migration)	NSPT, SPT (resective or regenerative surgery with EMD ± BG).	14 subjects: 2-month SPC intervals 7 subjects: 3–4 month SPC intervals	11.6 ± 1.6 (range: 10–15)	N/A
Barbe et al. (2020)[a,b]	3	1	Germany	2	a. 224 b. 220 c. 0	Mean age: Mean: 64 ± 12 (range: 32–90) Gender F/M: 111/113	Co-morbidities (n = 165)	N/A	WWC 1999—Loc/Gen. mild-severe ChP/AgP	NSPT, SPT	6-month SPC intervals	N/A	N/A
Baumer et al. (2020)[b]	4, 5	4	Germany	1	a. 100 b. 68 c. 68	Mean age: 35.3 ± 4.4 (range: 18–40) Gender F/M: 63/37 SE: 44% high, 34% moderate educational status	Non-contributory medical history at baseline	Current smokers: 15 (smoked 5–20 cigarettes/day) Former smokers: 40 Non-smokers: 45	WWC 1999—AgP	NSPT, SPT (includes regenerative therapy), ± adjunctive antibiotics	OHI, PMPR; Fluoride gel Re-treatment (46 subjects) Attendance: regular—at least 2 visits/year (n = 33); irregular (n = 67)	Mean 24.2 ± 6.5 (range: 10.2–35.4)	N/A
Ciurescu et al. (2021)[a]	N/A	2	Romania	1	a. 42 b. 38 c. 0	Mean age: 45.31 ± 9.78 Gender F/M: 22/20	Systemically healthy	Current smokers: 23	WWC 2017—Stages III or IV; Grade B	Control: NSPT in 1–4 sessions within 2 weeks Test: Diode laser therapy followed by a second round of laser treatment and NSPT of PPD ≥4 mm after 1 week. Third round of laser treatment of persistent sites	N/A	N/A	Millimetre-scaled 15 UNC colour-coded probe (PCPUNC 15, Hu Friedy) BoP recorded 30 s after probing
Collins et al. (2022)[a,b]	5	2	Dominican Republic	2	a. 40 b. 38 c. 0	Mean age: 52.7 (test); 51.55 (placebo) Gender F/M: 19/21	Systemic disease (n = 1)	Non-smokers	WWC 2017—Stages III or IV; Grades B–C	NSPT, SPT (access flaps/OFD) Test: metronidazole; Control: placebo (commenced after last surgery—1	OHI, PMPR; NSPT if needed	N/A	Examiner calibration 4 patients—correlation coefficient for PPD of 0.851 (95% confidence interval, CI

TABLE 1 (Continued)

Author, year of publication	Funding	Study design	Country	Setting	Patient sample size in: (a) journal article, (b) raw data received, (c) raw data received from subjects in SPC for ≥5 years	Demographics	Medical history of sample	Smoking history of sample	Definition and severity of periodontitis	Types of APT carried out	SPC regime	Duration of SPC for studies/ subjects answering FQ-2 (years)	Diagnostic method employed in study
													[0.811; 0.884]; $p < .001$). UNC 15-mm periodontal probe (Hu-Friedy) BoP assessed dichotomously
Cortellini et al. (2020)[a,b]	3	2	Italy	1	a. 50 b. 50 c. 50	Mean age: 51.2 ± 8.7 (control): 46.3 ± 8.9 (test) Gender F/M: 25/25	N/A	Current smokers: 5 (<20 cigarettes/ day)	WWC 2017—Stages III or IV (with at least a tooth with bone loss extending to or beyond the apex)	NSPT ± adjunctive antibiotics; SPT (including regeneration); Splinting of hypermobile teeth; Test: periodontal regeneration. Control: extraction and implant	3 month SPT intervals	9.68 years	N/A
De Wet et al. (2018)[a,b]	5	4	Netherlands	1	a. 54 b. 54 c. 54	Mean age: 45.31 ± 9.78 Gender F/M: 29/25		Current smokers: 12 Former smokers: 23 Non-smokers: 19	Van der Velden, 2000—Loc/gen: minor to severe	Non-surgical periodontal therapy; Surgical periodontal therapy	Adhered to protocol of regular 3–6-month SPC intervals ($n = 5$)	10 (±0.5)	N/A
Graetz et al. (2020)[a,b]	4, 5	4	Germany	2	a. 896 b. 50 c. 50	Mean age: 55.7 ± 11.3 Gender F/M: 21/28	DM: $n = 5$	Current smokers: 5 Former smokers: 23 Non-smokers: 21	WWC 1999—Loc/gen; ChP/AgP	NSPT (full mouth disinfection); SPT (OFD, resective treatment of furcation involved teeth; regenerative procedures)	Regime: • 3–6 month SPC intervals • OHI • NSPT of 'residual pockets' Regular: $n = 31$. Irregular: $n = 18$	10.1 ± 0.5	N/A
Jiao et al. (2017)[a]	2, 5	4	China	2	a. 10,789 b. 10,789 c. 418	Mean age: 45.12 ± 18.0 (range 18–79.92) Gender F/M: 5595/5194 Ethnicity: Chinese	Systemically healthy	Current smokers: 1870 Former smokers: 1407 Non-smokers: 7512	WWC 1999—ChP	NSPT	Regime: • 3–6 month SPC intervals • OHI • NSPT of residual pockets (PPD = 4 mm + BoP; PPD ≥ 5 mm)	≥5	Examiners were calibrated in pre-clinical programmes

tablet ×3/day for 7 days)

(Continues)

TABLE 1 (Continued)

