

REVIEW

Open Access



Efficacy of alternative or adjunctive measures to conventional treatment of peri-implant mucositis and peri-implantitis: a systematic review and meta-analysis

Frank Schwarz^{*}, Andrea Schmucker and Jürgen Becker

Abstract

In patients with peri-implant mucositis and peri-implantitis, what is the efficacy of nonsurgical (i.e. referring to peri-implant mucositis and peri-implantitis) and surgical (i.e. referring to peri-implantitis) treatments with alternative or adjunctive measures on changing signs of inflammation compared with conventional nonsurgical (i.e. mechanical/ultrasonic debridement) and surgical (i.e. open flap debridement) treatments alone? After electronic database and hand search, a total of 40 publications (reporting on 32 studies) were finally considered for the qualitative and quantitative assessment. The weighted mean changes (WM)/ and WM differences (WMD) were estimated for bleeding on probing scores (BOP) and probing pocket depths (PD) (random effect model). Peri-implant mucositis: WMD in BOP and PD reductions amounted to -8.16% [SE = 4.61] and -0.15 mm [SE = 0.13], not favouring adjunctive antiseptics/antibiotics (local and systemic) over control measures ($p > 0.05$). Peri-implantitis (nonsurgical): WMD in BOP scores amounted to -23.12% [SE = 4.81] and -16.53% [SE = 4.41], favouring alternative measures (glycine powder air polishing, Er:YAG laser) for plaque removal and adjunctive local antibiotics over control measures ($p < 0.001$), respectively. Peri-implantitis (surgical): WMD in BOP and PD reductions did not favour alternative over control measures for surface decontamination. WM reductions following open flap surgery (\pm resective therapy) and adjunctive augmentative therapy amounted to 34.81 and 50.73 % for BOP and 1.75 and 2.20 mm for PD, respectively. While mechanical debridement alone was found to be effective for the management of peri-implant mucositis, alternative/adjunctive measures may improve the efficacy over/of conventional nonsurgical treatments at peri-implantitis sites. Adjunctive resective and/or augmentative measures are promising; however, their beneficial effect on the clinical outcome of surgical treatments needs to be further investigated.

Review

Background

Peri-implant mucositis describes an inflammatory lesion that resides in the soft tissues compartment, while at peri-implantitis sites, this lesion has extended and also affects the implant supporting bone [1]. The 11th European Workshop on Periodontology has pointed to an “estimated weighted mean prevalence of peri-implant mucositis and peri-implantitis of 43 and 22 %, respectively” [2].

The main etiology of peri-implant mucositis refers to plaque accumulation [3, 4], and the conversion from mucositis to peri-implantitis was, particularly in the absence of a supportive maintenance care [5], positively correlated with the function time [2]. However, the presence of some independent systemic/patient-related (i.e. smoking) and local (i.e. residual cement, dimension of the keratinized tissue, surface roughness) risk indicators may increase the probability of the disease occurring [3].

* Correspondence: Frank.Schwarz@med.uni-duesseldorf.de
Department of Oral Surgery, Westdeutsche Kieferklinik, Universitätsklinikum
Düsseldorf, D-40225 Düsseldorf, Germany

According to the cause-related concept of therapy, professionally administered plaque removal is a key strategy for the prevention and management of peri-implant diseases [6]. In previous years, several alternative or adjunctive measures (e.g. local antibiotics, air polishing, laser application) have been proposed to improve the efficacy of nonsurgical treatment approaches [7–9]. At peri-implantitis sites, surgical protocols may involve different decontamination protocols, that may also be combined with resective (e.g. pocket elimination, bone re-contouring, implantoplasty) and/or augmentative approaches (e.g. bone substitutes or autografts with or without a supporting barrier membrane) [7, 10]. Accordingly, there is a need to identify the most effective interventions for the treatment of peri-implant diseases.

