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REVIEW ARTICLE

Clinical outcomes of peri-implantitis treatment and supportive care: A systematic review

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Abstract

Objectives: To report the clinical outcomes for patients with implants treated for peri-implantitis who subsequently received supportive care (supportive peri-implant/ periodontal therapy) for at least 3 years.

Material and methods: A systematic search of multiple electronic databases, grey literature and hand searching, without language restriction, to identify studies including ≥10 patients was constructed. Data and risk of bias were explored gualitatively. Estimated cumulative survival at the implant- and patient-level was pooled with random-effects meta-analysis and explored for publication bias (funnel plot) at different time intervals.

Results: The search identified 5,761 studies. Of 83 records selected during screening, 65 were excluded through independent review (kappa = 0.94), with 18 retained for qualitative and 13 of those for quantitative assessments. On average, studies included 26 patients (median, IQR 21-32), with 36 implants (median, IQR 26-45). Study designs (case definitions of peri-implantitis, peri-implantitis treatment, supportive care) and population characteristics (patient, implant and prosthesis characteristics) varied markedly. Data extraction was affected by reduced reporting quality, but over 75% of studies had low risk of bias. Implant survival was 81.73%-100% at 3 years (seven studies), 74.09%-100% at 4 years (three studies), 76.03%-100% at 5 years (four studies) and 69.63%-98.72% at 7 years (two studies). Success and recurrence definitions were reported in five and two studies respectively, were heterogeneous, and those outcomes were unable to be explored quantitatively.

Conclusion: Therapy of peri-implantitis followed by regular supportive care resulted in high patient- and implant-level survival in the medium to long term. Favourable results were reported, with clinical improvements and stable peri-implant bone levels in the majority of patients.

KEYWORDS

dental implants, dental restoration failure, long-term care, meta-analysis, peri-implantitis, periodontal maintenance, supportive periodontal therapy, surgical treatment, survival, systematic review

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1 | INTRODUCTION

Peri-implantitis is defined as the presence of inflammation in the soft tissues in addition to loss of supporting bone around an osseointegrated implant (Lindhe & Meyle, 2008). Controversy regarding the global prevalence of peri-implantitis exists largely due to the wide range of case definitions used across studies (Salvi, Cosgarea & Sculean, 2017). Nevertheless, it is recognized that peri-implantitis is not an uncommon finding. A recent cross-sectional study identified patients from the Swedish implant register (n > 24,716) who had implants in situ for 9 years and assessed the prevalence of moderate to severe peri-implantitis to be 15% (Case definition: bleeding on probing (BOP), suppuration and >2 mm of peri-implant bone loss) in 596 patients who attended a clinical examination out of 900 invitees (Derks et al., 2016); and a recent systematic review estimated a prevalence of 22% (Derks & Tomasi, 2015) across 11 studies.

Furthermore, there is general concern that the incidence of periimplantitis may increase as more implants are being placed by a greater number of clinicians with varying expertise. Therefore, as highlighted in the 11th European Workshop for Periodontology (Tonetti, Chapple, Jepsen & Sanz, 2015), there is a need for research to identify effective protocols for prevention and treatment of peri-implantitis. In addition, evaluation of effective supportive care protocols to maintain peri-implant tissue health once peri-implantitis is treated is also required.

Heitz-Mayfield and Mombelli (2014) in 2014 investigated periimplantitis treatment success at 12 months in a systematic review of seven studies, concluding that whilst favourable short-term outcomes were reported in the majority of patients; nonresolution, progression or recurrence could also occur.

Numerous peri-implantitis treatment protocols with clinical efficacy have been documented, including nonsurgical, surgical, resective, regenerative and combined approaches. However, the most effective management protocol across the general population or in specific patient groups has not been identified (Chan, Lin, Suarez, MacEachern & Wang, 2014; Daugela, Cicciu & Saulacic, 2016; Esposito, Grusovin & Worthington, 2012b; Heitz-Mayfield & Mombelli, 2014; Khoshkam et al., 2013, 2016; Mahato, Wu & Wang, 2016; Renvert, Polyzois & Rutger Persson, 2013; Suarez-Lopez Del Amo, Yu & Wang, 2016). It is likely that heterogeneity related to study design, patient characteristics, defect characteristics, implant design, prosthesis design, operator experience, clinical protocols, outcome measures and disease definitions have complicated data assessment. In addition, length of follow-up is a significant confounding factor, with Esposito and coworkers finding that recurrence of peri-implantitis occurred in up to 100% of cases in some of the study environments (Esposito et al., 2012b). In contrast, Renvert and coworkers found that stable clinical results could be achieved up to 5 years after initial therapy but highlighted that adequate oral cleanliness across this period appeared to be an essential prerequisite (Renvert et al., 2013).

Authors agree that extended follow-up periods are required to allow adequate assessment of stable treatment outcomes over time (Heitz-Mayfield & Mombelli, 2014; Khoshkam et al., 2016; Mahato et al., 2016). The role of supportive periodontal therapy (SPT) in stabilizing periodontal disease over the long term has been accepted for many years (Lindhe & Nyman, 1984; Matuliene et al., 2008), with recent evidence also concluding that "erratic" SPT attendees had a significantly higher risk of tooth loss compared with those who attended regularly (Lee, Huang, Sun & Karimbux, 2015). Regarding peri-implant outcomes and supportive therapy, Monje and coworkers investigated outcomes across 13 studies, finding that less frequent supportive care was correlated with an increased incidence of peri-implantitis at the implant level. However, this finding was confounded by whether there was a history of periodontal disease (Monje et al., 2016).

It is hypothesized that over the long term, supportive care influences the outcome of implants in general and those that have been treated for peri-implant disease specifically.

The aim of this systematic review was to explore the question: In patients with osseointegrated dental implants, who were enrolled in supportive peri-implant/periodontal therapy (SPT) for at least 3 years, following treatment for peri-implantitis, what proportion of patients and implants is estimated to experience success, survival or peri-implantitis recurrence?

2 | MATERIALS AND METHODS

The focus question, PICO, search design and selection process are outlined in Tables 1 and 2 and are summarized below. The proposed methods were registered with PROSPERO (CRD42017071602), and reporting has been guided by PRISMA. The search was completed in April 2017. Multiple electronic databases (MEDLINE (Ovid), Embase (Ovid), The Cochrane Library, Nonindexed OVID citations), grey literature (conference proceedings, expert contact, study registers), reference lists (included articles, relevant reviews) and selected journals were scrutinized systematically, without language restriction to identify relevant data for independent review. Dedicated electronic search strategies combined textwords, indexing terms (MESH or EMTREE), multipurpose fields, adjacency operators, truncations and Boolean operators.

Selection criteria were broad during identification and screening to decrease search specificity (low agreement between investigators anticipated, decreased risk of omitting relevant articles) and specific during inclusion to increase search precision (high agreement between investigators anticipated, relevant articles included). Clinical investigations where at least 10 participants with osseointegrated implants that required treatment for peri-implantitis and who were subsequently enrolled in a SPT for at least 3 years were included. Review articles were excluded.

The primary outcome was survival at the patient and implant level. Secondary outcomes were success, peri-implantitis recurrence, and implant loss at the patient and implant level. To report those outcomes, number of patients and implants in each category were extracted at 3 years, and other time intervals if reported. Outcome definitions were:

TABLE 1 Search strategy and selection criteria

Focus question	In patients with osseointegrated dental implants who have been enrolled in a supportive periodontal/peri-implant programme (SPT) for at least 3 years following treatment of peri-implan- titis, what is the implant failure rate or recur- rence of peri-implantitis?
Population	Patients with osseointegrated dental implants that were diagnosed with and received treatment by investigators for peri-implantitis
Intervention	Enrolment in SPT for a minimum of 3 years following treatment for peri-implantitis
Comparison	Nil
Outcome	Implant loss for any reason (failure), recurrence of peri-implantitis
Language	No restriction
Search date	Completed in April 2017
PROSPERO	CRD42017071602 registration number
Database search	n, No language restriction
Databases	MEDLINE (Ovid), Embase, Nonindexed citations (Ovid), The Cochrane Library. See further details in Table 2
Supplementary	hand search
Journals (Jan	Clinical Oral Implants Research
2015—April 2017)	International Journal of Oral and Maxillofacial Implants
	Clinical Implant Dentistry and Related Research
	International Journal of Prosthodontics
	Journal of Prosthetic Dentistry
	Journal of Periodontology
	Journal of Clinical Periodontology
References	Included articles and identified reviews
Grey literature	search
Conference	EAO, 2016
proceedings	EuroPerio, 2015
	Perio Master Clinic, European Federation of Periodontology, 2017
	ITI World Symposium, Basel 2017
	American Academy of Periodontology, 2016, 2017
	Academy of Osseointegration 2017
	Osteology Australasia 2017
Contact with experts	Authors of included articles; researchers with a known interest in peri-implantitis research
Study registers	Australia & New Zealand (ANZCTR, http://www. anzctr.org.au)
	China (ChiCTR, http://www.chictr.org.cn)
	EU (EU-CTR, https://www.clinicaltrialsregister.eu) Germany (DRKS, http://www.drks.de)
	UK (ISRCTN, http://www.isrctn.com)
	USA (ClinicalTrials.gov)
	Search terms: periimplantitis, peri-implantitis or peri-implantitis identified 79 studies, with 2 potentially relevant investigations