Author, year of publication	Funding	Study design	Country	Setting	Patient sample size in: (a) journal article, (b) raw data received, (c) raw data received from subjects in SPC for ≥5 years	Demographics	Medical history of sample	Smoking history of sample	Definition and severity of periodontitis	Types of APT carried out	SPC regime	Duration of SPC for studies/ subjects answering FQ-2 (years)	Diagnostic method employed in study
Jiao et al. (2018)	2, 5	4	China	2	a. 1004 b. 1004 c. 23	Mean age: 30.68 ± 4.97 (range 18–43) Gender F/M: 544/460 Ethnicity: Chinese	Systemically healthy	Current smokers: 118 Former smokers: 102 Non-smokers: 784	WWC 1999—AgP	NSPT	Regime: • 3-month intervals • OHI • PMPR • NSPT of residual PPD ≥ 4 mm	≥5	Examiners were calibrated in pre-clinical programmes
Nibali et al. (2017)[a,b]	1	4	United Kingdom	1	a. 100 b. 98 c. 98	Mean age: 53.04 ± 9.31 Gender F/M: 60/40 Ethnicity: White ($n = 93$); Asian ($n = 5$); Afro-Carribean ($n = 2$)	Hypertension: $n = 13$ DM: $n = 0$	Current smokers: 22 Former smokers: 20 Never smokers: 58	WWC 1999—ChP	NSPT, SPT (resective, regenerative, periodontal plastic surgery)	3–12 month individualized SPC intervals: • OHI • Supra- and subgingival PMPR	6.59	
Nibali et al. (2020)[b]	1	1	United Kingdom	2	a. 66 b. 63 c. 63	Age: 18–65 years Gender F/M: 39/27 Ethnicity: White ($n = 39$); Asian ($n = 7$); Afro-Carribean ($n = 17$); other ($n = 3$)	DM: $n = 2$ CVD: $n = 5$ Overweight + obese: $n = 38$ RA: $n = 2$	Current smokers: $n = 8$ Non-smokers: $n = 58$	WWC 1999—AgP	NSPT ± adjunctive antibiotics; SPT	Unknown (SPC with GDP) 24% optimal adherence with SPC	6.97	UNC-15 periodontal probe
Saleh et al. (2021)[b]	N/A	4	United States	2	a. 148 b. 166 c. 166	Mean age: 46.49 ± 11.53 Gender F/M: 80/68	N/A	N/A	N/A	NSPT, SPT	≥1 SPC visit/year	24.7 ± 7.6	N/A
Saydzai et al. (2022)[a,b]	5	3	United Kingdom	1	a. 97 b. 195 c. 155	Mean age: 56 ± 8.7 Gender F/M: 66/31 Ethnicity: Caucasian ($n = 93$); Asian ($n = 3$); mixed ($n = 1$) BMI: 24.8	Excluded: serious medical history that prevents patients from undergoing dental treatment	Current smokers: $n = 14$ Former smokers: $n = 33$ Non-smokers: $n = 50$	WWC 1999—ChP or AgP	NSPT, SPT (resective, regenerative, periodontal plastic surgery)	3–12 month individualized SPC intervals: • OHI • Supra- and subgingival PMPR (under LA when necessary)	≥5	UNC-15 periodontal probe

TABLE 1 (Continued)

Author, year of publication	Funding	Study design	Country	Setting	Patient sample size in: (a) journal article, (b) raw data received, (c) raw data received from subjects in SPC for ≥5 years	Demographics	Medical history of sample	Smoking history of sample	Definition and severity of periodontitis	Types of APT carried out	SPC regime	Duration of SPC for studies/ subjects answering FQ-2 (years)	Diagnostic method employed in study
Sonnenschein et al. (2017)[b]	4, 5	4	Germany	2	a. 39 b. 24 c. 24	Mean age: 56.6 (range: 37–76) Gender F/M: 22/17		Current smokers: $n = 6$ Former smokers: $n = 2$ Non-smokers: $n = 31$	WWC 1999—ChP/ AgP	NSPT (full mouth disinfection) + splint insertion; SPT	≥1 SPC visit/year • OHI • PMPR • Fluoride gel; • NSPT for 'residual sites'	≥7	Examiners were calibrated
Codes		1—None; 2—Government; 3—Private; 4—Self-funded; 5—University	1—Cross-sectional 2—RCT 3—Prospective cohort 4—Retrospective cohort	1—Private practice 2—University hospital		SE—socio-economics	DM—diabetes mellitus, CVD—cardiovascular disease; RA—rheumatoid arthritis		Loc—localised Gen—generalised ChP—chronic periodontitis AgP—aggressive periodontitis	NSPT—non-surgical periodontal therapy SPT—surgical periodontal therapy EMD—enamel matrix derivative BG—bone grafts OFD—open flap debridement	OHI—oral hygiene instructions PMPR—professional mechanical plaque removal		BoP—bleeding on probing

Abbreviations: GDP, general dental practitioner; N/A, not applicable; PPD, probing pocket depth; SPC, supportive periodontal care; UNC, University of North Carolina; WWC, World Workshop Classification.

[a]Full site-level data inclusive of BoP was available.

[b]Follows conventional active periodontal therapy (APT).

calculate the mean effect (Langan et al., 2017). Knapp–Hartung adjustments were used to calculate the CI around the pooled effect (Knapp & Hartung, 2003).

The extent and impact of inter-study heterogeneity was assessed by inspecting the forest plots and by calculating the τ^2 (absolute heterogeneity) and the I^2 statistics (relative heterogeneity), respectively. I^2 defined the proportion of total variability in the result explained by heterogeneity, and not chance, and we considered arbitrarily $I^2 > 75\%$ to represent considerable heterogeneity (Higgins et al., 2003).

Meta-analytical positive predictive values (PPV; a subject/tooth not meeting an endpoint and experiencing tooth loss) and negative predictive values (NPV; a subject/tooth meeting the endpoint and not experiencing tooth loss) were estimated at the subject and tooth level using pooled sensitivity and specificity for tooth loss across studies. For the meta-analytical pooling of the sensitivity and specificity, the bivariate approach was used as an improvement and extension of the traditional summary receiver operating characteristic (sROC) approach (Reitsma et al., 2005; Rutter & Gatsonis, 2001) and the *mada* function in R (Doebler & Holling, 2015).

3 | RESULTS

3.1 | Study selection

The initial search generated 1682 articles from all databases combined, 9 from manual search and 1 via editorial contact (Figure 1).

Following screening of titles and abstracts, 230 articles qualified for full-text screening (Supplemental Material S2). The Cohen's kappa value for inter-reviewer agreement was 0.93 at first stage of screening and 0.92 at the second stage. Corresponding authors of the 62 articles considered potentially suitable for inclusion were contacted for confirmation that all requested data were available. IPD were available for nine studies (Barbe et al., 2020; Ciurescu et al., 2021; Collins et al., 2022; Cortellini et al., 2020; De Wet et al., 2018; Nibali et al., 2017, 2020; Saleh et al., 2021; Saydzai et al., 2022) and summaries of the requested data were made available via completed contingency tables for a further six studies (Aimetti et al., 2020; Baumer et al., 2020; Graetz et al., 2020; Jiao et al., 2017, 2018; Sonnenschein et al., 2017). There were no important issues in checking IPD integrity.

3.1.1 | Focused question 1

A total of 15 studies (Aimetti et al., 2020; Barbe et al., 2020; Baumer et al., 2020; Ciurescu et al., 2021; Collins et al., 2022; Cortellini et al., 2020; De Wet et al., 2018; Graetz et al., 2020; Jiao et al., 2017, 2018; Nibali et al., 2017; Nibali et al., 2020; Saleh et al., 2021; Saydzai et al., 2022; Sonnenschein et al., 2017) were included in the qualitative and quantitative analyses (Tables 1 and 2). They included 3 RCTs (both test and control groups were considered in the analyses), 10 cohort (1 prospective and 9 retrospective) and 2 cross-sectional studies.