The aim of this systematic review was therefore to address the following focused question: in patients with peri-implant mucositis and peri-implantitis, what is the efficacy of nonsurgical (i.e. referring to peri-implant mucositis and peri-implantitis) and surgical (i.e. referring to peri-implantitis) treatments with alternative or adjunctive measures on changing signs of inflammation compared with conventional nonsurgical and surgical treatments alone?

Methods

This systematic review was structured and conducted according to the preferred reporting items of the PRISMA statement [11].

Focused question

The focused question serving for literature search was structured according to the PICO format [12]: “In patients with peri-implant mucositis and peri-implantitis, what is the efficacy of nonsurgical (i.e. referring to peri-implant mucositis and peri-implantitis) and surgical (i.e. referring to peri-implantitis) treatments with alternative or adjunctive measures on changing signs of inflammation compared with conventional nonsurgical and surgical treatments alone?”.

Population: patients with peri-implant mucositis and peri-implantitis based on case definitions used in respective publications

Intervention: alternative or adjunctive measures to nonsurgical and surgical treatments

Comparison: conventional measures for nonsurgical and surgical treatments

Outcome: changes in peri-implant mucosal inflammation

Search strategy

The PubMed database of the U.S. National Library of Medicine and the Web of Knowledge of Thomson Reuters were used as electronic databases to perform a systematic search for relevant articles published in the

dental literature between 1992 up to April 30, 2015. A commercially available software program (Endnote X7, Thomson, London, UK) was used for electronic title management. Screening was performed independently by two authors (F.S. and A.S.). Disagreement regarding inclusion during the first and second stage of study selection was resolved by discussion.

The combination of key words (i.e. Medical Subject Headings MeSH) and free text terms included:

“treatment” OR “nonsurgical treatment” OR “non-surgical treatment” OR “surgical treatment” OR “regenerative treatment” OR “augmentative treatment” OR “resective treatment” OR “reconstructive treatment” OR “therapy” OR “nonsurgical therapy” OR “non-surgical therapy” OR “surgical therapy” OR “regenerative therapy” OR “augmentative therapy” OR “resective therapy” OR “reconstructive therapy” OR “antiseptic treatment” OR “antibiotic treatment” OR “adjunctive treatment” OR “antiseptic therapy” OR “antibiotic therapy” OR “adjunctive therapy”

AND

“peri-implant disease” OR “periimplant disease” OR “peri-implant infection” OR “periimplant infection” OR “mucositis” (MeSH) OR “peri-implant mucositis” OR “periimplant mucositis” OR “Periimplantitis” (MeSH) OR “peri-implantitis”.

Electronic search was complemented by a hand search of the following journals:

Clinical Implant Dentistry and Related Research; Clinical Oral Implants Research; International Journal of Oral and Maxillofacial Implants; Journal of Clinical Periodontology; Journal of Periodontology. Finally, the references of all selected full-text articles and related reviews were scanned. If required, the corresponding authors were contacted and requested to provide missing data or information.

Study inclusion and exclusion criteria

During the first stage of study selection, the titles and abstracts were screened and evaluated according to the following inclusion criteria:

- 1) English language.
- 2) Prospective randomized controlled (RCT), or non-randomized controlled (CCT) studies (split-mouth or parallel group designs) in humans comparing alternative (i.e. for biofilm removal) or adjunctive measures (i.e. for biofilm removal, or adjunctive antiseptic/antibiotic therapy, or regenerative/resective approaches) to conventional nonsurgical (i.e. mechanical/ultrasonic debridement) or surgical (i.e. open flap debridement) treatments.
- 3) Data on the clinical changes in mucosal inflammation (i.e. bleeding scores) and probing

pocket depths (PD) following nonsurgical (referring to peri-implant mucositis and peri-implantitis) or surgical (referring to peri-implantitis) treatments in respective groups.

