The Efficacy of Supportive Peri-Implant Therapies in Preventing Peri-Implantitis and Implant Loss: a Systematic Review of the Literature

Ausra Ramanauskaite[1], Tellervo Tervonen[2,3]

[1]Department of Dental and Oral Pathology, Lithuanian University of Health Sciences, Lithuania.
[2]Department of Periodontology and Geriatric Dentistry, Unit of Oral Health Sciences, University of Oulu, Finland.
[3]Medical Research Center Oulu (MRC Oulu), University of Oulu and Oulu University Hospital, Finland.

Corresponding Author:
Tellervo Tervonen
Department of Periodontology and Geriatric Dentistry, Unit of Oral Health Sciences
University of Oulu
P.O. Box 8100, FI-90014 University of Oulu
Finland
E-mail: tellervo.tervonen@oulu.fi

ABSTRACT

Objectives: To study the efficacy of supportive peri-implant therapies in preventing clinical and radiological signs of peri-implantitis and implant loss.
Material and Methods: Longitudinal human studies, published between January 1, 2006, and February 1, 2016, were included based on an electronic search using MEDLINE and EMBASE databases and complemented by a manual search. Articles were included only if 1) they comprised a group of patients involved in/adhering to regular supportive peri-implant therapies (SPTs) and a control group without such therapies or with poor adherence to them, 2) the protocol of the SPTs was clearly described and 3) the outcome was indicated by means of clinical/radiological changes or implant loss.
Results: After initially identifying a total of 710 titles and abstracts, 12 full text articles were selected for eligibility assessment. Seven studies, three prospective and four retrospective, fulfilled the inclusion criteria for this review.
The frequency of recall visits varied between the studies from a minimum of one visit every three months to an individually tailored regimen. In all the studies a lack of SPTs or poor adherence to them resulted in significantly higher frequencies of sites with mucosal bleeding, deepened peri-implant pockets or alveolar bone loss. In line with the above, a lack of/poor adherence to SPTs was associated with higher implant loss.
Conclusions: To prevent peri-implantitis, an individually tailored supportive programme based on patient motivation and re-instruction in oral hygiene measures combined with professional implant cleaning seem to be crucial.

Keywords: compliance; dental implant; maintenance; peri-implantitis.

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INTRODUCTION

Despite the overall satisfactory survival rates of dental implants [1], it is well known that a proportion of implants are unsuccessful due to various inflammatory pathoses in peri-implant tissues. These include two main disease entities: peri-implant mucositis, which is a condition limited to the mucosa surrounding the implant, and peri-implantitis, characterised by a loss of peri-implant bone [2]. In the recent 11th European Workshop on Periodontology consensus conference, weighted mean prevalences of 43% and 22% of peri-implant mucositis and peri-implantitis, respectively, were reported [3]. Both animal and human studies have provided evidence that the primary aetiologic factor in peri-implant inflammation is accumulation of plaque around the mucosal margins of implants [4,5], as is the case in gingivitis of natural teeth. To confirm the biofilm-related aetiology of peri-implant inflammation, several studies have shown that, subsequent to plaque removal, resolution of peri-implant mucositis is evident [5-7].

It is generally agreed that gingivitis of natural teeth and peri-implant mucositis of implants are precursors of their advanced forms, periodontitis and peri-implantitis, respectively [8]. Therefore, prevention and management of peri-implant mucositis are critical in long-term maintenance of implants. While no studies on primary prevention of peri-implant mucositis are available, it is evident from recent systematic reviews and meta-analyses that a reduction in clinical signs of peri-implant inflammation is possible after patient-performed [9] or professional [10] plaque control. Of note is, however, that complete resolution of inflammation cannot be achieved in all patients.

Hultin et al. [11] studied whether supportive treatment is effective in the prevention of biological complications of implant therapy and fixture loss. The review was based on nine studies of 749 implants at a 10-year examination. In only two of the reviewed studies the patients were enrolled in an individualised maintenance programme; in the remaining studies the treatment provided at the recall visits was not reported. Therefore, the group called for new studies to suggest the frequency of recall visits and to propose specific hygiene treatments. A later systematic review and meta-analysis [12], based on qualitative and quantitative analyses of 13 and 10 studies, respectively, assessed the impact of supportive maintenance therapies on peri-implant conditions. This review showed a positive effect of the therapies, and the authors recommended implementation of a maintenance programme after implant placement and restorative treatment.