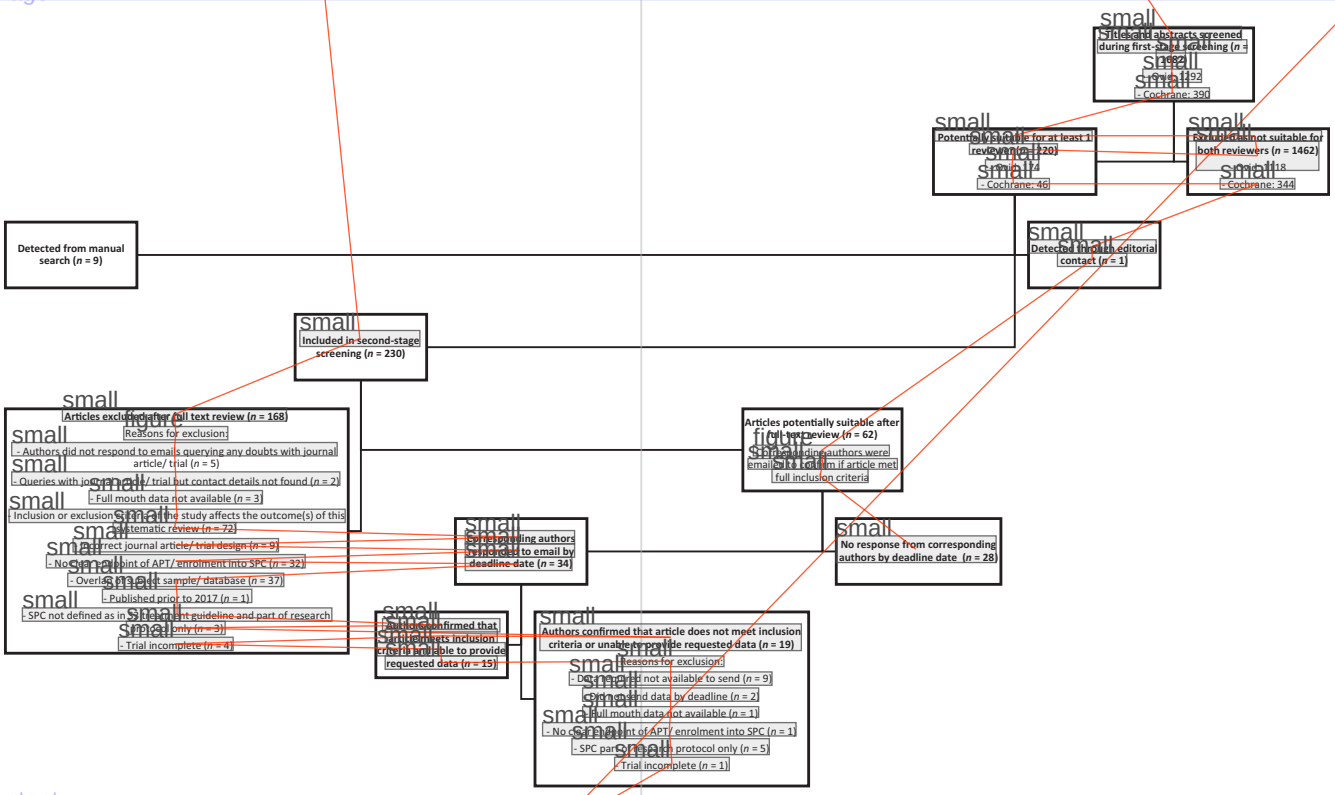

FIGURE 1 Flowchart detailing screening process. APT, active periodontal therapy; SPC, supportive periodontal care.

TABLE 2 Prevalence of reaching different endpoints at the start of supportive periodontal care at the subject and tooth level.

			'Stable periodontitis'—WWC 2017		'Endpoints of therapy'—EFP S3 treatment guidelines		'Controlled periodontitis' Prevalence of successfully meeting endpoint		PPD < 5 mm		PPD < 6 mm	
			Prevalence of successfully meeting endpoint		Prevalence of successfully meeting endpoint				Prevalence of successfully meeting endpoint		Prevalence of successfully meeting endpoint	
Author, year		Total	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Aimetti et al. (2020)	Subjects	21	5	23.81	17	80.95	8	38.10	11	52.38	21	100
	Teeth	403	309	76.67	394	97.77	N/A		384	95.29	403	100
Barbe et al. (2020)	Subjects	224	22	9.82	46	20.54	97	43.30	32	14.29	97	43.30
	Teeth	4685	3338	71.25	4010	85.59	N/A		3683	78.61	4276	91/27
Baumer et al. (2020)	Subjects	68	N/A		N/A		67	98.53	53	77.94	60	88.24
	Teeth	1658	N/A		N/A		N/A		1629	98.25	1644	99.16
Ciurescu et al. (2021)	Subjects	38	5	13.16	12	31.58	18	47.37	10	26.32	18	47.37
	Teeth	878	503	57.29	632	71.98	N/A		583	66.40	718	81.78
Collins et al. (2022)	Subjects	38	2	5.26	13	34.21	27	71.05	11	28.95	23	60.53
	Teeth	796	651	81.78	737	92.59	N/A		719	90.33	773	97.11
Cortellini et al. (2020)	Subjects	50	2	4	11	22	31	62	11	22	34	68
	Teeth	1233	1012	82.08	1133	91.89	N/A		1111	90.11	1205	97.73
De Wet et al. (2018)	Subjects	54	0	0	3	5.56	10	18.52	1	1.85	12	22.22
	Teeth	1362	885	64.98	1114	81.79	N/A		1002	73.57	1207	88.62
Graetz et al. (2020)	Subjects	50	3	6	11	22	30	60	6	12	18	36
	Teeth	1178	937	79.54	1068	90.66	N/A		1022	86.76	1114	94.57
Jiao et al., 2017	Subjects	10,789	94	0.87	1136	10.53	3747	34.73	615	5.70	3252	30.14
	Teeth	271,085	147,939	54.57	200,287	73.88	N/A		185,887	68.57	238,168	87.86
Jiao et al. (2018)	Subjects	1004	1	0.10	32	3.19	143	14.24	16	1.59	129	12.85
	Teeth	25,805	10,125	39.24	15,167	58.78	N/A		13,767	53.35	19,707	76.37
Nibali et al. (2017)	Subjects	98	11	11.22	31	31.63	67	68.37	23	23.47	61	62.24
	Teeth	2510	2132	84.94	2351	93.67	N/A		2251	89.68	2428	96.73
Nibali et al. (2020)	Subjects	63	N/A		N/A		21	33.33	5	7.94	17	26.98
	Teeth	1687	N/A		N/A		N/A		1187	70.36	1400	82.99
Saleh et al. (2021)	Subjects	166	N/A		N/A		44	26.51	17	10.24	57	34.34
	Teeth	4309	N/A		N/A		N/A		3143	72.94	3736	86.70
Saydzai et al. (2022)	Subjects	197	24	12.18	70	35.53	143	72.59	44	22.34	106	53.81
	Teeth	5028	4424	87.99	4761	94.69	N/A		4589	91.27	4874	96.94
Sonnenschein et al. (2017)	Subjects	24	N/A		N/A		7	29.17	8	33.33	18	75
	Teeth	494	N/A		N/A		N/A		444	89.88	472	95.55
Totals												
All studies[a]	Subjects	12,884	169	1.35	1382	11.00	4460	34.62	863	6.70	3923	30.45
	Teeth	323,111	172,255	54.69	231,654	73.55	N/A		221,401	68.52	282,125	87.32
Sub-analysis of studies following conventional APT[b]	Subjects	1053	69	9.43	202	27.60	552	52.42	222	21.08	524	49.76
	Teeth	25,343	13,688	79.60	15,568	90.54	N/A		21,164	83.51	23,532	92.85