(Continues)

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TABLE 1	(Continued)
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Selection proces	55
Inclusion criteria	Clinical investigations of any study design related to the focus question
	Minimum 10 patients followed for at least 3 years
	Must specify: number of participants, number of implants, follow-up duration, number of failures, definition for peri-implantitis
Contact with authors	Research potentially met the inclusion criteria, but full-text article was unavailable
	Research potentially met the inclusion criteria, but data reporting was incomplete or unclear
	Research identified through grey literature search
Exclusion	Topic not relevant to the focus question
criteria	Reviews
	In vitro study
	Animal study
	Insufficient patient numbers
	Insufficient follow-up
	Insufficient participant information, and no response from investigators when seeking clarification
	Previous investigations reporting on the same patient population (excluded, but retained for reference)
Identification process	Records were reviewed by at least two investiga- tors independently, disagreements were resolved by discussion, and authors were contacted for clarification when required
	Records in languages other than English that potentially fulfilled inclusion criteria were translated initially by the investigators, colleagues or "Google Translator." No investiga- tions met the inclusion criteria, and therefore no formal translations were completed

- Survival—implant presence, regardless of the health of the surrounding tissues.
- Success-if defined by the authors.
- Peri-implantitis recurrence-if defined by the authors.
- Implant loss—implants that were removed for any reason, including those unrelated to peri-implantitis.

The data extraction form, risk of bias assessment form and explanatory instructions were drafted, trialled (two investigators) modified (two investigators) and completed (in duplicate, independently). Discrepancies were resolved by discussion, with authors also contacted to seek additional information.

Data extraction included the methodology, participant demographics, implant details, author's outcome definitions, periimplantitis treatment method, SPT method, primary outcomes, secondary outcomes and other unexpected outcomes that could be of interest. WII FV— CLINICAL ORAL IMPLANTS RESEARCH

TAE	BLE	2	Electronic	database	search	strategies
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Databases	Search strategy	Description
MEDLINE (Ovid)	(peri-implant adj3 disease*).mp or (peri-implant adj3 infection*).mp or implantitis.mp or ((Dental implants. mp and (bone loss*).mp)) or ((Dental implants.mp and (suppurat*).mp))	The multipurpose (.mp) field was used to search words used by authors in the title, original title and abstract as well as indexing terms allocated to the bibliometric record. OVID operators "OR", "AND" and "ADJ" allowed terms to be combined exclusively (AND), inclusively (OR) or specifically (ADJ3: retrieving records where terms were within 3 words of each other). For example, "Peri-implant adj3 disease*" retrieves both "peri-implant disease" and "Diseases of the peri-implant tissues"
MEDLINE(R) Epub Ahead of Print, In-Process & Other NonIndexed Citations and Ovid MEDLINE(R) (Ovid)	((peri-implant adj3 disease*) or (peri-implant adj3 infection*) or implantitis or ((Dental adj3 implants) and (bone adj3 loss*)) or ((Dental adj3 implants) and suppurat*)).mp	Nonindexed records were searched with the search philosophy outlined for MEDLINE (Ovid). The search differs, because the records are not yet indexed with MeSH terms. However, the ".mp" field was used to structure the search as it also identifies data in textword fields
Embase (Ovid)	((peri-implant adj3 disease*) or (peri-implant adj3 infection*) or implantitis or ((Dental adj3 implants) and (bone adj3 loss*)) or ((Dental adj3 implants) and suppurat*)).mp. or (Tooth implants.sh. and bone loss*.mp.) or (Tooth implants.sh. and suppurat*.mp.)	Embase records were searched with the search philosophy outlined for MEDLINE (Ovid). However, MeSH and EMTREE terms differed for implant subject headings and the MeSH term "Dental implant" was substituted for the EMTREE term "Tooth implant"
The Cochrane Library	(peri implant disease:ti,ab,kw) OR (peri implant infection*:ti,ab,kw) OR (implantitis:ti,ab,kw) OR (bone loss*:ti,ab,kw and dental implants:ti,ab,kw) OR (suppurat*:ti,ab,kw and dental implants:ti,ab,kw)	Cochrane fields of ".ti", ".ab" and ".kw" were used to search the title, abstract and index term for the Cochrane Library

Note. mp (multipurpose field: title, original title, abstract, subject heading, name of substance, and registry word fields); adj3 (adjacency operator: retrieves records where terms are within 3 words of each other); * (truncation operator); sh (MeSH subject heading field), ab (abstract field), ti (title field), kw (keyword field).

Risk of bias was assessed on a modified Newcastle–Ottawa Scale (NOS). The criteria were customized for number of study groups (one or multiple) and assessment of subjective outcomes specific to this review (peri-implant probing, radiograph assessment, peri-implantitis recurrence definition and failure definition) (Table 3). The impact of potential bias on outcomes was explored qualitatively.

2.1 | Statistics and data presentation

Research details were tabulated and discussed qualitatively. Where available, implant- and patient-level survival and success across 3, 4, 5 and 7 years was tallied. The number of implants and patients at the study inception, and those that became lost to follow-up, failed or experienced recurrence were tallied to calculate survival and success. Those lost to follow-up were assumed to occur randomly across time (nonsystematic), with life-table analysis and Greenwood's formula used to calculate the estimated cumulative survival (ECSurv), estimated cumulative success (ECSucc) and 95% confidence interval (CI). Confidence intervals that extended beyond 100% were truncated.

Data was weighted and pooled with meta-analysis (Stata 11.2, StataCorp) where appropriate. Heterogeneity was assessed with Cochran's Q (p < 0.1 indicated reduced homogeneity) and *I*-squared (variation in summary estimate that may be attributable to heterogeneity). Fixed or random-effects (if there was reduced statistical homogeneity) meta-analysis was used to calculate the pooled summary estimate and 95% CI. A funnel plot investigated

whether publication or other small-study biases may have been present.

3 | RESULTS

3.1 | Systematic search

The systematic search flow is outlined in Figure 1. Of 5,754 studies from multiple electronic databases, six studies from grey literature searches and one study from hand searching were screened (total n = 5,761). Eighty-three records were identified as potentially relevant during screening, 65 records were excluded through independent full-text review (Kappa = 0.94). All corresponding researchers were contacted to request clarification or further information. Four records were excluded as double-data, with the most relevant data retained for analysis (Froum, Rosen, Wang, Froum & Vinayak, 2018; Romeo, Lops, Chiapasco, Ghisolfi & Vogel, 2007; Roos-Jansåker, Lindahl, Persson & Renvert, 2011; Schwarz, Hegewald, John, Sahm & Becker, 2013). Eighteen studies were included in qualitative assessments, with 13 in quantitative assessments. Additional records were consulted if data had been presented in related publications, and these are listed in Table 4.

A single investigator identified records from multiple electronic databases, sought grey literature and completed the hand search. Two independent investigators completed screening (Kappa = 0.25, low agreement as anticipated, reflecting the wide variety of

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potentially relevant articles gathered) and eligibility assessments (Kappa = 0.94, high agreement).

3.2 | Qualitative assessment

3.2.1 | Study characteristics

Table 4 describes the main features of the individual studies including: study design and setting; population characteristics; periimplantitis case definition; peri-implantitis treatment provided; and supportive care during follow-up. The majority of studies (n = 15) were small convenience samples (range 16–38 participants, 19–86 implants) of patients referred for peri-implantitis treatment. One study followed 100 participants with 179 implants (Carcuac et al., 2017), and two studies followed 100 (Froum, Froum & Rosen, 2015) and 245 participants (Charalampakis, Rabe, Leonhardt & Dahlen, 2011) respectively, but it was unclear how many were followed for at least 3 years. Average participant age ranged between 44.9 and 66.3 years, with age ranges also reported from 22 to 87 years.

Studies were prospective (n = 16) and retrospective (n = 2), followed one participant group (n = 11) or multiple participant groups (n = 7), and were completed in University (n = 9), private practice (n = 6) and combined environment (n = 3).