Although biological complications associated with dental implants cannot be completely avoided, it is likely that the overall long-term success of implant therapy can be improved by the establishment of supportive peri-implant therapies (SPTs) [9,12]. While the 11th European Workshop on Periodontology consensus conference focused on the efficacy of preventive measures in managing peri-implant mucositis, only scarce evidence of the effectiveness of supportive therapies in managing biological complications beyond mucositis is available. Therefore, we conducted a systematic review of the literature to study the efficacy of SPTs on peri-implantitis-associated clinical and radiologic signs and implant loss.

MATERIAL AND METHODS

Protocol and registration

The methods of the analysis and inclusion criteria were specified in advance and documented in a protocol. The review was registered in PROSPERO, an international prospective register of systematic reviews. The protocol can be accessed at: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016035621

The reporting of this systematic analysis adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) Statement [13].

Focus question and outcomes

The following focus question was developed according to the population, intervention, comparison and outcome (PICO) study design:

- What is the efficacy of supportive peri-implant therapies evaluated by means of clinical (bleeding and/or probing depth) and/or radiological (marginal bone level) changes around dental implants and/or implant loss for patients with osseointegrated dental implant(s)?
- Primary outcome: occurrence of various signs of peri-implantitis (peri-implant bleeding/deepened peri-implant pockets/peri-implant bone loss).
- Secondary outcome: implant loss/survival.

Information sources

The search strategy incorporated an examination of the electronic database Scopus, which covers the whole MEDLINE database (Ovid) and a greater

part (90%) of the EMBASE database. Additionally, a manual search was conducted in the following journals: "Clinical Oral Implants Research", "Implant Dentistry", "International Journal of Oral & Maxillofacial Implants", "International Journal of Periodontics and Restorative Dentistry", "Journal of Clinical Periodontology" and "Journal of Periodontology".

The references of each relevant study were screened to find additional relevant publications and to improve the sensitivity of the search.

Search

The keywords and search inquiries used during the primary stage were: ("implant loss" OR "implant survival" OR "peri-implantitis" OR periimplantitis OR "peri-mucositis" OR perimucositis OR "peri-implant mucositis" OR "periimplant mucositis" OR "biological complication") AND ("prevention" OR "maintain" OR "maintenance" OR "support" OR "supportive therapy"). The choice of keywords was intended to be broad to collect as much relevant data as possible without relying on electronic means alone to refine the search results.

Selection of studies

The review included all human prospective or retrospective follow-up studies (clinical trials, cohort studies and case-control studies) in the English language published between January 1, 2006, and February 1, 2016.

Titles and abstracts derived from this broad search were independently screened by both authors to eliminate irrelevant publications (Figure 1). The final stage of screening involved reading the full texts to confirm each study's eligibility based on the inclusion criteria below.

Inclusion criteria

Studies were included in this review only if they met the following inclusion criteria:

- The subjects must have had at least one osseointegrated dental implant;
- A group of subjects involved in/adhering to regular SPTs and a control group without such therapies or with poor adherence were included;
- The protocol of the supportive peri-implant therapy was clearly described;
- The efficacy of supportive peri-implant therapy was evaluated by means of clinical (plaque, bleeding and/or probing depth scores) and/or radiological (marginal bone level) changes around dental implant(s), and/or implant loss at the end of the follow-up period.

The following types of articles were excluded: letters, editorials, theses, commentaries, consensus statements, reviews and meta-analyses. Furthermore, animal and *in vitro* studies were excluded. In case of unclear data, the authors were contacted to obtain the data.

Data extraction and data items

The data were independently extracted from the studies according to the aims and themes of the present review as follows (Table 1):

- "Author" - revealed the authors of the study and the year of publication.
- "Study design and follow-up" - revealed the type of study and the time period in months/years during which the patients in the test and control groups were followed.
- "Population" - revealed the size and characteristics of the study population.
- "Test group" - revealed the regimen of SPTs applied and the numbers of patients and implants (if available).
- "Control group" - revealed the numbers of patients and implants (if available) included.
- "Results" - described the efficacy of supportive peri-implant therapies evaluated by means of clinical (bleeding on probing and/or probing depth) and/or radiological (bone level) changes around dental implant(s), and/or implant loss.