Abbreviations: EFP, European Federation of Periodontology; N/A, not applicable; PPD, probing pocket depth; WWC, World Workshop Classification.
[a]From all studies, 12,563 subjects and 314,963 teeth have complete site-level data.
[b]In studies following conventional active periodontal therapy (APT), 732 subjects and 17,185 teeth have complete site-level data.

The publication year ranged from 2017 to 2022. Eleven studies were undertaken in Europe, two in China and one each in the Dominican Republic and United States. Eight studies were based in university hospitals and seven studies in private practice. A total of 12,884 subjects were included. Of these, 12,563 subjects from 11 studies had complete site-level data (inclusive of BoP). Three

TABLE 3 Statistical analyses of different endpoints in relation to tooth loss (TL) at the subject and tooth level.

		All studies					Sub-analysis of studies following conventional APT				
		'Stable periodontitis'—WWC 2017 (Chapple et al., 2018)	'Endpoints of therapy'—EFP's S3 treatment guideline (Sanz et al., 2020)	'Controlled periodontitis' (Feres et al., 2020)	PPD < 5 mm	PPD < 6 mm	'Stable periodontitis'—WWC 2017 (Chapple et al., 2018)	'Endpoints of therapy'—EFP's S3 treatment guideline (Sanz et al., 2020)	'Controlled periodontitis' (Feres et al., 2020)	PPD < 5 mm	PPD < 6 mm
Subject-level	RR of TL (95% CI)	1.36 (0.88–2.12)	1.46 (0.92–2.32)	2.57 (1.50–4.42)	1.59 (1.11–2.26)	1.98 (1.19–3.52)	1.36 (0.74–2.50)	1.67 (0.70–3.96)	2.78 (1.45–5.33)	1.70 (1.13–2.58)	2.08 (0.99–4.39)
	p-Value	.1221	.0886	.0030*	.0160*	.0275*	.2072	.1762	.0068*	.0179*	.0523
	I^2 (%)	0	0	72	0	69	0	19	72	0	74
	τ^2	0	0	0.4553	0	0.4290	0	0.12	0.56	0	0.68
	No. of subjects included in meta-analysis	792	828	1190	1190	1169	324	428	749	749	728
	No. of subjects in SPC ≥ 5 years	869	869	1190	1190	1190	428	428	749	749	749
	Positive predictive value (PPV) (%)	20.6	8.8	5.1	10.0	5.1	20.6	8.7	5.1	10.0	5.1
	Negative predictive value (NPV) (%)	99.9	99.6	97.8	99.6	98.09	99.9	99.6	97.8	99.6	98.0
Tooth-level	RR of TL (95% CI)	**10.33 (5.15–20.73)**	**16.34 (5.17–51.63)**	N/A	**9.66 (5.34–17.48)**	**10.87 (4.93–23.99)**	**10.27 (3.73–28.32)**	**14.86 (2.37–93.16)**	N/A	**8.22 (4.34–15.56)**	**9.38 (3.53–24.90)**
	p-Value	<.0001*	.0010*	N/A	<.0001*	<.0001*	<.0001*	.0151*	N/A	<.0001*	.0007
	I^2 (%)	67	85	N/A	79	92	66	77.5	N/A	59	86
	τ^2	0.5852	1.6809	N/A	0.9808	1.8889	1.08	1.85	N/A	0.51	1.45
	No. of teeth included in meta-analysis	21,661	21,661	N/A	29,809	29,406	10,631	10,631	N/A	18,779	18,376
	No. of teeth overall	21,661	21,661	N/A	29,809	29,809	10,631	10,631	N/A	18,779	18,779
	PPV (%)	15.1	14.6	N/A	14.6	12.8	15.1	14.6	N/A	14.6	12.8
	NPV (%)	88.2	67.3	N/A	68.0	29.3	88.2	67.2	N/A	68.0	29.3

Note: Bold was used for figures that showed statistically significant associations.

Abbreviations: APT, active periodontal therapy; CI, confidence interval; EFP, European Federation of Periodontology; N/A, not applicable; PPD, probing pocket depth; RR, relative risk; SPC, supportive periodontal care; WWC, World Workshop Classification.

*Statistically significant association.

TABLE 4 Incidence of tooth loss (TL) related to different endpoints within a minimum duration of 5-years supportive periodontal care (SPC) (subject-level).

					World Workshop Classification (WWC) 2017—'Stable periodontitis'							EFP S3 treatment guidelines 'Endpoints of therapy'						
			Subjects who underwent ≥5 years SPC (*n*)		Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL		Prevalence of not successfully meeting endpoint (*n*)	Prevalence of not successfully meeting endpoint with TL			Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL		Prevalence of not successfully meeting endpoint	Prevalence of not successfully meeting endpoint with TL		
Author, year	Periodontitis-related TL [a]	non-specific TL [b]	Overall (*n*)	Had TL (*n*)		*n*	%		*n*	%			*n*	%		*n*	%	
Aimetti et al. (2020)	a		21	0	5	0	0	16	0	0		17	0	0	4	0	0	
Baumer et al. (2020)	a		68	9	N/A	N/A	N/A	N/A	N/A	N/A		N/A	N/A		N/A	N/A	N/A	
Cortellini et al. (2020)	a		50	12	2	0	0	48	12	25		11	0	0	39	12	30.77	
De Wet et al. (2018)	b		54	36	0	0	0	54	36	66.67		3	1	33.33	51	35	68.63	
Graetz et al. (2020)	b		50	25	3	1	33.33	47	24	51.06		13	4	36.36	39	21	53.85	
Jiao et al. (2017)	b		43	11	2	0	0	41	11	27.88		24	5	20.83	39	11	28.17	
Jiao et al. (2018)	b		23	9	0	0	0	23	9	39.13		2	0	0	21	9	42.86	
Nibali et al., 2019	b		98	36	11	3	27.27	87	27	31.03		36	9	29.03	67	21	31.34	
Nibali et al. (2020)	b		63	27	N/A	N/A	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	
Saleh et al. (2021)	a		166	75	N/A	N/A	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	
Saydzai et al. (2022)	a		155	14	18	0	0	137	14	10.22		58	1	1.72	97	13	13.40	
Sonnenschein et al. (2017)	b		24	7	N/A	N/A	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	
Totals																		
All studies			1190	360	41	4	9.76	828	238	28.74		157	20	12.74	712	222	31.18	
Sub-analysis of studies following conventional APT			749	235	39	4	11.76	389	113	29.05		131	15	11.45	297	102	34.34	
Sub-analysis of studies reporting periodontitis-related TL only			460	110	25	0	0	201	26	12.94		86	1	1.16	140	25	17.86	