3.2.2 | Outcomes

Studies reported outcomes of implant success (n = 5, Table 5), survival (n = 13, Figures 2 and 3) and disease recurrence (n = 2) at the implant-level, patient-level or both. No studies evaluated patient-reported outcomes.

3.2.3 | Methodological Heterogeneity

Peri-implantitis definitions, peri-implantitis treatment protocols, success definitions and recurrence definitions varied considerably between groups, contributing to marked methodological heterogeneity between studies. However, participants were treated equally within studies and within study groups, reducing heterogeneity within the data. The between-study variations impact on how results are interpreted, inter-related and translated into practice.

Across the studies, all peri-implantitis case definitions included the presence of clinical signs of inflammation and bone loss, but the thresholds defined for bone loss and probing depths were heterogeneous.

Peri-implantitis treatment protocols differed across all categories: pretreatment phase; surgical approach (i.e., resective, regenerative, combination); implant surface decontamination method; biomaterials used; adjunctive treatment (e.g., soft tissue grafting); and peri-operative antimicrobials.

Definitions for success were reported by five studies and varied markedly (Table 5). For this reason, it was not possible to assess implant- and patient-level success quantitatively. Studies with strict definition generally reported lower success figures, but studies with less strict definitions did not necessarily achieve better outcomes. The ECSucc calculated from the data reported in each study for "successfully" treated implants ranged from 34% to 57% (at 3 years), 71% to 75% (at 5 years) and 7% to 41% (at 7 years) across studies. However, at these time points, the majority of implants survived, and remained in situ (Figure 2).

Disease "recurrence" was described in two of the 18 papers (Heitz-Mayfield et al., 2016; Serino, Turri & Lang, 2015). Heitz-Mayfield and coworkers defined recurrence of disease where implants required additional treatment (i.e., with PD > 5 mm with concomitant BoP or suppuration and/or continued bone loss), which occurred in 12% (three of 24 patients) at 5 years. Serino and coworkers reported that none of the implants (86 patients) which obtained healthy peri-implant tissues following treatment had recurrence of disease, which was described as increased probing depth (Serino et al., 2015).

3.2.4 | Supportive care protocols

Few studies provided detailed information about the supportive care regimen during follow-up, while some described the recall frequency; operator; instrumentation; and individual risk analysis performed. One study used soft tissue grafting during supportive care to augment keratinized peri-implant mucosa for some patients (Roccuzzo, Pittoni, Roccuzzo, Charrier & Dalmasso, 2017). No studies compared supportive care protocols.

3.2.5 | Factors influencing treatment outcome

Two studies reported treatment success for different implant surfaces (Carcuac et al., 2017; Roccuzzo et al., 2017; Table 5). In one study implants with a rough titanium plasma-sprayed surface (TPS) had lower success at 7 years than implants with a moderately rough surface (sandblasted large-grit acid etched [SLA]), but similar survival (Roccuzzo et al., 2017). In the second study implants with modified implant surfaces had lower success at 3 years compared to implants with a nonmodified surface (Carcuac et al., 2017).

3.2.6 | Risk of bias assessment

The 18 included studies were assessed for methodological risks that may impact on the results (Figure 4). The NOS was modified to apply to both multiple and single group studies. Ten studies reported on a single patient group and eight reported on multiple patient groups.

Fourteen of the studies (78%) met over 80% of the criteria and were considered to have low risk of bias. All studies included participants in a manner that reduced risk of bias (Domain 1: Selection), with the participants comparable with each other within all studies (Domain 2: Comparability). However, assessments of outcomes were not always standardized and definitions of outcome measures were not always clearly reported across the studies (Domain 3: Outcome). Over 80% (16 of 18) of the studies did not clearly define peri-implantitis

TABLE 3	Risk of bias assessment form,	, modified from NOS.	. Studies with more tha	n one group could att	ract 13 stars (*), a	and studies with
a single grou	up could attract 12 stars (*)					

	Торіс	Question	Details
Selectio	on		
1	Representativeness	Are the patients in the study representative of similar patients who would present with peri-implantitis to a private practice, university or hospital?	
		1. Yes, generally representative of the average patient who may need treatment in a private practice, university clinic or hospital clinic? (*)	
		2. No, it is a selected group (e.g. Nurses, volunteers, students)	
		3. Unclear, there is no description of how the cohort was selected	
2	Second group representativeness	Does the study have two groups? If yes, answer this question. If no, skip this question and continue with Question 3. If there are two cohorts, was the second cohort	
		1. Drawn from the same community as the first cohort (*)	
		2. Drawn from a different source	
		3. Unclear, There is no description of how the second cohort was selected	
3	Ascertainment of	How do you know that the group was exposed?	
	exposure	1. Secure record (e.g. Surgical record, Clinical Notes, Author provided the exposure etc.) (*) $(*)$	
		2. Structured interview (*)	
		3. Written self-report	
		4. Unclear, No description	
4	When did the outcome occur	Is it clear that the outcome of interest (see definition above) was not present at the start of the study? 1. Yes (*)	
		2. No	
Compa	rability		
5	Different cohorts	Does the study have two groups? If yes, answer this question. If no, skip this question and continue with Question 6. Are subjects in different cohorts comparable with each other?	
		1. Yes. This is because cohorts were randomly selected with allocation concealment (**)	
		 Yes. Although selection was nonrandomized, authors adjusted for/reported/excluded/considered more than one important confounding factor. Please list the factors in the "details" column. (**) 	
		3. Yes. Although selection was nonrandomized, authors adjusted for/reported/excluded/considered <u>one</u> important confounding factor only. Please list the single factor in the "details" column. (*)	
		4. No, subjects in each cohort appeared to differ substantially from each other.	
		5. No, details were not reported	
6	Same cohort	Does the study have one group? If yes, answer this question. If no, skip this question and continue with Question 7. Are subjects within the same cohort comparable with each other?	
		1. Yes. This is because authors adjusted for/reported/excluded/considered <u>more than one</u> important confounding factor. Please list the factors in the "details" column. (**)	
		2. Yes. This is because authors adjusted for/reported/excluded/considered <u>one</u> important confounding factor only. Please list the single factor in the "details" column. (*)	
		3. No, subjects appeared to differ substantially from each other in the same group.	
		4. No, details were not reported	
Outcon	nes		
7	Subjective outcomes	How were the subjective outcomes assessed (probing, radiographic bone loss)?	
		1. Independent blind assessment with calibrated examiners (*)	
		 Nonblinded assessment with calibrated examiners, because blinding was not appropriate or practical (*) 	
		3. Non calibrated multiple examiners	
		4. Self-report, by patient	
		5. Unclear, no description	

	Торіс	Question	Details
8	Probing	Was peri-implant probing standardized? Yes (*) No	
9	Radiographs	Were radiographs standardized? Yes (*) No	
10	Recurrence	Were criteria for peri-implantitis "recurrence" clearly reported? Yes (*) No	
11	Failure	Were reasons/criteria for implant removal clearly reported? Yes (*) No	
12	Follow-up completeness	Was the follow-up long enough for outcomes to occur? 1. Yes (*) (State the maximum follow-up in the "details" box) 2. No	
13	Loss to follow-up	 Was the follow-up of the cohorts adequate? 1. Complete follow-up, with all subjects accounted for (*) 2. Some subjects were lost to follow-up, but in your opinion this was unlikely to introduce bias or be the result of selective reporting. Authors provided reasons for lost to follow-up where practical and these indicate that such losses were unlikely to introduce bias. (State the number that were lost to follow-up and the total number in the study; the percentage lost to follow-up; reasons for lost to follow-up in the details box) (*) 3. Follow-up rate was high, and there was no description of those lost 4. Unclear, not reported 	

recurrence, over a quarter (five of 19) did not clearly standardize the radiographic technique and another quarter (five of 19) did not clearly standardize the probing technique. These factors impact on how results can be generalized to other patient populations.

3.3 | Quantitative assessment

Quantitative assessment of survival at the implant- (n = 13 studies, Figure 2) and patient-levels (n = 12 studies, Figure 3) are outlined below. There was heterogeneity between studies in the reporting of treatment outcomes. While all included studies reported on implant-level survival, the reason for implant loss/removal was not always stated.

Four studies reported at two time points each: Heitz-Mayfield et al. (2016) (3 year, 5 year), Roccuzzo et al. (2017) (3 year through personal communication, 7 year), Roos-Jansåker, Persson, Lindahl & Renvert (2014) (3 year, 5 year) and Schwarz, John, Schmucker, Sahm & Becker (2016) (4 year, 7 year).