Due to great heterogeneity in the methodologies (aims, outcomes, study populations, treatment protocols) between the included studies we preferred a qualitative analysis and a quantitative data synthesis for meta-analysis was not considered.

Assessment of methodological quality

The quality of all included studies was assessed during the data extraction process and involved evaluating the methodological elements that might influence the outcome of each study (Table 2). The Cochrane Collaboration's two-part tool for assessing risk of bias [14] was used to assess bias across the studies and to identify papers with intrinsic methodological and design flaws. Based on the information given in each study the potential risk of bias was categorized into 'low', 'unclear' or 'high' by one of the authors (AR).

Table 1. Descriptive information of the included studies

Author	Year of publication	Study design	Follow-up	Population	Test group	Control group	Results
Anner et al. [20]	2010	Retrospective study	1 - 114 months	475 patients 1626 implants	Patients participating in recall visits for oral hygiene instruction and re-enforcement as well as professional cleaning every 3 - 6 months. (246 patients; 873 implants)	Patients who only attended annual free-of-charge implant examinations. (229 patients; 753 implants)	The proportion of patients with failed implants (P = 0.0114) and the frequency of failed implants (P = 0.0028) were lower in patients attending a structured SPT programme. Patients not attending a SPT had an OR of 1.89 for implant failure.
Costa et al. [21]	2012	Retrospective study	5 years	80 PHP and PCP diagnosed with peri-implant mucositis	Patients with preventive maintenance (GTP group): at least five dental visits during the 5-year evaluation period. During the visits periodontal and peri-implant status assessment was performed. Oral hygiene instructions and mechanical debridement, when needed. (39 patients; 156 implants)	No maintenance (GNTP group). (41 patients; 180 implants)	The incidence rates of peri-implantitis observed in the GTP group (18%) were significantly lower than those observed in the GNTP group (44%) (P < 0.01). Absence of maintenance was associated with a higher incidence of peri-implantitis.
Fricsh et al. [22]	2014	Retrospective study	3 years	236 PHP and PCP 540 implants	Grade 1: One prophylaxis appointment per year; Grade 2: Two prophylaxis appointments per year; Grade 3: Three prophylaxis appointments per year; Grade 4: Four prophylaxis appointments per year. During the sessions, patient motivation was reinforced, patients were re-instructed in home-based plaque -control techniques and the implants and teeth were professionally cleaned with polishing paste and a rubber cup. (192 patients)	Grade 0: No prophylaxis appointments per year; Grade 00: patients without any appointment in the entire observation period. (44 patients)	A significant correlation between lower compliance and increased PPD was detected (P = 0.032). 3-month recalls recommended.
Rinke et al [23]	2011	Retrospective study	68.2 (SD 24.8) months	89 PHP and PCP 540 implants	Regular prophylaxis (including re-instruction and re-motivation in effective plaque control, professional tooth cleaning and polishing using rubber cups and polishing paste and application of fluoride gel) every 6 months was performed in patients without a history of periodontal disease, and SPT (supportive periodontal therapy) in patients with a history of periodontal disease. Subgingival scaling of implants using an ultrasonic tip and hand instruments was performed is sites with PD ≥ 5 mm. (58 patients)	Irregular prophylaxis (31 patients)	Patients who did not participate in regular post-treatment programmes bore an 11-fold higher chance of peri-implantitis than patients showing good compliance (OR = 0.09, CI = 0.01 to 0.58, P = 0.011).
Roccuzzo et al. [24]	2010	Prospective cohort study	10 years	28 PHP, 37 moderate PCP, 36 severe PCP 246 implants	An individually tailored SPT including continuous evaluation, motivation, reinstruction, instrumentation and treatment of re-infected sites. The treatment of peri-implant biologic complications according to CIST. Recall intervals depending on the initial diagnosis and treatment results. (79 patients)	22 patients not adhering to SPTs	- Moderate PCP: the number of patients with bone loss ≥ 3 mm (P = 0.003) or implant loss (P = 0.005) was higher among patients not adhering than in those adhering to SPTs; - Severe PCP: the number of patients with implant loss was higher in subjects not adhering than in those adhering to SPTs (P = 0.016)
Roccuzzo et al. [25]	2012	Prospective cohort study	10 years	28 PHP, 37 moderate PCP, 36 severe PCP 246 implants	An individually tailored SPT programme including continuous evaluation, motivation, reinstruction, instrumentation and treatment of re-infected sites. The treatment of peri-implant biologic complications according to CIST. Recall intervals depending on the initial diagnosis and treatment results. (79 patients)	22 patients not adhering to SPT	Compared with patients adhering to SPTs, at 10 years those not adhering had: - In moderate PCP: a significantly higher proportion of sites with BOP (P = 0.0001), greater mean deepest PD (P = 0.0001) and higher proportions of implants with deepest PD ≥ 6 mm (P = 0.001); - In severe PCP: a significantly higher proportion of sites with BOP (P = 0.0006), greater mean deepest PD (P = 0.009), higher proportions of implants with PD ≥ 6 mm (P = 0.01).
Roccuzzo et al. [26]	2014	Prospective cohort study	10 years	32 PHP, 46 moderate PCP, 45 severe PCP 252 implants	An individually tailored SPT programme including continuous evaluation, reinstruction, instrumentation and treatment of re-infected sites. The diagnosis and treatment of peri-implant biological complications according to CIST. (75 patients)	48 patients not adhering to SPT	Compared with patients adhering to SPTs, at 10 years those not adhering had: - In moderate PCP: a higher proportion of sites with BOP (P = 0.018), greater mean deepest PD at implants (P = 0.02) and higher frequency of implants with at least one site with PD ≥ 6 mm (P < 0.001); - In severe PCP: greater mean deepest PD (P = 0.01), higher frequency of implants with at least one site with PD ≥ 6 mm (P = 0.001) and higher number of lost teeth (P = 0.03).