(Continues)

TABLE 4 (Continued)

Author, year	Periodontitis-related TL[a], non-specific TL[b]	Subjects who underwent ≥5 years SPC (*n*)		'Controlled periodontitis'				PPD < 5 mm				Prevalence of not successfully meeting endpoint with TL	
		Overall (*n*)	Had TL (*n*)	Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL	Prevalence of not successfully meeting endpoint (*n*)	Prevalence of not successfully meeting endpoint with TL	Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL	Prevalence of not successfully meeting endpoint	Prevalence of not successfully meeting endpoint with TL		
				n	%	*n*	%		*n*	%		*n*	%
Aimetti et al. (2020)	a	21	0	8	0	13	0	11	0	0	10	0	0
Baumer et al. (2020)	a	68	9	67	11.94	1	100	53	6	11.32	15	3	20
Cortellini et al. (2020)	a	50	12	31	6.45	19	52.63	11	0	0	39	12	30.77
De Wet et al. (2018)	b	54	36	10	30	44	75	18	0	0	53	36	67.92
Graetz et al. (2020)	b	50	25	30	36.67	20	70	6	2	33.33	44	23	52.27
Jiao et al. (2017)	b	418	116	100	21	318	95	29.87	7	28.57	411	114	27.74
Jiao et al. (2018)	b	23	9	4	0	19	9	47.37	1	0	22	9	40.91
Nibali et al. (2017)	b	98	30	67	18	31	12	38.71	23	4	75	26	34.67
Nibali et al. (2020)	b	63	27	21	2	42	25	59.52	5	0	58	27	46.55
Saleh et al. (2021)	a	166	75	44	11	122	64	52.46	17	5	149	70	46.98
Saydzai et al. (2022)	a	155	14	110	5	45	9	20	3	0	120	14	11.67
Sonnenschein et al. (2017)	b	24	7	7	3	17	4	23.53	8	3	16	4	25
Totals													
All studies		1190	360	499	84	691	276	39.94	178	22	1012	338	33.40
Sub-analysis of studies following conventional APT		749	235	395	63	354	172	48.59	170	20	579	215	37.13
Sub-analysis of studies reporting periodontitis-related TL only		460	110	260	26	200	84	42	127	11	8.66	333	99	29.73

Author, year	Periodontitis-related TL[a], non-specific TL[b]	Subjects who underwent ≥5 years SPC (*n*)		PPD < 6 mm					
		Overall (*n*)	Had TL (*n*)	Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL		Prevalence of not successfully meeting endpoint	Prevalence of not successfully meeting endpoint with TL	
					n	%		*n*	%
Aimetti et al. (2020)	a	21	0	21	0	0	0	0	0
Baumer et al. (2020)	a	68	9	60	7	11.67	8	2	25
Cortellini et al. (2020)	a	50	12	34	1	2.94	16	11	68.75
De Wet et al. (2018)	b	54	36	12	9	75	42	27	64.29

TABLE 4 (Continued)

Author, year	Periodontitis-related TL[a], non-specific TL[b]	Subjects who underwent ≥5 years SPC (*n*)		PPD < 6 mm					
		Overall (*n*)	Had TL (*n*)	Prevalence of successfully meeting endpoint (*n*)	Prevalence of successfully meeting endpoint with TL		Prevalence of not successfully meeting endpoint	Prevalence of not successfully meeting endpoint with TL	
					n	%		*n*	%
Graetz et al. (2020)	b	50	25	18	11	61.11	32	14	43.75
Jiao et al. (2017)	b	418	116	85	15	17.65	333	101	30.33
Jiao et al. (2018)	b	23	9	6	1	16.67	17	8	47.06
Nibali et al. (2017)	b	98	30	61	17	27.87	37	13	35.14
Nibali et al. (2020)	b	63	27	17	2	11.76	46	25	54.35
Saleh et al. (2021)	a	166	75	57	17	29.32	109	58	53.21
Saydzai et al. (2022)	a	155	14	86	3	3.48	69	11	15.94
Sonnenschein et al. (2017)	b	24	7	18	3	16.67	6	4	66.67
Totals									
All studies		1190	360	475	86	18.11	715	274	38.32
Sub-analysis of studies following conventional APT		749	235	384	70	18.23	365	165	45.21
Sub-analysis of studies reporting periodontitis-related TL only		460	110	258	28	10.85	202	82	40.59

Abbreviations: APT, active periodontal therapy; EFP, European Federation of Periodontology; N/A, not applicable; PPD, probing pocket depth.

[a]highlights studies where periodontitis-related TL was reported.

[b]highlights studies where non-specific TL was reported.

studies did not follow conventional APT: one RCT (Ciurescu et al., 2021) included NSPT and laser only, and two retrospective cohort studies (Jiao et al., 2017, 2018) included only NSPT.

3.1.2 | Focused question 2

A total of 12 studies (Aimetti et al., 2020; Baumer et al., 2020; Cortellini et al., 2020; De Wet et al., 2018; Graetz et al., 2020; Jiao et al., 2017, 2018; Nibali et al., 2017, 2020; Saleh et al., 2021; Saydzai et al., 2022; Sonnenschein et al., 2017) including 1190 subjects had a minimum of 5 years of follow-up in SPC and were included in the qualitative and quantitative analyses (Tables 1, 3 and 4). Eight studies including 869 subjects had complete site-level data and so were used in the analyses assessing the relationships between 'stable periodontitis' and 'endpoints of therapy' and subsequent tooth loss. Ten studies followed conventional APT. Five studies reported on periodontitis-related tooth loss, and so this data were used when available. Studies without two arms (i.e., zero subjects or teeth when assessing tooth loss in relation to successfully or unsuccessfully reaching the endpoints) were subsequently not included in the corresponding meta-analyses when analysing the WWC 2017 (De Wet et al., 2018; Jiao et al., 2018) and PPD ≥ 6 mm (Aimetti et al., 2020).