Two studies reported data cumulatively, and were included in pooled summaries corresponding to their mean time in situ: Froum, Froum & Rosen (2012) (3 year results, μ = 3.7), and Zablotsky (1998) (4 year results, μ = 4.5).

Seven studies reported on single, and six studies reported on multiple treatment groups. Of those six studies, results of each

group were reported separately (n = 1; Schwarz, Sahm, Bieling & Becker, 2009), results of the test group only were reported because the control group was observed for less than 3 years (n = 1; Romeo et al., 2005) and results were combined because authors observed no differences between groups (n = 4; Carcuac et al., 2017; Khoury & Buchmann, 2001; Roos-Jansåker et al., 2014; Schwarz et al., 2016).

Implant survival across seven studies at 3 years ranged from 81.73% (lower 95% CI) to 100% (upper 95% CI). Implant survival across three studies (one with two groups) at 4 years ranged from 74.09% (lower 95% CI) to 100% (upper 95% CI). Implant survival across four studies at 5 years ranged from 76.03% (lower 95% CI) to 100% (upper 95% CI). Implant survival across two studies at 7 years ranged from 69.63% (lower 95% CI) to 98.72% (upper 95% CI).

Patient-level survival across eight studies at 3 years ranged from 78.64% (lower 95% CI) to 100% (upper 95% CI). Patient-level survival across three studies (one with two groups) at 4 years ranged from 71.29% (lower 95% CI) to 100% (upper 95% CI). Patient-level survival across three studies at 5 years ranged from 56.14% (lower 95% CI) to 100% (upper 95% CI). Patient-level survival across two studies at 7 years ranged from 69.63% (lower 95% CI) to 98.42% (upper 95% CI).

Pooled meta-analysis results showed implant-level ECSurv of 99.95% at 3 years (n = 7 studies), 99.97% at 4 years (n = 3 studies) and 91.82% at 5 years (n = 4 studies). Corresponding 95% Cls



FIGURE 1 PRISMA systematic search flow diagram

estimating the precision of the mean summary effect are reported in Figures 2 and 3. Pooled meta-analysis results showed patientlevel ECSurv of 99.99% at 3 years (n = 8 studies), 99.99% at 4 years (n = 3 studies) and 86.08% at 5 years (n = 3 studies). Corresponding 95% CIs estimating the precision of the mean summary effect are reported in Figures 2 and 3. Data at 7 years was not pooled, as there were less than 3 studies. Across the 13 implant-level studies and 12 patient-level studies, seven groups reported no implant losses (and 100% survival). It is likely that this has markedly influenced the pooled weighting and overestimated the true effect.

A combined funnel plot (Figure 5) explored the point estimate versus the standard error of implant-level survival in the 3 year (blue legend, n = 7 studies), 4 year (red legend, n = 4 studies), 5 year (green legend, n = 4 studies) and 7 year (yellow legend, n = 2 studies) subgroups. Data for nine studies appeared once in the plot, and data for four studies appeared twice in the plot (n = 3, reported at multiple time points, n = 1, two study groups analysed). Seven studies reported 100% survival and these data points are clustered at the peak of three of the funnels (3, 4 and 5 year). Data was skewed or potentially skewed at all time points, meaning that it was likely that small patient cohorts with less favourable outcomes existed, but remained either unpublished or difficult to find. Therefore, the pooled results likely overestimate the true clinical effect and care should be taken when applying the pooled estimate to patient groups.

4 | DISCUSSION

This review assessed clinical outcomes in patients treated for peri-implantitis who were enrolled in a supportive care program for at least 3 years, with 3, 4, 5 and 7 year results collated. This review shows that after 3, 4, 5, and 7 years the great majority of patients enrolled in a supportive care program (SPT), with regular professional biofilm removal at both implants and teeth, will not lose their implants. This review did not aim to identify the most effective peri-implantitis treatment protocol or supportive care regimen, or to quantify risk factors that may modify outcomes. However, as there was considerable heterogeneity within and between studies with respect to the study design (peri-implantitis definition, outcome definitions, treatment protocols, supportive care protocols) and population characteristics (patient, implant and prosthesis characteristics), these factors are examined further in the discussion.

The perception among clinicians that peri-implantitis treatment is unpredictable and may not lead to successful clinical outcomes is not uncommon. In a systematic review (Esposito, Grusovin & Worthington, 2012a) it was found that recurrence of peri-implantitis in up to 100% of treated cases occurred in some studies with a follow-up longer than 1 year. In contrast, the present systematic review shows that favourable treatment outcomes documented in studies with 12-month results (Heitz-Mayfield & Mombelli, 2014) may be

	Supportive care	SPT operator: NR SPT frequency: 6 months SPT description: Dental hygiene + diode laser	SPT operator: NR SPT frequency: 3 months for the first year, then annually SPT description: Regimen unclear, OHI as required	SPT operator: Referring clinician SPT frequency: 3 -4 monthly SPT description: 1st year-OHI every 3 months. Thereafter according to individual needs	SPT operator: Hygienist SPT frequency: 3-5 month SPT description: NR
	nent	Adjunctive treatment: Mucogingival corrections, if necessary Surface decontamination: Gp1: NR, Gp2: Diode laser Peri-operative Antibiotics: NR	Adjunctive treatment: No Surface decontamination: APB Peri-operative Antibiotics: MTR	Adjunctive treatment: No Surface decontamination: titanium curettes, saline (Gp2 & 4)/CHX (Gp 1 & 3) Peri-operative Antibiotics: In Gp 1 & 2	Adjunctive treatment: Retreatment 1-8 times Surface decontamination: ErYAG Laser + CHX irrigation + MIN ointment injection Peri-operative Antibiotics: NR
Treatment provided	Initial peri-implantitis treatr	Pretreatment phase: Yes Surgical treatment: Combination RES + regenerative	Pretreatment phase: Yes lodine irrigation for 4 weeks Surgical treatment: Regenerative ABG block (n = 18) ABG particulate (n = 7)	Pretreatment phase: Yes Professional supramu- cosal cleaning/OHI Surgical treatment: RES: pocket elimination Gp 1: ATB+/CHX+ Gp 2: ATB+/CHX+ Gp 3: ATB-/CHX- Gp 4: ATB-/CHX-	Pretreatment phase: NR Nonsurgical treatment: Curettage of the granulation tissue
	Inclusion	Inclusion Criteria: Evidence of marginal bone loss, PD > 5 mm, overall BoP, Clinical signs of inflammation Exclusion Criteria: Serious illness, alcohol abuse, nicotine use, lack of compliance	Inclusion Criteria: Peri-implan- titis crater defects, PD > 5 mm, crater-like BL < 90% implant length Exclusion Criteria: No systemic illnesses	Inclusion Criteria: Advanced peri-implantitis—PD ≥6 mm, BoP/SUP, bone loss >3 mm Exclusion Criteria: compro- mised general health, systemic antibiotic therapy during past 6 months	Inclusion Criteria: PD >4 mm, BL >2 mm, BoP/PUS, Plaque Exclusion Criteria: NR
	Population baseline	Patients: n = 30 G1: n = 15 G2: n = 15 Implants: NR Prostheses: NR	Patients: n = 17 6 M, 11 F Mean age: 51.7 yrs Implants: n = 25 Straumann Prostheses: NR	Patients: n = 100 35 M, 65 F Mean age 66.3 (21-60 yrs) Implants: n = 179 Prostheses: NR	Patients: n = 16 10 M, 6 F Mean age: 56.2 \pm 10.6 yrs HX treated PDD n = 12 DM + CVD n = 3 CVD n = 3 Implants: n = 31 Prostheses: SICs = 5, FDPs = 26
Study details	Design	Prospective, two groups Private practice Operators–NR Funding: NR Follow-up: 5 yrs	Prospective, one group University Single Operator- periodontist Funding: NR Follow-up: 3 yrs	Prospective RCT, four groups University Multiple operators; 5 periodontists Funding: Swedish Research Council Follow-up: 3 yrs	Retrospective, 1 group University Operators–NR Funding: NR Follow-up: 5 yrs
	Authors/Year	1. Bach et al. (2000)	2. Behneke et al. (2000)	3. Carcuac et al. (2017) Related publication: Carcuac et al. (2016)	4. Chang, Park, Kim, Kim and Lee (2015)