At the second stage of selection, all full-text articles identified during the first stage were acquired. During this procedure, the pre-selected publications were evaluated according to the following exclusion criteria:

- 1) Inclusion of less than five patients
- 2) Inadequate case definition [13]
- 3) Lack of clinical data on the changes in mucosal inflammation and PD

Quality assessment of selected studies

A quality assessment of all selected full-text articles was performed according to the Cochrane collaborations tool for assessing risk of bias (low, high, unclear) including the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data [14]. Quality assessment was performed in two different phases. In particular, during phase I, quality assessment was based on the published full-text article performed independently by both authors. In phase II, disagreements were resolved by discussion.

Data extraction and method of analysis

A data extraction template was generated and based on the study design, population, case definition, observation period, interventions, comparisons, and primary and secondary outcomes as well as the study quality. For data analysis, the bleeding index (BI)/bleeding on probing (BOP) and PD scores after respective healing periods were defined as primary outcomes. Secondary outcomes included changes in marginal bone levels, immunological/microbiological parameters and the resolution of peri-implant diseases, based on case definitions used in respective publications. RCTs and CCTs not implementing appropriate control measures but reporting on changes in primary outcomes were used for the estimation of the overall efficacy of treatments.

Heterogeneity between RCTs, meta-analysis (i.e. weighted mean changes/differences and 95 % confidence intervals, random effect model to account for potential methodological differences between studies), forest plots and publication bias (Egger's regression to quantify the bias captured by funnel plots) were assessed using a commercially available software program (Comprehensive Meta-Analysis V2, Biostat, Englewood, NJ 07631 USA).

Results

Study selection

A total of 368 potentially relevant titles and abstracts were found during the electronic and manual search. During the first stage of study selection, 319 publications were excluded based on title and abstract. For the second phase, the complete full-text articles of the remaining 49 publications were thoroughly evaluated. A total of 19 papers had to be excluded at this stage because they did not fulfil the inclusion criteria of the present systematic review (Table 1).

Finally, a total of 40 publications (reporting on 32 studies) were considered for the qualitative and quantitative assessment (Fig. 1).

Quality and risk of bias assessment of selected studies

The review author's judgement about each risk of bias item for each included RCT is presented in Table 2. In particular, the percentages across all included studies for high, low and unclear risk of bias items were 34.1, 54.8 and 11.1 %, respectively (Table 2).

Subdivision of selected studies

All selected publications were subdivided according to differences in the treatment protocol:

- o Nonsurgical treatment of peri-implant mucositis—alternative or adjunctive measures for biofilm removal (2 RCTs and 1 CCT) (Table 3)
- o Nonsurgical treatment of peri-implant mucositis—adjunctive antiseptic therapy (3 RCTs) (Table 4)
- o Nonsurgical treatment of peri-implant mucositis—adjunctive antibiotic therapy (2 RCTs) (Table 5).
- o Nonsurgical treatment of peri-implantitis—alternative measures for biofilm removal (6 RCTs) (Table 6)
- o Nonsurgical treatment of peri-implantitis—adjunctive antiseptic therapy (1 RCT) (Table 7)
- o Nonsurgical treatment of peri-implantitis—adjunctive antibiotic therapy (4 RCTs) (Table 8)
- o Surgical treatment of peri-implantitis—alternative measures for surface decontamination (3 RCTs and 1 CCT) (Table 9)
- o Surgical treatment of peri-implantitis—adjunctive resective therapy (1 RCT) (Table 10)
- o Surgical treatment of peri-implantitis—adjunctive augmentative therapy (4 RCTs, 4 CCTs) (Table 11)

Nonsurgical treatment of peri-implant mucositis

The case definitions markedly differed among the studies investigated. While three studies considered mucosal inflammation in the absence of radiographic bone loss [15–17], four studies also accepted a bone resorption of up to 3 mm for defining peri-implant mucositis [18–21]. Moreover, these studies used several clinical parameters

Table 1 Excluded clinical studies at the second stage of selection and the reason for exclusion