SPT = supportive peri-implant therapy; PHP = periodontally healthy patients; PCP = periodontally compromised patients; GTP = a group with preventive maintenance; GNTP = a group without preventive maintenance; CIST = cumulative interceptive supportive therapy; OR = odds ratio; CI = confidence interval; BOP = bleeding on probing; PD = pocket depth; PPD = periodontal probing depth.

Table 2. Assessment of the risk of bias

Author	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias
Anner et al. [20]	?	?	-	+	?	+
Costa et al. [21]	?	?	?	-	?	+
Frisch et al. [22]	?	?	?	-	?	+
Rinke et al. [23]	?	?	?	+	?	+
Roccuzzo et al. [24]	?	?	+	+	?	+
Roccuzzo et al. [25]	?	?	+	+	?	+
Roccuzzo et al. [26]	?	?	+	+	?	+

+ = low risk; ? = unclear risk; - = high risk.

RESULTS

Search results

The article review and data extraction were performed according to the PRISMA flow diagram (Figure 1). The initial database search displayed 716 results and one result was obtained from the manual search. Abstracts were available for 710 articles. Preliminary exclusion was done by relevancy; 51 non-relevant titles and abstracts were excluded. Of the remaining 659 results, 17 case reports and 65 systematic reviews or meta-analyses were further filtered. After exclusion of abstracts (n = 566) that did not include information on the selected topic, 12 full text articles were assessed for eligibility. Another exclusion was done because information on the SPT regimen was not available [15] or because there was no control group [16-19]. Finally, seven articles were included in the review (Figure 1).

Description of the included studies

Anner et al. [20] evaluated the influence of SPT on long-term implant survival in a retrospective study of 475 patients with 1626 inserted implants.