3.1.3 | Prevalence of stable and successfully treated periodontitis subjects at the start of SPC

Table 2 and Supplemental Material S4 display the prevalence data of each of the 15 studies at the subject and tooth level for achieving the endpoints.

Subject-level data

Of 12,563 subjects who had complete site-level data, 1.35% ($n = 169$) fulfilled the criteria of 'stable periodontitis' and 11.00% ($n = 1382$) met the 'endpoints of therapy'. 'Controlled periodontitis' was achieved in 34.62% ($n = 4460$) of the 12,884 subjects, while PPD < 5 mm and PPD < 6 mm were achieved in 6.70% ($n = 863$) and 30.45% ($n = 3923$) of subjects, respectively. Achievement of endpoints varied greatly across studies. The prevalence of reaching each of the five subject-level endpoints increased when studies following conventional APT were analysed (9.43% fulfilled the criteria of 'stable periodontitis', 27.6% met the 'endpoints of therapy', 52.42% achieved 'controlled periodontitis', while 21.08% and 49.76% achieved PPD < 5 mm and PPD < 6 mm, respectively).

Tooth-level data

Of 323,111 teeth, 314,963 teeth had complete site-level data. A total of 54.69% and 73.55% of teeth met the composite measures described in 'stable periodontitis' and 'endpoints of therapy', respectively, and 68.52% and 87.32% of all included teeth had PPD < 5 mm and PPD < 6 mm, respectively. Maxillary molars achieved tooth-level endpoints least frequently (24.18% and 47.20%, respectively, for 'stable periodontitis' and 'endpoints of therapy'), closely followed by mandibular molars (Supplemental Material S5). As per WWC 2017, there were 11.36 and 11.51 'diseased' teeth per patient after APT among all 12,563 subjects and 12,394 'unstable' subjects, respectively. This reduced to 4.79 and 5.29 'diseased' teeth in all 732 subjects and 663 'unstable' subjects, respectively, from studies following conventional APT.

3.1.4 | Tooth loss at 5 years according to endpoints at the start of SPC

Figures 2 and 3 display subject- and tooth-level meta-analyses of not achieving the various endpoints and tooth loss. Table 3 outlines the statistical analyses.

Subject-level data

Table 4 shows that less than a third (30.25%) of all subjects lost their teeth during an average SPC period of 9.88 years. Unsuccessful achievement of 'controlled periodontitis' (RR = 2.57; $p = .0030$), PPD < 5 mm (RR = 1.59; $p = .0160$) and PPD < 6 mm (RR = 1.98; $p = .0275$) were associated with tooth loss (Figure 2). Unsuccessful attainment of 'stable periodontitis' ($p = .1221$) and 'endpoints of therapy' ($p = .0886$) failed to reach statistical significance for association with tooth loss. PPVs and NPVs of the five subject-level endpoints ranged between 5.1% ('controlled periodontitis' and PPD < 6 mm) and 20.6% ('stable periodontitis') and between 97.8% ('controlled periodontitis') and 99.9% ('stable periodontitis'), respectively (Table 3). Studies following conventional APT showed statistically significant associations for not achieving 'controlled periodontitis' (RR = 2.78, $p = .0068$) and PPD < 5 mm (RR = 1.70, $p = .0179$) over an average SPC period of 12.75 years (Supplemental Material S5). Supplemental Material S6 reports results relative to studies reporting periodontitis-related tooth loss. Heterogeneity in subject-level studies/analyses varied from unimportant to substantial but did not seem to affect the direction of effects but affected only the precision with which the summary effect was calculated. Contour-enhanced funnel plots showed small sample bias among all meta-analyses. Studies showing statistically significant results were most frequently found in analyses of 'controlled periodontitis' and 'PPD < 6 mm'.

Tooth-level data

Of 29,809 teeth in subjects who were in SPC during an average period of 9.88 years, 3.14% ($n = 936$) were extracted for all reasons (Supplemental Material S7). Non-achievement of all endpoints at the tooth level was statistically significant and associated with an increased risk of tooth loss (Figure 3) ('stable periodontitis' [RR = 10.33; $p < .0001$]; 'endpoints of therapy' [RR = 16.34; $p = .001$]; PPD < 5 mm [RR = 9.66; $p < .0001$]; PPD < 6 mm [RR = 10.87; $p < .0001$]). The results remained largely unchanged in sub-analyses of studies following conventional APT (Table 4; Supplemental Material S8) and those reporting periodontitis-related tooth loss (Supplemental Material S9).

PPVs and NPVs of the four tooth-level endpoints ranged between 12.8% (PPD < 6 mm) and 15.1% ('stable periodontitis') and