Publication	Reason for exclusion
Lavigne et al. [63]	Experimental sites without BOP at baseline
Ciancio et al. [64]	Homecare plaque control protocol
Felo et al. [65]	Homecare plaque control protocol
Bach et al. [66]	Lack of clinical data defined for the present systematic review
Dörtbudak et al. [67]	Lack of a conventional control treatment
Khoury and Buchmann [68]	Changes in mucosal inflammation not reported
Roos-Jansaker et al. [69]	Observational study
Duarte et al. [70]	Observational study reporting on the same study population as [71]
Maximo et al. [71]	Observational study
Ramberg et al. [72]	Homecare plaque control protocol
Corbella et al. [73]	Prevention of peri-implant diseases
Heitz-Mayfield et al. [74]	Homecare plaque control protocol
Costa et al. [5]	Observational study
De Angelis et al. [75]	Lack of subgroup analyses
Salvi et al. [76]	Observational study
Deppe et al. [59]	Observational study
De Siena et al. [77]	Homecare plaque control protocol
McKenna et al. [78]	Case definition not reported
Flichy-Fernandez et al. [79]	Cross-over study design

to assess mucosal inflammation, employed various oral hygiene instructions (OHI) and defined different intervals for maintenance care. Despite significant improvements in all of the clinical parameters investigated, test (i.e. alternative or adjunctive methods for biofilm removal, adjunctive antiseptic therapy, or adjunctive antibiotic therapy) and control treatments were commonly associated with residual gingival index (GI), BI, and/or BOP scores at 3 to 12 months after therapy (Tables 3, 4 and 5).

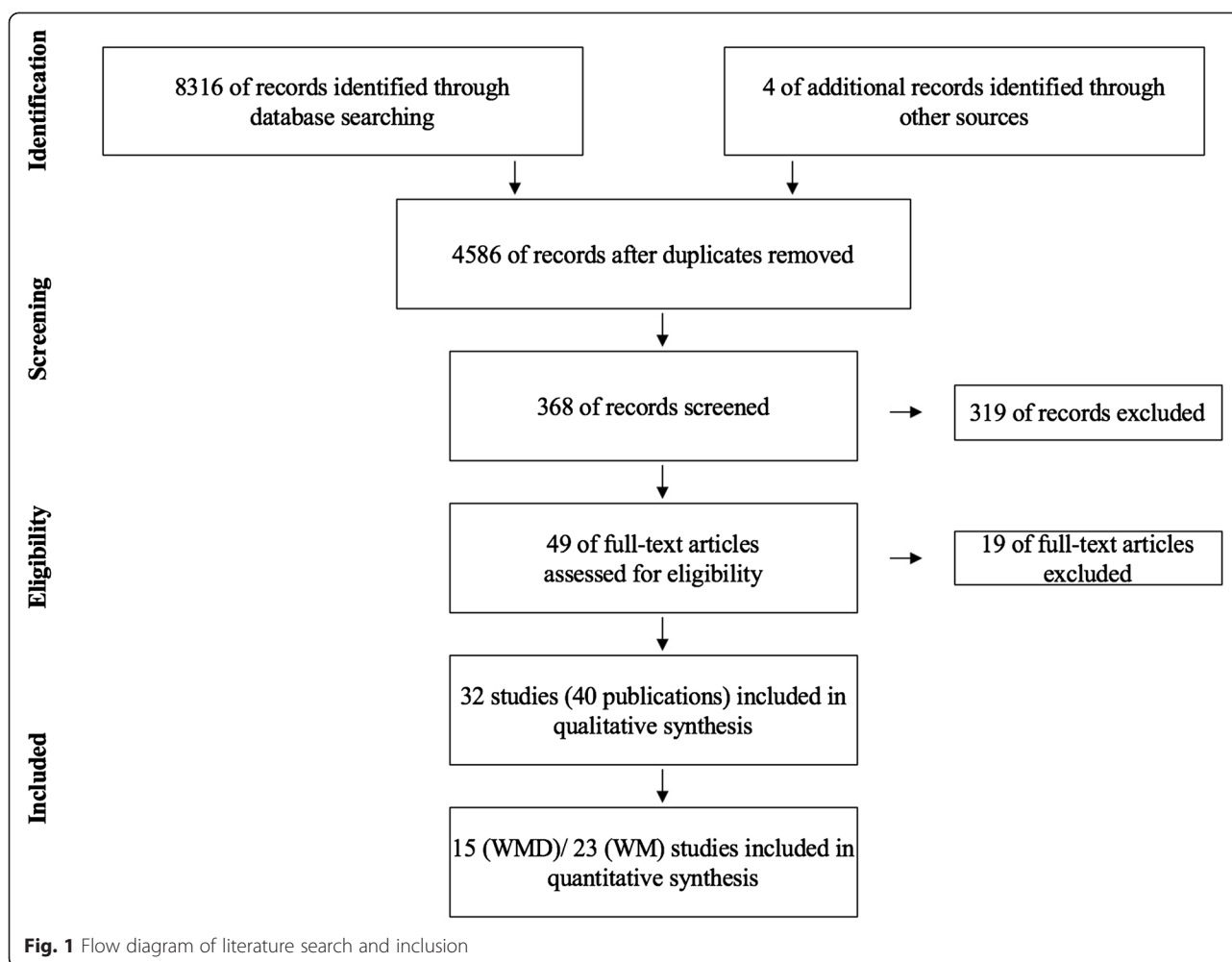
Alternative or adjunctive measures for biofilm removal