TABLE 4 Study description

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	Study details			Treatment provided		
Authors/Year	Design	Population baseline	Inclusion	Initial peri-implantitis treatm	hent	Supportive care
5. Charalampakis et al. (2011)	Retrospective Multiple operators Funding–Oral Microbiology Gothenburg Follow-up: 9 months to 13 yrs. 45 patients ≥ 4 yrs	Patients 245 (45 patients followed for ≥4 yrs) Implants: NR Prostheses: NR	Inclusion Criteria: BOP/Sup with PD ≥5 mm and bone loss ≥1.8 mm after 1 year in function Exclusion Criteria: NR	Pretreatment phase: NR Nonsurgical (46 patients) Surgical treatment: 6 different surgical approaches used RES, regenerative (various materials)	Adjunctive treatment: NR Surface decontamination: Various antiseptics (NaCl, H ₂ O ₂ , CHX, iodine) Peri-operative Antibiotics: Various, based on microbio- logical testing results Some local antibiotics	SPT operator: multiple SPT frequency: 3 monthly for first year then annually SPT description: OHI patient motivation, supragingival plaque control, "subgingival scaling" at implant sites with residual bleeding
6. Deppe, Horch and Neff (2007)	Prospective, 4 groups University Operators–NR Funding: NR Follow-up: 5 yrs	Patients: n = 32 Implants: n = 73 G1: n = 17, G2: n = 22 G3: n = 15, G4: n = 19 IMZ, Frialit, Brånemark, Straumann Prostheses: Cement and screw retained SICs and FDPs	Inclusion Criteria: PD >5 mm, progressive BL or BoP Exclusion Criteria: NR	Pretreatment phase: Yes Non surgical debride- ment + CHX rinsing Surgical treatment: Multiple G1: Regenerative (TCP, ABG, ePTFE) G2: RES G3: Regenerative (TCP, ABG, ePTFE) G4: RES	Adjunctive treatment: No Surface decontamination: G1 & G2: APB + CO ₂ Laser G3 & G4: APB Peri-operative Antibiotics: No	SPT operator: NR SPT frequency NR SPT description: NR
7. Froum et al. (2012) Related publications: Froum et al. (2015, 2018)	Prospective, 1 group Private practice Single operator Funding: NR Follow-up: 3 to 7.5 yrs	Patients: n = 38 18 M, 20 F Mean age: approx. 58 yrs, range 29-81 yrs Implants: n = 51 8 brands: S Prostheses: NR	Inclusion criteria: PD >6 mm, BoP, BL >4 mm Exclusion Criteria: DM, OP, chemotherapy, radiation therapy	Pretreatment phase: Yes FMD 1 month prior surgery Surgical treatment: Regenerative EMD, XBM, PDGF, CM CTG (if KT <2 mm)	Adjunctive treatment: No Surface decontamination: CFC, TC, APB, CHX Peri-operative Antibiotics: AMX/CLI for 10 days	SPT operator: NR SPT frequency: 2-3 monthly SPT description: Rubber cup polishing 2 month post-op. interproximal brush soaked in CHX 3x day
8. Froum et al. (2015) Related publications: Froum et al. (2012, 2018)	Prospective, 1 group Private practice Operators–NR Funding: NR Follow-up: up to 10 yrs	Patients: n = 100, unknown for ≥3 yrs 47 M, 53 F Implants: n = 170, unknown for ≥3 yrs Prostheses: NR	Inclusion Criteria: BoP, PD ≥5 mm, BL ≥3 mm from implant platform Exclusion Criteria: DM, OP, BIP chemotherapy radiation therapy	Pretreatment phase: Yes Surgical treatment: Regenerative EMD or PDGF XBM, CM CTG (if KT <2 mm)	Adjunctive treatment: Additional surgical procedure if required Surface decontamination: MIN, TET, CHX, APB Peri-operative Antibiotics: NR	SPT operator: NR SPT frequency: 2-3 month SPT description: NR

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TABLE 4 (Continued)

	Study details			Treatment provided		
Authors/Year	Design	Population baseline	Inclusion	Initial peri-implantitis treatm	nent	Supportive care
9. Heitz-Mayfield et al. (2016) Related publication: Heitz-Mayfield et al. (2012)	Prospective, 1 group Multi-centre Private practice & University Multiple operators Funding: ITI grant Follow-up: 5 yrs	Patients: n = 24 13 M, 11 F Mean age: 56±8.5 yrs Hx treated PDD n = 8 Smokers n = 6 Implants: n = 36 Various brands Prostheses: Cement and screw-retained SICs and FDPs	Inclusion Criteria: BL ≥2 mm + PD ≥5 mm + BoP/PUS Exclusion Criteria: Inadequate implant, restoration contours, uncontrolled DM, heavy smokers	Pretreatment phase: Yes FMPS < 25% & FMBS < 25% Surgical treatment: Access flap	Adjunctive treatment: No Surface decontamination: TC + saline Peri-operative Antibiotics: AMX and MTR for 7 days	SPT operator: Periodontist SPT frequency: 3 monthly for 12 months, then at least 6 monthly according to patient's needs SPT description: Motivation, OHI, FMD
10. Khoury & Buchmann (2001)	Prospective, 3 groups Private practice & University Single operator Funding: NR Follow-up: 3 yrs	Patients: $n = 25$ Gp1: $n = 12$, Gp2: $n = 20$, Gp3: $n = 9$ 3 M, 22 F Mean age: 48.2 ± 6.3 yrs Implants: $n = 41$ IMZ, Friadent Prostheses: FDPs and RDPs	Inclusion Criteria: BL >50% Exclusion Criteria: NR	Pretreatment phase: Yes 0.2% CHX irrigation Implant scaling + systemic ATB Weekly OHI prophylaxis program Surgical treatment: Regenerative Gp 1: ABG (n = 12) Gp 2: ABG + ePTFE (n = 20) Gp 3: ABG + CM (n = 9)	Adjunctive treatment: No Surface decontamination: CHX, CA, H ₂ 0 ₂ , saline Peri-operative Antibiotics: Various, 6 months prior surgery	SPT operator: NR SPT frequency: 3-6 month SPT description: Regimen unclear, OHI as required
11. Mercado et al. (2018)	Prospective, 1 group Private practice Single operator Funding: National Health and Medical Research Council Follow-up: 3 yrs	Patients: n = 30 11 M, 19 F Mean age: 44.9±11 yrs Implants: n = 30 Brånemark TiUnite, Astra Tech, Straumann SLA Prostheses: Cement or screw-retained SICs	Inclusion Criteria: BoP/PUS, BL > 20%, PD > 4 mm, Implants >2 yrs in function Exclusion Criteria: DM, OP, pregnant/lactating, autoimmune disorders, warfarin intake, >2 implants, UPD, smoking	Pretreatment phase: Yes Surgical treatment: Regenerative (XMB + EMD + DOX mix) + CTG (n = 8)	Adjunctive treatment: CTG (n = 8) Surface decontamination: DOX 100 mg mixed with XMB Peri-operative Antibiotics: No	SPT operator: Periodontist SPT frequency: 3-4 month SPT description: OHI, FMD with mild ultrasonic implant debridement

TABLE 4 (Continued)

(Continues)

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	Study details			Treatment provided		
Authors/Year	Design	Population baseline	Inclusion	Initial peri-implantitis treatm	lent	Supportive care
12. Roccuzzo et al. (2017)	Prospective, 1 group Private practice Single operator Funding: NR Follow-up: 7 yrs	Patients: n = 26 11 M, 15 F Mean age: 60±7.9 yrs Hx treated PDD Smokers N = 4 Implants: n = 26 Straumann, 12 SLA & 14 TPS Prostheses: Cement retained SICs and FDPs	Inclusion Criteria: Crater-like BL, PD ≥6 mm Exclusion Criteria: Poor implant placement, HC, adjacent defects, Implant mobility	Pretreatment phase: Yes FMPS < 20% & FMBS < 20% Surgical treatment: Regenerative DBBMC	Adjunctive treatment: CTG when no KT Surface decontamination: EDTA gel (24%) + CHX gel (1%) Peri-operative Antibiotics: AUG 1 g twice a day, for 6 days	SPT operator: Dental hygienist + Periodontist SPT frequency: According to individual risk assessment SPT description: Motivation, OH reinstruc- tion, FMD Additional treatment ATB, FGG
13. Romeo et al. (2005)	Prospective, 2 groups University Multiple operators Funding: NR Follow-up: 3 yrs	Patients: $n = 17$ Gp1: $n = 10$, Gp2: $n = 7$, 2 smokers >10 cig./day Implants: $n = 35$ Straumann, TPS: HS n = 11, S $n = 24Prostheses: NR$	Inclusion Criteria: PD >4 mm, BoP/PUS, Evident BL Exclusion Criteria: Implant mobility	Pretreatment phase: Yes Systemic ATB and FMD Surgical treatment: Resective Gp1: RES + IPP (10 pts, 19 impl.) Gp2: RES (7 pts, 16 impl.); Not followed for 3 yrs	Adjunctive treatment: NR Surface decontamination: MTR gel + TET solution Peri-operative Antibiotics: AMX	SPT operator: NR SPT frequency: NR SPT description: Regimen unclear
14. Roos-Jansåker et al. (2014) Related publications: Roos-Jansåker et al. (2007, 2011)	Prospective, 2 groups University Single operator Funding: NR Follow-up: 5 yrs	Patients: $n = 36$ Gp1: $n = 17$ 7 M, 10 F Mean age: 65.6 ± 7.4 yrs Smokers $n = 12$ Gp2: $n = 19$ 5 M, 12 F Mean age: 66.3 ± 6.8 yrs Smokers $n = 13$ Implants: $n = 65$ G1: $n = 29$, G2: $n = 36$ Astra Tech, Brånemark Prostheses: Screw	Inclusion Criteria: BL ≥1.8 mm, BoP/PUS Exclusion Criteria: Horizontal bone loss or no crater-like bone defect	Pretreatment phase: Yes Surgical treatment: Regenerative Gp 1: PCC + RSM (n = 19) Gp 2: PCC (n = 17)	Adjunctive treatment: NA Surface decontamination: H ₂ O ₂ Peri-operative Antibiotics: AMX and MET for 10 days	SPT operator: NR SPT frequency: 3 month SPT description: OHI and rubber cup polishing