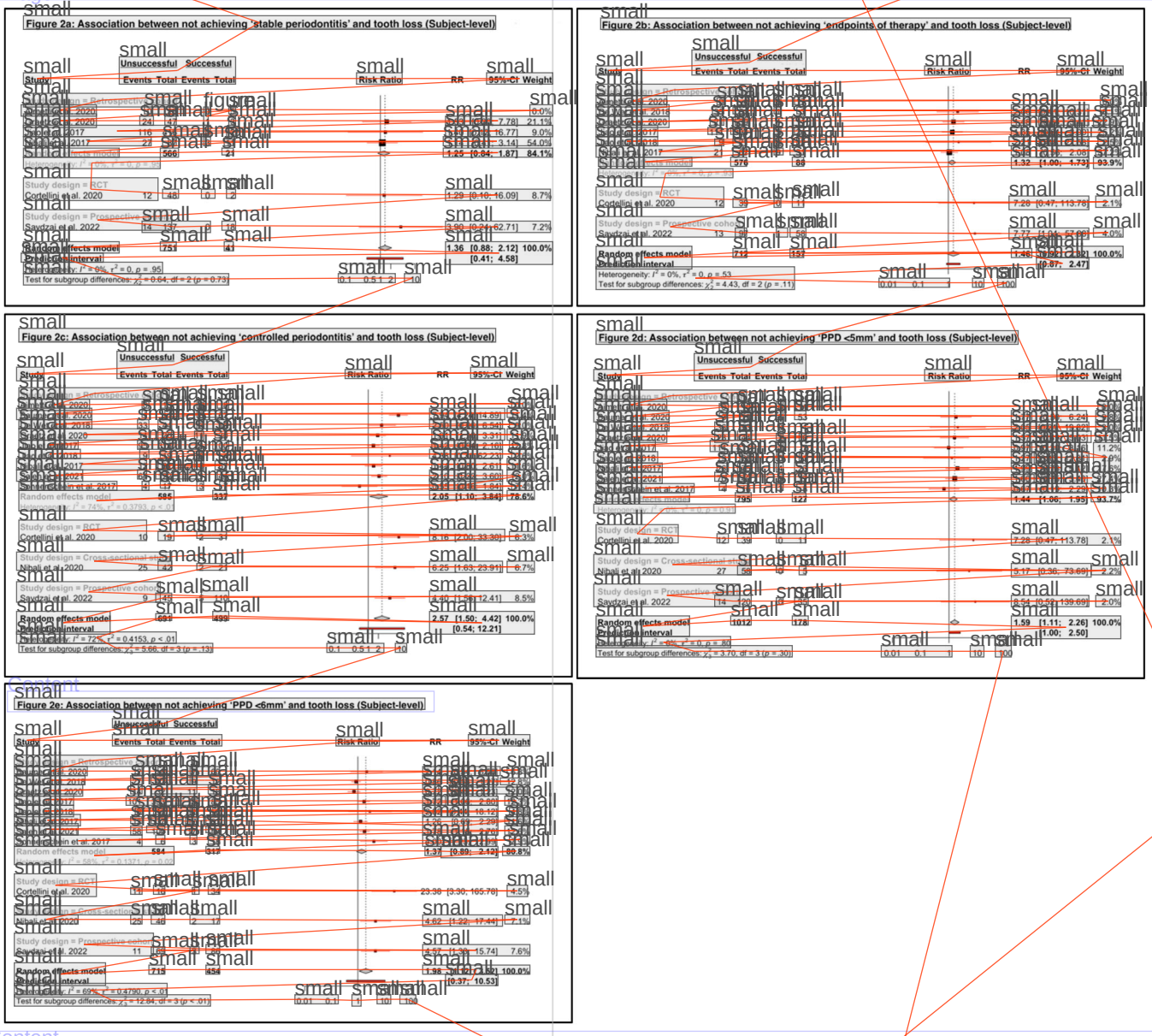

FIGURE 2 Meta-analyses of not achieving various endpoints and their association to tooth loss (subject level). CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.

between 29.3% ('PPD < 6 mm') and 88.2% ('stable periodontitis'), respectively (Table 3). The total number of teeth lost per patient per year of SPC was 0.08 (all studies: average of 9.88 SPC years) and 0.06 (conventional APT studies: average of 12.75 SPC years). Heterogeneity in the tooth-level studies/analyses varied from unimportant to considerably higher compared to the subject-level findings but did not affect the direction of effects (i.e., lack of periodontal stability led to tooth loss) and only affected the precision with which the summary effect was calculated.

3.2 | RoB assessment

Supplemental Material S10 reports the RoB assessments for RCTs, cohort and cross-sectional studies. RoB for cohort studies ranged from 5 to 6 stars, with the item 'comparability' always scored as 0. RCTs showed low RoB or some concerns due to missing data in follow-up studies.

4 | DISCUSSION

This systematic review confirms that very few periodontitis cases achieve the proposed endpoints following steps 1, 2 and 3 of periodontal therapy. In studies following conventional APT, 9.43% of subjects achieved 'stable periodontitis' and 27.6% achieved the desirable 'endpoints of therapy'. Our data showed that 54.2% of subjects achieved 'controlled periodontitis', coinciding with a multi-centre study where approximately 50% of the population was within the limits of 'controlled periodontitis' (Feres et al., 2020). The prevalence

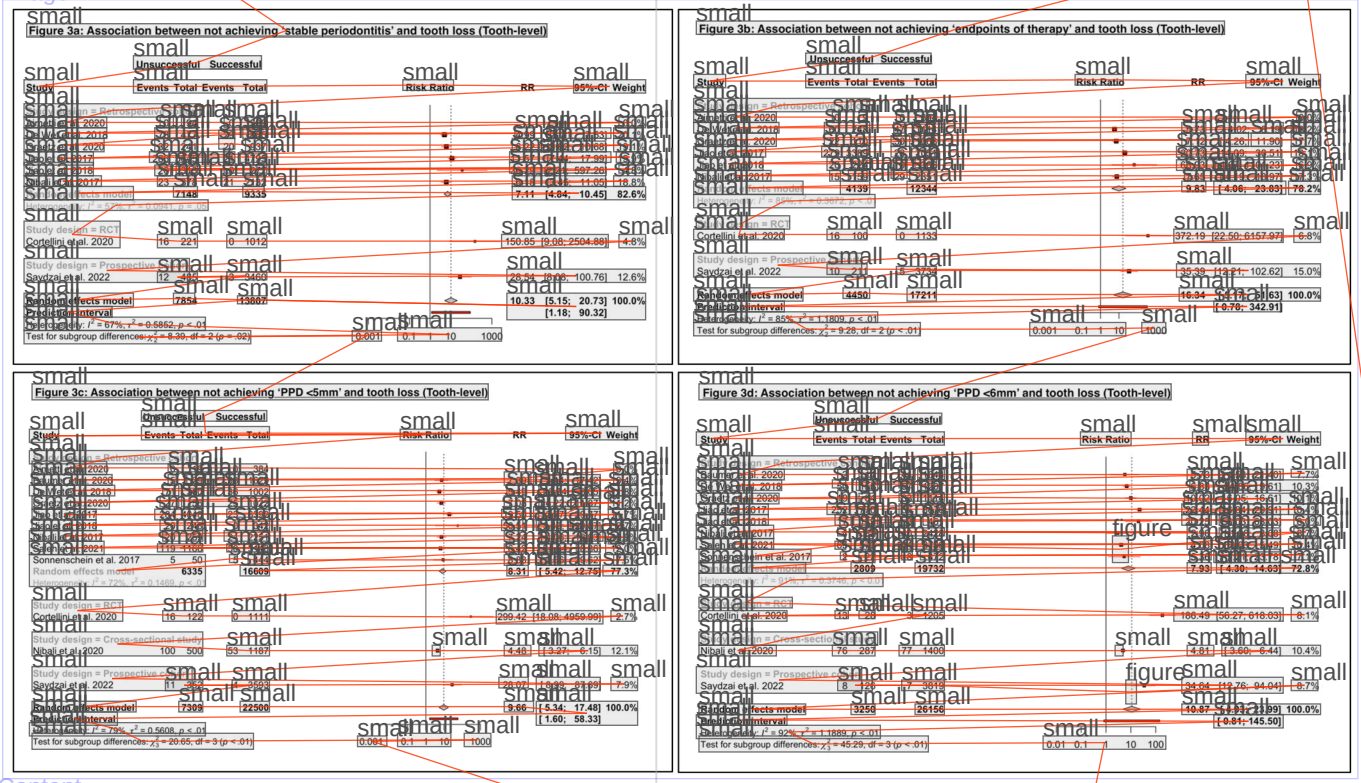

FIGURE 3 Meta-analyses of not achieving various endpoints and their association to tooth loss (tooth level). CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.

of achieving and sustaining these endpoints is likely to be reduced further with increased time of SPC (Bertl et al., 2022) and reduced operator experience (Fleischer et al., 1989). Therefore, the reality of successfully achieving or sustaining these endpoints in general dental practice is likely to be limited further.