Three studies reported on alternative or adjunctive measures for biofilm removal (Table 3).

In particular, one RCT and one CCT compared the clinical efficacy of adjunctive air polishing (glycine powder) to OHI and mechanical debridement using either ultrasonic scalers or hand instruments [15, 18]. Both test and control groups were associated with significant improvements in mean BI and PD scores after therapy. When evaluating absolute values at 6 months, mean BI and PD scores were significantly lower following adjunctive air polishing to teflon curettes [18]. One RCT compared a repeated (3 and 6 months) monotherapy using an air abrasive device to ultrasonic scaling. After a healing period of 12 months, both groups revealed comparable BOP reductions and frequencies of diseased sites [21] (Table 3).

Adjunctive antiseptic therapy Three RCTs reported on the adjunctive antiseptic therapy to OHI and mechanical debridement [17, 20, 22] (Table 4).

In particular, one RCT assessed the adjunctive application of phosphoric acid gel to carbon curettes and rubber cup polishing, which was provided once every month in both groups. At 5 months, test sites revealed a significantly higher reduction in mean gingival index (GI) (modified, but not specified) and colony-forming units when compared with control sites, respectively [22]. Porras et al. [20] compared OHI + mechanical debridement with and without local pocket irrigation using chlorhexidine digluconate (CHX) + topical CHX gel application + CHX mouthwash (twice for 10 days). At 3 months, mean mucosal bleeding (mBI), BOP scores and microbiological parameters did not significantly differ between test and control groups. However, the test group revealed a significantly higher change in mean PD scores [20]. In another RCT, topical CHX gel application + full mouth disinfection + CHX mouthrinse (2×/day) and tonsil spraying (1×/day) for 14 days was compared with OHI + mechanical debridement (plastic scaler + polyetheretherketone-coated ultrasonic instruments) + full mouth scaling alone. While both treatment procedures were associated with significant PD reductions at 8 months, the BOP scores did not significantly differ to baseline in both groups [17] (Table 4).



Adjunctive antibiotic therapy Two studies reported on the adjunctive antibiotic (i.e. local or systemic) therapy to OHI and mechanical debridement [16, 19] (Table 5).