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TABLE 4 (Continued)

	Study details			Treatment provided		
Authors/Year	Design	Population baseline	Inclusion	Initial peri-implantitis treatm	hent	Supportive care
15. Schwarz et al. (2009) Related publications: Schwarz et al. (2006, 2008)	Prospective, 2 groups University Single operator Funding: NR Follow-up: 4 yrs	Patients: n = 22 Gp1: n = 11 Gp2: n = 11 8 M, 14 F Mean age: 54.4±12.5 yrs Implants: n = 22 7 brands: S Prostheses: NR	Inclusion Criteria: PD > 6 mm, intrabony BL > 3 mm Exclusion Criteria: Implant mobility, occlusal overload, no KM, UPD, poor OH, DM, OP, heavy smokers (> 10 cig./day), HS	Pretreatment phase: Yes Non surgical debride- ment with PS, CHX irrigation & gel Surgical treatment: Regenerative Gp1: NHA+ CM Gp2: NBM	Adjunctive treatment: NR Surface decontamination: PC Peri-operative Antibiotics: No	SPT operator: 2 of the authors SPT frequency Fortnightly for 2 month, Monthly until 6 month, then 6 monthly until 48 month SPT description: Supragingival professional implant/tooth cleaning OHI
16. Schwarz et al. (2017) Related publications: Schwarz et al. (2012, 2013)	Prospective, 2 groups University Single operator Funding: NR Follow-up: 7 yrs	Patients: $n = 32$ Gp1: $n = 16$ Gp2: $n = 16$ J1 M, 21 F Mean age: 60.8±10.9 yrs Implants: $n = 38$ 10 different brands Prostheses: NR	Inclusion Criteria: PD > 6 mm, Intrabony BL > 3 mm Exclusion Criteria: HC, Implant mobility, unhealthy patients, UPD, lack of proper periodontal maintenance, heavy smokers (> 10 cig./ day)	Pretreatment phase: Yes Surgical treatment: Combined Regenerative XMB (Bio-Oss), CM (BioGide) + resective (IPP)	Adjunctive treatment: CTG when no KT Surface decontamination: Gp 1: ER:YAG laser (ERL), PC + saline GP 2: PC + saline Peri-operative Antibiotics: AMX for 5 days	SPT operator: Single operator first 6 month One visit annually, University, Maintenance provided by the referring practitioner SPT frequency 2 weeks during the first 2 month, then monthly until 6 month, then yearly SPT description: OHI, professional cleaning
17. Serino et al. (2015) Related publications: Serino et al. (2011)	Prospective, 1 group University Multiple operators-peri- odontists Funding: NR Follow-up: 5 yrs	Patients: n = 31 13 M, 11 F Mean age: 63.2±8.7 yrs Smokers n = 8 Implants: n = 86 Astra, ITI, Brånemark: S Prostheses: Screw-re- tained restorations removed before treatment	Inclusion Criteria: PPD ≥ 6 mm, BoP/PUS, BL ≥ 2 mm Exclusion Criteria: BIP	Pretreatment phase: Yes Supra/subgingival debridement, adjustment prosthesis if required Surgical treatment: Combined Access flap + RES	Adjunctive treatment: No Surface decontamination: US + CHX irrigation Peri-operative Antibiotics: CLI for 7 days	SPT operator: Periodontist SPT frequency: 6 month SPT description: Supragingival plaque control Sub-gingival scaling at implants with residual pockets using US metal tips instrument under CHX 0.12% irrigation

TABLE 4 (Continued)

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	Study details			Treatment provided		
Authors/Year	Design	Population baseline	Inclusion	Initial peri-implantitis treatm	hent	Supportive care
18. Zablotsky (1998)	Retrospective, 1 group Private practice Operators–NR Funding: NR Follow-up: 3 yrs	Patients: n = 21 Age range: 22-87 yrs Implants: n = 42 Multiple brands, various surfaces: TPS n = 22, HA HS n = 15, Ti n = 5 Prostheses: NR	Inclusion Criteria: Implant stability (periotest values <10), BL <70%, PD >4 mm, BoP/PUS, previously treated with hard and/or soft tissue augmentation Excessive BL BoP/PUS Exclusion criteria: NR	Pretreatment phase: Yes LDD: Actisite (n = 8) Systemic ATB (n = 6) Surgical treatment: Multiple 17 GBR, 11 RES, 9 STG, 5 combination	Adjunctive treatment: Unstable implants were retreated Surface decontamination: CA Peri-operative Antibiotics: NR	SPT operator: NR SPT frequency: 3-4 month SPT description: NR
I · hone lose: PD· nrol	hing denth: RoD: hleedin	s on prohing: NR: not report	ed: SLID/DLIS: summiration			

BL: bone loss; PD: probing depth; BoP: bleeding on probing; NR: not reported; SUP/PUS: suppuration.

Population baseline: FDP: fixed dental prosthesis; HA: hydroxyapatite-coated implants; Hx treated PDD: history of treated periodontal disease; HS: hollow-screw; RDP: removable dental prosthesis; S: screw-shaped; SIC: single-implant crown, Ti: titanium; TPS: titanium plasma-sprayed; HC: Hollow cylinder.

Inclusion/Exclusion criteria: BIP: bisphosphonate therapy; DM: diabetes mellitus; CVD: cardiovascular diseases; OP: osteoporosis; UPD: untreated periodontal disease.

Surgical treatment and regenerative materials: ABG: autogenous bone graft; CM: collagen membrane; DBBMC: demineralized bovine bone mineral with collagen; EMD: enamel matrix derivate; ePTFE: Antibiotics: AMX: amoxicillin; ATB: antibiotics; AUG: augmentin; CLI: clindamycin; DOX: doxycycline; LDD: local delivery device; MIN: minocycline; MTR: metronidazole; TET: tetracycline.

expanded polytetrafluoroethylene membrane; GBR: guided bone regeneration; NBM: natural bone mineral; NHA: nanocrystalline hydroxyapatite; PCC: phytogenic calcium carbonate (Algipore); PDGF: platelets derived growth factor; RES: resective; RSM: resorbable synthetic membrane; STG: soft tissue grafting; TCP: beta-tricalcium phosphate; XBM: xenogenic bone mineral (Bio-Oss). Adjunctive treatment: FGG: free gingival graft; CTG: connective tissue graft; KT: keratinized tissue.

Surface decontamination: CA: citric acid; CHX: chlorhexidine; EDTA: ethylenediamine tetra-acetate; IPP: implantoplasty; PC: plastic curette; PS: plastic scaler; TC: titanium curettes; US: ultrasonic instrumentation.

Supportive care: APB: air-powder abrasive with sodium bicarbonate powder; FMD: full-mouth debridement; OHI: oral hygiene instruction.