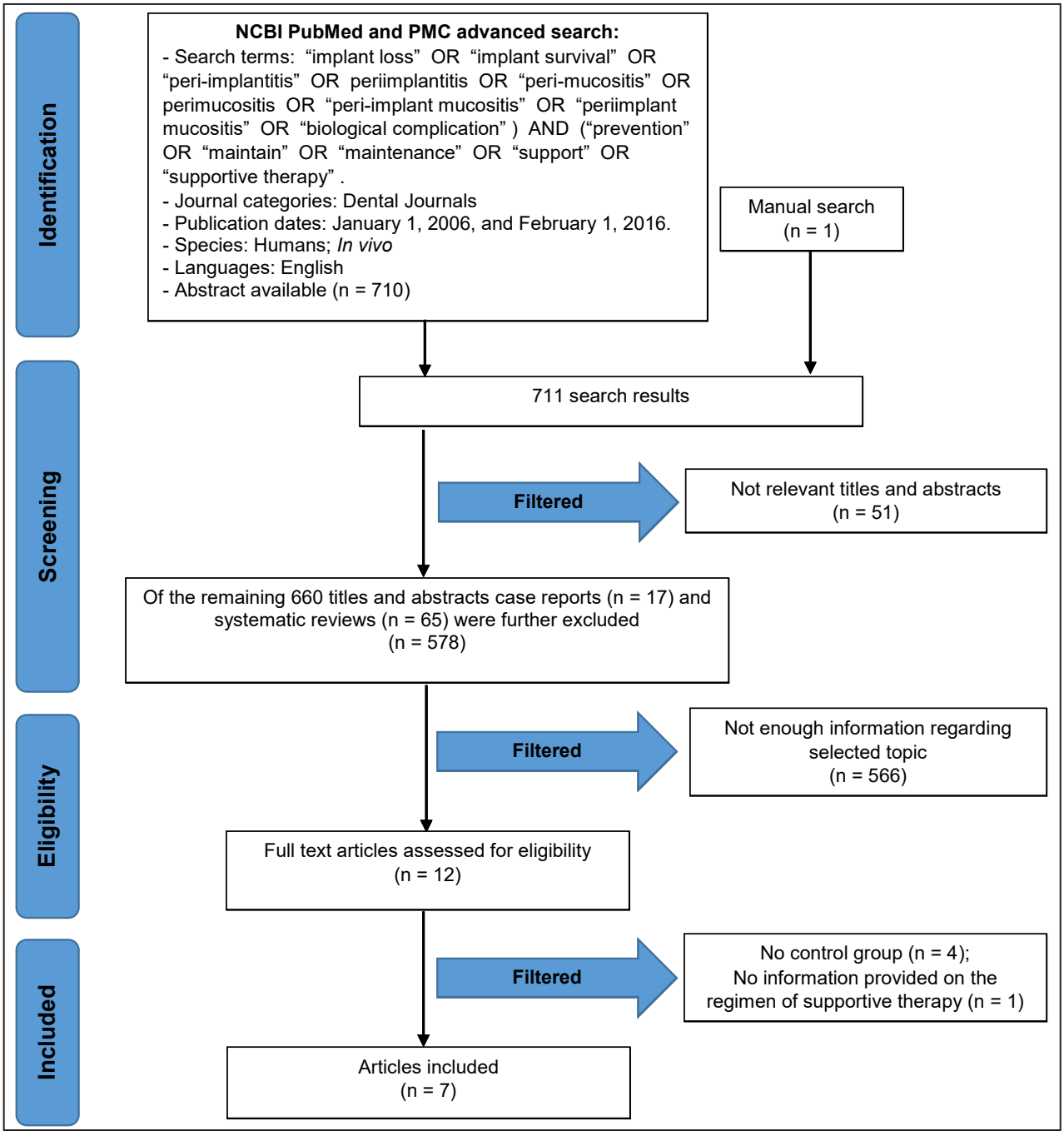

Figure 1. PRISMA flow diagram.

According to personal communication with the authors, the SPT regimen included oral hygiene instruction and re-enforcement as well as professional cleaning every 3 - 6 months. Overall, 77 implants (4.7%) were lost in 58 patients (12.2%). Patients not attending the SPT programme had an odds ratio of 1.89 for implant failure.