In particular, one RCT compared the adjunctive local delivery of tetracycline HCl (25 %) fibres for 10 days (test) to mechanical debridement alone (control). A complete or partial fibre loss was noted at three implants after 7 to 10 following application. While test sites were associated with marked BOP improvements, control sites revealed a further increase of BOP scores at 3 months [16]. In another RCT, a total of 45 patients were randomly allocated to either OHI + mechanical debridement (titanium curettes + rubber polishing) + systemic antibiotic medication (Azithromycin® 500 mg day 1 and 250 mg days 2–4) (test), or OHI + mechanical debridement alone (control). The subject-based, per-protocol analysis at 6 months did not reveal any significant differences between test and control groups for all clinical and microbiological parameters investigated [19] (Table 5).

Nonsurgical treatment of peri-implantitis

In all studies investigated, peri-implantitis was commonly defined by BOP and a radiographic bone loss. However, the reference points (i.e. baseline radiographs) and thresholds used to identify bone level changes were either not specified [23–25] or exhibited large variations [26–34]. Radiographic bone level changes as treatment outcome were merely assessed in three studies [28–30].

Despite significant improvements in all of the clinical and microbiological parameters investigated, test (i.e. alternative methods for biofilm removal, adjunctive antiseptic therapy, or adjunctive antibiotic therapy) and control treatments were commonly associated with residual BI and BOP scores at 3 to 12 months after therapy (Tables 6, 7 and 8).

Alternative measures for biofilm removal Six RCTs (corresponding to 7 publications) reported on the efficacy of alternative measures for biofilm removal (Table 6). In particular, two studies employed the same type of an ultrasonic device used with a hydroxyapatite

Table 2 Risk of bias summary for finally selected randomized studies

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data
Schenk et al. [16]	?	–	–	–	+
Strooker et al. [22]	?	–	–	–	+
Porras et al. [20]	?	–	–	+	–
Büchter et al. [26]	+	–	–	?	+
Romeo et al. [42, 57]	?	–	–	–	+
Karring et al. [28]	?	+	–	+	+
Schwarz et al. [25]	+	–	–	+	+
Renvert et al. [32]	+	+	–	+	+
Schwarz et al. [24]	+	–	–	+	+
Schwarz et al. [48, 51, 54]	+	–	–	+	+
Renvert et al. [29]	+	+	–	+	+
Renvert et al. [31]	+	?	–	+	+
Renvert et al. [30]	+	–	–	+	+
Sahm et al.; John et al. [27, 33]	+	–	–	+	+
Thone-Mühling et al. [17]	–	?	–	–	+
Hallström et al. [19]	+	?	–	–	+
Schwarz et al. [49, 50, 52]	+	–	–	+	+
Aghanzadeh et al. [43]	?	?	–	+	+
Machtei et al. [23]	+	+	?	+	+
Wohlfahrt et al. [55, 58]	+	+	–	+	+
deWaal et al. [38]	+	+	?	+	+
McKenna et al. [78]	+	–	+	+	–
Schär et al.; Bassetti et al. [34, 37]	+	–	–	+	
deWaal et al. [39]	+	+	?	+	+
Ji et al. [15]	+	?	–	+	+
Papadopoulos et al. [41]	+	–	–	+	+
Riben Grundström et al. [21]	+	+	–	+	+

+ low, – high, ? unclear

fluid polish [28, 31], while two studies reported on erbium-doped yttrium aluminum garnet (Er:YAG) laser monotherapy [24, 25] and two publications on glycine powder air polishing [27, 33]. One study compared Er:YAG laser monotherapy versus air polishing [30].

At 3 months after therapy, nonsurgical ultrasonic debridement was associated with a reduction in mean BOP scores, whereas these values further increased at control sites (i.e. carbon fibre currettes). However, these differences, as well as those noted for mean PD and radiographic bone level changes, did not reach statistical significance between groups [28]. Similarly, when comparing ultrasonic scaling with mechanical debridement using titanium currettes, Renvert et al. [31] also failed to identify

any significant between group differences in mean BI and PD reductions at 6 months. Furthermore, both procedures did not reduce bacterial load [35] (Table 6).