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		Peri-implanti	tis			Results	at the lon	gest follo	w-up tim	е			
Date	Author	Ķ	Group	Time in situ	Imp N	LTF N	Succ N	Recur N	Fail N	ECSucc (%)	Lower 95% CI	Upper 95% CI	Success Criteria
2017	Carcuac et al.	Res	4 Groups combined	3 years	179	31	40	NR	20	33.94	26.69	41.20	Success = No BL > 0.5 mm, +PD ≤5 mm, + No BoP + No Sup
2018	Mercado F, Hamlet S, Ivanovski S	2	1 Group	3 years	30	0	17	X	0	56.67	38.93	74.41	Success = No further BL + No BoP + No Sup + PD <5 mm + Recession of <0.5-1.5 mm
1998	Zablotsky MH.	Various	1 Group	3.5 years to 7.0 years, μ=4.5 years	42	4	32	NR	4	85.00	73.93	70.66	Not clearly reported
2015	Serino G, Turri A, Lang NP.	Res	1 Group	5 years	86	ω	58	6	11	75.61	66.32	84.9	Success = PD < 4 mm + No BoP + No Sup
2016	Heitz-Mayfield LJ et al.	Access flap	1 Group	5 years	36	œ	19	Ŋ	4	71.88	56.30	87.46	Success = No further BL + No PD 25 mm with BoP +No Sup
2017	Roccuzzo M et al.	ц	Gp 1: TPS	7 years	14	2	2	NR	5	7.69	0.00	22.18	Success = No further BL + PD ≤5 mm + No BoP + No Sup
			Gp 2: SLA		12	0	7	NR	2	41.67	13.77	69.56	
Peri-impl	antitis abbreviations: R: 1	regenerative, R	ecur: recurrence	, Res: resective, ⁻	Fx: treatme	nt.							

 TABLE 5
 Implant-level success for the longest follow-up time reported, and success definitions as reported

Other abbreviations: BL: bone loss, BoP: bleeding on probing, ECSucc: estimated cumulative success, LTF: loss to follow-up, N: number, NR: not reported, PD: peri-implant probing depth, Succ:

success, Sup: suppuration, TPS: titanium plasma sprayed, SLA: sandblasted large grit acid-etched.

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Author	Date	PI Tx	Time (yr) in situ	Imp N	LTF N	Surv N	Fail N		
Khoury F, Buchmann R.	2001	R	3	41	0	41	0		
Romeo E et al.	2005	Res	3	19	0	19	0		
Froum SJ, Froum SH, Rosen PS.	2012	R	3 to 7.5 μ=3.7	51	0	51	0		
Heitz-Mayfield LJ, et al.	2016	NR	3	36	4	30	2		
Mercado F, Hamlet S, Ivanovski S	2017	R	3	30	0	30	0		
Roccuzzo M, et al.	2017	R	3	26	1	23	2		
Carcuac O. et. al.	2017	Res	3	179	31	128	20		
	I-squar Weight	ed = 77.9% s are from	, P<0.001 random effe	cts an	alysis	1			
Zablotsky MH.	1998	С	3.5 to 7.0 u=4.5	42	4	34	4		
Schwarz F et al	2009	R	4	11	0	11	0		
Schwarz F et al	2009	R	4	11	0	11	0		
Schwarz F et al	2016	R	4	38	17	17	4		
	I-squared = 67%, P=0.028 Weights are from random effects analysis								
Roos-Jansaker AM et al	2014	R	5	45	15	30	0		
Chang HY et al	2015	NS	5	31	0	28	3		
Serino G, Turri A, Lang NP.	2015	Res	5	86	8	67	11		
Heitz-Mayfield LJ et al	2016	NR	5	36	8	24	4		
	I-squar Weight	ed = 85.4% s are from	, P<0.001 random effe	cts an	alysis				
Schwarz F et al.	2016	R	7	38	19	15	4		
Roccuzzo M et al	2017	R	7	26	2	20	4		
	I-squar Less th	ed = 0%, P an 3 studie	=0.84 es, Meta ana	lysis n	ot con	pleted			

ò 20 40 60 80 100 C=Combination, ECSurv=Estimated cumulative survival, LTF=Loss to follow up, NR=Non-Regenerative, PI tx=Peri-implantitis treatment, Pt = Patient, R=Regenerative, Res=Resective, Surv=Survival

FIGURE 2 Forest plot of the estimated cumulative survival of dental implants treated for peri-implantitis across 3, 4, 5 and 7 years

Author	Date	PI Tx	Time (yr) in situ	Pt N	LTF N	Surv N	Fail N		ECSurv %	Lower 95%Cl	Upper 95%Cl	Weight
Khoury F, Buchmann R.	2001	R	3	25	0	25	0	•	100.00	99.80	100.00	19.98
Romeo E et al.	2005	Res	3	10	0	10	0	•	100.00	99.80	100.00	19.98
Froum SJ, Froum SH, Rosen PS.	2012	R	3 to 7.5 μ=3.7	38	0	38	0	-	100.00	99.80	100.00	19.98
Roos-Jansaker AM et al	2014	R	3	38	6	32	0	-	100.00	99.80	100.00	19.98
Heitz-Mayfield LJ et al.	2016	NR	3	24	2	20	2		91.30	79.78	100.00	0.02
Mercado F, Hamlet S, Ivanovski S	2017	R	3	30	0	30	0	-	100.00	99.80	100.00	19.98
Roccuzzo M, et al.	2017	R	3	26	1	23	2		92.16	81.73	100.00	0.03
Carcuac O. et. al.	2017	Res	3	100	17	70	13		85.79	78.64	92.95	0.06
	I-squared Weights a	= 64.1% re from	%%, P=0.0.00 a random eff	07 ects ar	nalysis				99.99	99.81	100.00	100.00
Zablotsky MH.	1998	С	3.5 to 7.0 µ=4.5	21	2	17	2		90.00	76.85	100.00	0.06
Schwarz F et al	2009	R	4	11	0	11	0	•	100.00	99.80	100.00	49.95
Schwarz F et al	2009	R	4	11	0	11	0	-	100.00	99.80	100.00	49.95
Schwarz F et al	2016	R	4	32	11	17	4		84.91	71.29	98.53	0.05
	I-squared Weights a	= 56.7% ire from	%, P=0.074 random eff	ects ar	nalysis				99.99	99.68	100.00	100.00
Roos-Jansaker AM et al	2014	R	5	38	13	25	0	٠	100.00	99.80	100.00	39.15
Serino G, Turri A, Lang NP.	2015	Res	5	31	4	19	8		72.41	56.14	88.68	30.36
Heitz-Mayfield LJ et al	2016	NR	5	24	4	16	4		81.82	65.71	97.93	30.49
	I-squared Weights a	= 87.5% re from	%, P<0.001 i random eff	ects ar	nalysis			\bigcirc	86.08	67.17	100.00	100.00
Schwarz F et al.	2016	R	7	32	13	15	4		84.31	70.20	98.42	NA
Roccuzzo M et al	2017	R	7	26	2	20	4		84.00	69.63	98.37	NA
	I-squared Less than	= 0%, F 3 stud	P=0.98 ies, Meta an	alysis	not com	pleted			NA	NA	NA	NA
								0 20 40 60 80 100				

C=Combination, ECSurv=Estimated cumulative survival, LTF=Loss to follow up, NR=Non-Regenerative, PI tx = Peri-Implantitis treatment, Pt = Patient, R=Regenerative, Res=Resective, Surv=Survival

FIGURE 3 Forest plot of the estimated cumulative survival of dental implants in patients treated for peri-implantitis across 3, 4, 5 and 7 years

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3	4	7

			SELE	CTION		COMPA	RABILITY				оитсом	E			TOTAL
		1	2	3	4	5	6	7	8	9	10	11	12	13	
		Representativeness	Second group representativeness	Ascertainment of exposure	When did the outcome occur	Different cohorts	Single cohort	Subjective outcomes	Probing	Radiographs	Recurrence	Failure	Follow up completeness	Loss to follow up	
Studies with a single group		1	1	1							1	1		1	
Behneke A, Behneke N, d'Hoedt B	2000	*	NA	*	*	NA	**	?	*	*	*	*	*	*	10/12
Chang HY et al	2015	*	NA	*	*	NA	**	*	*	*	×	*	*	*	11/12
Charalampakis G et al	2011	*	NA	*	*	NA	*	×	*	×	*	*	*	?	6/12
Froum SJ, Froum SH, Rosen PS.	2015	*	NA	*	*	NA	**	*	*	*	×	*	*	*	11/12
Froum SJ, Froum SH, Rosen PS.	2012	*	NA	*	*	NA	**	*	*	*	×	*	*	*	11/12
Heitz-Mayfield LJ et al	2016	*	NA	*	*	NA	**	*	*	*	*	*	*	*	12/12
Mercado F, Hamlet S, Ivanovski S	2017	*	NA	*	*	NA	**	*	*	*	*	*	*	*	12/12
Roccuzzo M et al	2017	*	NA	*	*	NA	**	*	*	*	×	*	*	*	11/12
Serino G, Turri A, Lang NP	2015	*	NA	*	*	NA	**	*	*	×	*	*	*	*	11/12
Zablotsky MH	1998	*	NA	*	*	NA	**	?	*	*	*	*	*	*	8/12
Studies with more than one group															
Bach G et al	2000	*	*	*	*	*	NA	?	*	*	*	*	*	?	8/13
Carcuac et al	2017	*	*	*	*	**	NA	*	*	*	*	*	*	*	12/13
Deppe H, Horch HH, Neff A	2007	*	*	*	*	*	NA	*	*	*	*	*	*	*	6/13
Roos-Jansaker AM et al	2014	*	*	*	*	**	NA	*	*	*	*	*	*	*	11/13
Schwarz F et al	2016	*	*	*	*	**	NA	*	*	*	×	*	*	*	11/13
Schwarz F te al	2009	*	*	*	*	**	NA	*	*	*	×	*	*	*	11/13
Khoury F, Buchmann R. [^]	2001	*	*	*	*	*	NA	*	*	*	×	*	*	*	11/13
Romeo E et al*	2005	*	*	*	*	**	NA	*	*	*	*	*	*	*	12/13