The outcome of a five-year retrospective study by Costa et al. [21] highlighted the importance of SPT in preventing the onset of peri-implantitis. The frequency of maintenance visits was at least one visit per year. After being diagnosed with peri-implant mucositis, 18% of the subjects enrolled in SPT progressed to peri-implantitis, while the incidence of peri-implantitis amounted to 44% in subjects without SPT. The lack of preventive maintenance within the overall sample was significantly associated with peri-implantitis in a logistic model (OR = 5.92). The authors highlight the necessity of preventive maintenance and continuous monitoring of clinical peri-implant parameters when mucositis is present.

A retrospective study by Frisch et al. [22] evaluated patient compliance to supportive post-implant therapy (SIT) over a three-year period. The yearly assessed compliance rate, which was categorised into five grades, ranged from four prophylaxis appointments per year to no compliance to prophylaxis at all. This study revealed high rates of patient compliance (86 - 94%) to a SIT programme over the first three years. A significant correlation was found between lower compliance and increased pocket probing depth (P = 0.032). In addition, higher plaque rates were found in individuals with lower compliance rates (P = 0.087). However, the results of the study did not reveal a statistically significant correlation between compliance and peri-implant tissue inflammation (BOP+ values).

The prevalence rates of peri-implant mucositis and peri-implantitis were evaluated by Rinke et al. [23] in 89 patients, who were classified into being on 'regular prophylaxis/SPT' (those who did not exceed the recommended intervals for prophylaxis/SPT by more than 100%) and 'irregular prophylaxis/SPT' (patients who exceeded the recommended interval at least once by more than 100%). Prophylaxis (in patients without a history of periodontitis) and SPT (in patients with a history of periodontitis) were rendered to most patients at three-month intervals during the first year after implant placement and later on at six-month intervals. Based on the finding of this study, patients who did not participate in regular post-treatment programmes bore an 11-fold higher chance of peri-implantitis than patients showing good compliance (OR = 0.09; CI = 0.01 to 0.58; P = 0.011).

The long-term outcomes of implant therapies in relation to adhesion to SPTs were studied in three-arm prospective cohort studies by Roccuzzo and co-authors [24-26]. Implants were placed at the end of periodontal therapy and the outcomes of the treatment were evaluated during the SPTs and at 10 years. Based on their initial periodontal status, the patients were divided into periodontally healthy (PHP) and either moderately or severely periodontally compromised patients (PCP), and the treatment outcomes were measured as presence of plaque, bleeding on probing, probing pocket depth, peri-implant bone loss, treatment need according to CIST (interceptive supportive therapy) principle and implant loss. In periodontally healthy patients, no statistically significant differences in any of the periodontal variables were observed between patients adhering and not adhering to SPTs at 10 years. In the moderately and severely compromised groups, lack of adhesion to SPTs was associated with higher plaque and bleeding scores, deeper probing pocket depths both during the SPTs and at 10 years and a higher frequency of implant loss. In addition, a tendency of a higher need for antibiotic and surgical implant therapies was reported in the group of patients not adhering to SPTs [26].

Risk of bias within studies

Summarising the risk of bias for each study, all the studies were judged to have an unclear risk (of bias in more than one domain) (Table 2).

DISCUSSION

All the studies in the current review reported a significant positive effect of SPTs on peri-implant conditions. In addition, it became evident that peri-implant mucositis, if left untreated, may progress to peri-implantitis. In all the studies the preventive programmes comprised re-instruction/re-enforcement of oral home care and professionally performed prophylaxis or mechanical debridement/submucosal scaling of implant surfaces. Thus, the main conclusion drawn from this review is that providing such treatments for every patient after surgical and prosthetic phases is crucial to improving the long-term success of implant therapy.

Based on a qualitative analysis of 13 studies, Monje et al. [12] likewise concluded that peri-implant maintenance therapy is needed 'to potentially prevent biological complications and hence heighten the long-term success rate' of implant therapy.

While studies clearly reporting the frequency of peri-implant maintenance therapy were included in their qualitative analysis, we required, in addition, that the included studies also reported the protocol of the SPTs and had a control group.