An average of 11.36 teeth per patient were considered 'diseased' after APT. This result needs to be interpreted in light of the proven efficacy of steps 1 and 2 of periodontal therapy, which show an overall proportion of 74% of 'pocket closure' (PPD ≤ 4 mm and an absence of BoP; Suvan et al., 2020), bearing in mind that the efficiency of NSPT is reduced in areas of difficult access, such as furcations or deep pockets (Caffesse et al., 1986; Fleischer et al., 1989; Tomasi et al., 2007).

Analysing long-term outcomes showed that 29.05% of 'unstable' subjects, as per WWC 2017 and following conventional APT, experienced tooth loss during a mean observation period of 12.75 years. Yet, only 8.49% of teeth responsible for an 'unstable' diagnosis were extracted. The lack of a statistically significant association of tooth loss at the subject level (RR = 1.36; $p = .2072$) within this data supports that an 'unstable' periodontitis subject does not increase the risk for periodontitis-related tooth loss among subjects strongly compliant with SPC (Bertl et al., 2022). Consideration of this endpoint may be important when planning treatment at the tooth level, for example, utilising a 'stable' abutment tooth where our data highlight an RR = 10.27 for tooth loss if the tooth is 'unstable'.

Although approximately one third (34.34%) of the subjects not meeting the 'endpoints of therapy' lost teeth during SPC after conventional APT, similarly, statistical significance was reached only at the tooth level (RR = 14.86; $p = .0151$). This may be due to BoP, a variable of these composite endpoints, which has been found to be a useful predictor of periodontal progression and subsequent tooth loss only at the tooth level (Claffey & Egelberg, 1995; Matuliene et al., 2008). Yet, the effect of smoking on masking the predictive ability of BoP cannot be excluded (Bergström & Boström, 2001). Less than 20% of subjects within this dataset were current smokers.

'Controlled periodontitis' was the most frequently achieved endpoint (52.42%) among studies following conventional APT. At the subject level, it has an RR of 2.78 ($p = .0068$) of tooth loss during SPC when not achieved, which is similar to the findings reported elsewhere (Siow et al., 2022). Unlike other subject-level endpoints, this endpoint considers multiple residual sites, which is relevant, as subject- and tooth-level factors can affect the treatment response, particularly in relation to specific tooth types (Tomasi et al., 2007). All endpoints showed low PPVs and high NPVs at the subject level, supporting existing literature (Saydzai et al., 2022).

The number of teeth lost per subject per year of SPC varied between 0.06 and 0.08, corroborating that a small number of teeth are lost in a small proportion of the population (Hirschfeld & Wasserman, 1978; McFall, 1982; Needleman et al., 2018; Nibali et al., 2017). Optimal adherence to long-term SPC has been shown to

effectively reduce the progression of periodontitis and tooth loss, particularly in private practice and university-based hospitals (Axelsson & Lindhe, 1981; Chambrone et al., 2010; Leow et al., 2022). This is supported by our data at the subject and tooth level, respectively, where the highest incidence of tooth loss was reported in studies where <10% of subjects adhered to the recommended SPC regime (De Wet et al., 2018) and where SPC regimes were executed by the subjects' general dental practices (Nibali et al., 2020). With maxillary molar teeth being the most frequently lost teeth within SPC, this raises the question whether endpoints should be individualized to the tooth type, as their complex anatomy may affect 'pocket closure' (Tomasi et al., 2007).

This systematic review has many strengths including analyses of very large amount of clinical data from several settings and countries reflecting global periodontal practices, which increases its external validity and power. Limitations are evident, such as potential selection bias due to exclusion of studies, cases with no available data and restriction to studies published from 2017. Most included studies were retrospective cohort studies. Information and residual confounding bias cannot be excluded because of the unavailability of some of the required data. Multi-level and meta-regression analyses were not performed, as not all required data were available. Therefore, the low tooth loss rate may not be generalizable for all periodontitis patients. Including different stages of periodontitis and APT protocols may affect the discriminative power of the study. Study selection was limited to those published after 2017, as they better reflect current practice globally, particularly since official endpoints were proposed by the WWC 2017. IPD analyses are resource-intensive and we felt a 5-year restriction, which still included 12,884 subjects, would be pragmatic.

Further research is required to assess the different endpoints and their accuracy when predicting tooth loss, oral-health-related quality of life and the systemic impact of periodontitis, which collectively form the true endpoints of periodontitis.

Overall, the data collected from 12,884 periodontitis subjects and presented here demonstrate the following:

- An overwhelming majority of subjects and teeth do not successfully achieve 'stability' or meet the recommended 'endpoints of therapy' of current guidelines following APT. This suggests that either periodontal treatment still has a long way to go before being considered efficacious or the currently proposed endpoints are not realistic. We, with a certain degree of optimism based on the relatively low tooth loss during SPC, would like to believe in the latter.
- Certain surrogate endpoints may be more relevant at the tooth level than at the subject level. Endpoints should be specific to the tooth type if more personalised treatment approaches are required.
- The present findings apply to patients compliant with SPC. Yet, non-compliant patients represent a major proportion of treated patients. The generalisability of the results may depend on the extent, stage and grade of periodontitis.

Periodontally involved teeth can be well maintained when compliant with SPC. Rethinking endpoint selection may resolve any controversy surrounding periodontal treatment efficacy, particularly in relation to 5-year tooth survival rates, and prevent unnecessary overtreatment. Furthermore, as healthcare moves towards personalised medicine and the paradigm surrounding pathogenesis of periodontitis has shifted to consider the individual's host immune–inflammatory response, it may be justified to consider individualized endpoints acknowledging the patients' demographic, systemic and lifestyle factors.

AUTHOR CONTRIBUTIONS

L. Nibali conceived this systematic review. L. Nibali and V. Rattu wrote the review protocol and D. Raindi provided revisions. V. Rattu created the search strategy. V. Rattu and D. Raindi performed the literature search. D. Raindi performed the RoB assessments, which were reviewed by V. Rattu. V. Rattu extracted the data and this was reviewed by D. Raindi. The meta-analyses were performed by G. Antonoglou. V. Rattu prepared the draft manuscript, which was reviewed and edited by D. Raindi, G. Antonoglou and L. Nibali. L. Nibali supervised, reviewed and provided commentary or revisions at each stage.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the tables, figures and supplemental material of this article. The individual patient data from studies cannot be made available without permission from the corresponding authors. Contour enhanced funnel plots can be made available upon request.

ETHICS STATEMENT

We ensure that all research is conducted in accordance with ethical principles.

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