^3 groups in paper, but the authors combined the results during reporting

* 2 groups in the paper, but one was used for this analysis because the control group was followed for less than 3 years. Green: Criteria fulfilled: Orange: Unclear if criteria fulfilled: Red: Criteria not fulfilled: NA: Not applicable.

FIGURE 4 Risk of bias assessment results, modified from NOS. Studies with more than one group could attract 13 stars (*), and studies with a single group could attract 12 stars (*).

maintained over the medium to long term (3-7 years), when patients are enrolled in a supportive care program.

4.1 | 3-7-year outcomes

Across the studies, anti-infective treatment protocols aimed at implant surface decontamination with or without a reconstructive approach using bone graft/substitutes resulted in clinical improvements for the majority of patients and implants. It should be recognized however, that some studies in this review documented the need for additional interventions (connective tissue grafting, surgical intervention, systemic antimicrobials) in some patients,



Estimated Cumulative Survival (%)

FIGURE 5 Funnel plot, analysed by implant-level survival outcomes across 3 year (blue line), 4 year (red line), 5 year (green line) and 7 year (yellow line) subgroups

to achieve the desired outcome (Roccuzzo et al., 2017) or manage disease recurrence (Heitz-Mayfield et al., 2016; Zablotsky, 1998).

The 3-year treatment outcomes were favourable with high patient- and implant-level survival. However, in several studies where multiple follow-up time points were available, additional implant loss was noted with time due to disease progression resulting in the removal of the implants (Froum et al., 2015; Heitz-Mayfield et al., 2016; Roccuzzo et al., 2017).

The implant-level and patient-level pooled meta-analyses showed that over 90% of implants in over 85% of patients that had treatment were expected to still have their implants after 5 years. At 7 years there was less evidence, but data still indicated that over 80% of patients with treated implants might retain their implants. Although results are not definitive, the review suggests that anti-infective protocols will stabilize those infections for the medium- to long term for the majority of patients, and as such, pursuing treatment could be considered to be worthwhile.

Five papers defined success, with each using composite criteria relating to BoP, suppuration, and probing depth (n = 5), bone level (n = 4) and recession (n = 1). Due to the heterogeneity of success criteria, it was not possible to pool data or make meaningful comparisons. While complete resolution of disease, as defined by the total absence of BoP, may not be a requirement for treatment success, one study observed that absence of bleeding/suppuration on probing was predictive of stable bone levels 3 years after treatment (Carcuac et al., 2017).

Across the 18 studies, disease recurrence was not commonly discussed or defined. Recession of the peri-implant mucosa following treatment was documented in two studies. (Heitz-Mavfield et al., 2016: Mercado, Hamlet & Ivanovski, 2018) which might impact on aesthetics, V— CLINICAL ORAL IMPLANTS RESEARCH

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phonetics and comfort. However, patient-reported outcome measures (PROMs) such as aesthetic outcomes; quality of life; and patient satisfaction; as well as cost satisfaction analyses were not reported in the included studies. These outcomes are relevant to clinical decisions and would be important areas to address in future research.

The quality of conduct of the included studies was generally high, with over 75% assessed to have low risk of bias. However, the quality of reporting in some areas, in particular outcome definitions was low. This hindered data extraction and has reduced the potential utility of this systematic review.

4.2 | Anti-infective treatment

Anti-infective treatment protocols described included a pretreatment phase (nonsurgical supramucosal biofilm removal) followed by decontamination of the implant surface using a range of techniques with and without antiseptics. Implant surface decontamination was performed during surgical access. Peri-operative systemic antimicrobials were prescribed in the majority of studies. Postoperative infection control included the use of antiseptic rinsing for periods of several weeks following treatment. Supportive care protocols all involved professional biofilm removal at implants and teeth at varying time intervals from three monthly to annually. Some studies described recall frequency based on an individual risk assessment. There was no indication that recall frequency was related to patient attrition. While there were no studies comparing supportive care protocols it appears that the regular and thorough removal of biofilm at implants and teeth is necessary for a positive treatment outcome.

4.3 | Confounding factors

Local factors which may influence local plaque control and hence the outcome of peri-implantitis treatment include: implant placement/positioning; prosthesis design; presence of keratinized mucosa; implant surface and design. The association between inadequate access for oral hygiene due to prosthesis design/contours, and the presence of peri-implantitis was previously demonstrated (Serino & Strom, 2009). It is also important to consider access for adequate local plaque control after the peri-implantitis has been treated. Two studies in the present review excluded patients with implants considered inappropriate to treat due to either poor implant positioning (Roccuzzo et al., 2017) or inadequate contour of the prosthesis (Heitz-Mayfield et al., 2016). In some instances, it may be appropriate to remake the implant prosthesis or remove the implant if there is no possibility to achieve adequate plaque control.

While the majority of studies in this systematic review did not report full-mouth plaque scores (FMPS), low FMPS (<20%) such as those reported by (Heitz-Mayfield et al., 2016) may be important in achieving sufficient infection control and treatment success.

A number of studies in the systematic review incorporated a soft tissue graft as part of the treatment procedure (Bach, Neckel, Mall & Krekeler, 2000; Froum et al., 2012, 2015; Mercado et al., 2018) or during supportive care (Roccuzzo et al., 2017). It has been suggested that the absence of an adequate band of keratinized peri-implant mucosa may negatively influence treatment outcomes due to discomfort when performing oral hygiene resulting in increased plaque accumulation (Roccuzzo, Grasso & Dalmasso, 2016).

Implant design and surface characteristics may also influence the treatment outcome. Most studies included a variety of implant designs and surfaces and it was not possible to evaluate the effect on treatment outcome due to the heterogeneity. One study found that success following resective peri-implantitis treatment was affected by implant surface characteristics. Implants with a nonmodified ("turned") surface achieved success more frequently than implants with modified surfaces at 3 years (Carcuac et al., 2017). In another study with 7 years follow-up of reconstructive peri-implantitis treatment using a bone substitute (deproteinized bovine bone mineral with 10% collagen), patients with TPS implant surfaces had lower implant survival and success than those with a SLA implant surface (Roccuzzo et al., 2017).

Other possible confounding factors that could not be assessed in this review due to heterogeneity, low participant numbers and nonreporting include: patient systemic factors (e.g., diabetes, cardiovascular disease); medications; history of periodontitis; smoking status and prosthesis design.

4.4 | Limitations of the review

This review sought published and unpublished data across the peri-implantitis treatment field. Three of the included studies (20%) were identified through grey literature. This is a substantial number and indicates that multiple teams are actively researching in this field. Therefore, it is possible that additional grey data exists, but was unintentionally overlooked during the search. It also suggests that knowledge in this field will continue to evolve, possibly quickly, and care should be taken to interpret results from this review in the light of more recent evidence that was not available at its inception.

The outcomes from this review are limited by the heterogeneity between studies. The utility of results from this review is limited by the outcome measure, survival. Other outcome measures could not be assessed. Survival does not account for surrounding tissue health, tissue appearance, or patient satisfaction. Although peri-implantitis treatment can retain implants for patients, a surviving implant in one patient might be markedly different to a surviving implant in another patient.

5 | CONCLUSIONS

The results of this review confirm that peri-implantitis can be successfully treated in patients adhering to a supportive care programme which involves professional biofilm removal at implants and teeth. High survival rates can be achieved in the medium to long term. Implant surface may influence the treatment outcomes. Some implants in some patients may require retreatment, adjunctive therapies or implant removal.

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SUPPORTING INFORMATION

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