The primary question in this systematic review was 'To what extent can peri-implantitis be prevented by SPTs?' Thus, we focused on prevention of inflammatory changes beyond peri-implant mucositis, which, according to the recent consensus by the 11th European Workshop of Periodontology consensus conference, was found to be largely preventable [9]. The advanced biological complications, peri-implantitis and implant loss, can be considered end-points in the continuum from healthy peri-implant tissues to loss of peri-implant bone via inflammation of mucosal soft tissues (peri-implant mucositis) and deepening of peri-implant pockets. Overall, three studies in this review related a lack of/poor adherence to SPTs to deepening of peri-implant pockets [24-26], two studies to peri-implantitis [21,23], two studies to peri-implant bone loss [21,24] and two studies to implant loss [20,24]. Albeit deepened peri-implant pockets 'per se' have not been considered diagnostic criteria for peri-implantitis by prominent authorities [8,27,28], we used, parallel with many studies [29,30], deepened peri-implant pockets as one of the clinical end-points in this review. Generally speaking, it is not precisely known how valid as tools the clinical measures adopted from studies of natural teeth (for example bleeding on probing, probing pocket depth and clinical attachment level) are for studies of peri-implant diseases [29,30].

The benefits of supportive therapies in long-term maintenance of natural teeth have been shown in a two studies [31,32]. As for periodontal diseases, prevention of peri-implant diseases should be tailored according to each individual's needs through diagnosis and risk profiling [33-35]. In daily practice this means monitoring/diagnosing peri-implant conditions, motivating and educating the patient in oral self-care, professional mechanical plaque removal and, if manageable, control of risk factors. In the reviewed studies a few important risk factors such as smoking, susceptibility to periodontitis/periodontal disease history, diabetes and greater geographic distances to the study centre were recognised. An important finding here was that even under 'state-of-the-art' SPTs, peri-implantitis occurred/progressed in some patients, more often in those with compromised periodontal condition [24-26].

The risk profile of the patient is an important element in determining the recall interval of the SPTs. In three of the reviewed studies the interval varied between 3 to 6 months [20,22,23] and in the Roccuzzo studies [24-26] the treatment was delivered according to individual needs. In the Costa et al. study [21] the patients had a minimum of five visits during the five-year follow-up period. Monje et al. [12] made an attempt to define a 'reasonable' recall interval in preventing peri-implant infections and ended up with 5 - 6 months. The authors emphasised, however, that the maintenance therapy should in any case be customised according to the patients' risk profiling.

Unlike Hultin et al. [11], who selected studies presenting long-term clinical outcomes of ten years and more for their review, no restrictions were made here with regard to the length of the follow-up period. The positive effects of SPTs, verified as significantly decreased rates of peri-implant inflammation or bone loss, were evident already at five [21] or six [23] years, or during the course of the 10-year SPT as in the Roccuzzo studies [24-26]. Both human and animal studies show that the progression of an inflammatory lesion subsequent to plaque accumulation is more aggressive and the resolution of inflammation is slower at implant sites than at tooth sites [4,5]. Therefore, it is imperative that continuous monitoring of peri-implant health and preventive practices be started as a continuum to the prosthetic phase of the implant therapy.

Limitations

All the studies included in this review were judged to be of unclear risk of bias, which, according to the Cochrane Collaboration's tool, is sufficient to affect the interpretation of the results [14]. The limitations, to mention here a few, should therefore be considered when applying the results of this review to daily implant practices. Generally taken, it is unethical to leave patients with progressing peri-implant infections untreated, and therefore no 'golden standard' type of controlled/randomised controlled trials related to prevention can be performed. A majority of the included studies were retrospective by design and originally not intended to specifically assess the efficacy of preventive therapies on peri-implant infections. Moreover, many of the studies had small sample sizes and were therefore likely underpowered. In six studies the patients were recruited from private clinics specialised in periodontal or implant therapies and in one study from private and university clinics; caution should therefore be exercised in generalising the results to the population level.

CONCLUSIONS

In light of the microbial aetiology of peri-implant infections, supportive peri-implant therapies targeting the removal of infectious agents at implant sites are needed. Within the limitations of the present systematic review, it can be concluded:

1. A lack of poor adherence to supportive peri-implant therapies results in significantly higher frequencies of sites with mucosal inflammation and peri-implant bone loss as well as more frequent implant loss.
2. Individually tailored supportive peri-implant therapies based on patient motivation and re-instruction in oral hygiene measures combined with professional implant cleaning should be an integral part of implant therapy.

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