In two RCTs, the efficacy of Er:YAG laser monotherapy was compared to that of mechanical debridement using carbon fibre currettes + adjunctive local antiseptic CHX irrigation/application [24, 25]. After 6 months of healing, Er:YAG laser application was associated with significantly lower mean BOP scores than the control treatment. However, these improvements failed to reach statistical significance at 12 months, particularly at advanced sites [24, 25] (Table 6). In one RCT, glycine powder air polishing resulted in a significantly higher reduction of mean BOP scores at 3, 6, and 12 months

Table 3 Included studies—nonsurgical treatment of peri-implant mucositis: alternative or adjunctive measures for biofilm removal

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Ji et al. [15]	RCT, parallel	24 patients 33 implants Molar/premolar sites 1 implant system	PD \geq 4 mm, BOP + no radiographic bone loss compared with baseline (i.e. immediately after prosthesis installation)	3 months	OHI + mechanical debridement (ultrasonic scaler with carbon fibre tips) + air abrasive device, glycine powder (sites with PD \geq 4 mm)	OHI + mechanical debridement (ultrasonic scaler with carbon fibre tips)	Test Bl: 1.4 (0.57) (BL) to 1.1 (0.58) (3 months, subject level) Bl: 1.7 (0.93) (BL) to 1.1 (0.98) (3 months, implant level) Sites without bleeding: 29.3 % PD: 3.6 (0.47) (BL) to 3.2 (0.48) mm (3 months, subject level) Control Bl: 1.5 (0.65) (BL) to 1.0 (0.85) (3 months, subject level) Bl: 1.7 (1.0) (BL) to 0.9 (1.1) (3 months, implant level) Sites without bleeding: 42 % PD: 3.5 (0.5) (BL) to 3.1 (0.38) mm (3 months, subject level)
De Siena et al. [18]	CCT, parallel	30 patients No information on number and types of implants	BOP or spontaneous bleeding with local swelling PD \leq 3.5 mm Bone loss \leq 3.0 mm	6 months	OHI + mechanical debridement Teflon curettes, polishing) + air abrasive device, glycine powder	OHI + mechanical debridement Teflon curettes, polishing)	Test PD: 3.0 (0.4) (BL) to 2.4 (0.5) mm (6 months, subject level) 13 patients did not present bleeding at 6 months Control PD: 2.9 (0.4) (BL) to 3.0 (0.6) mm (6 months, subject level) 9 patients did not present bleeding at 6 months

Table 3 Included studies—nonsurgical treatment of peri-implant mucositis: alternative or adjunctive measures for biofilm removal (Continued)

Riben Grundström et al. [21]	RCT, parallel	37 patients	PD \geq 4 mm, BOP + with or without suppuration	12 months	OHI + air abrasive device, glycine powder	OHI + mechanical debridement (ultrasonic scaler with plastic coated tips)	BI and PD scores sign. lower in the test group at 6 months
		One implant per subject used	Bone loss \leq 2 mm from implant shoulder		Repeated treatment at 3 and 6 months	Repeated treatment at 3 and 6 months	Test BOP: 43.9 (7.3) (BL) to 12.1 (3.8) % (12 months, subject level)
		Test N = 19					Number of diseased sites (pocket depth \geq 4 mm with bleeding/ suppuration)
		Control N = 18					38 % (BL) to 8 % (12 months, subject level) Control BOP: 53.7 (7.9) (BL) to 18.6 (6.4) % (12 months, subject level)

BI bleeding index, BL baseline, BOP bleeding on probing, CCT non-randomized controlled clinical study, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

Table 4 Included studies—nonsurgical treatment of peri-implant mucositis: adjunctive antiseptic therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Strooker et al. [22]	RCT Split-mouth design	16 patients each with 4 mandibular implants and bar retained over denture	Not reported	5 months	Supra-/subgingival scaling (carbon curettes) + polishing (rubber cup) + phosphoric acid gel (35 %) in sulcus for 1 min Once every month	Supra-/subgingival scaling (carbon curettes) + polishing (rubber cup) Once every month	Test (subject level) BOP: 30.5 (27.5) (BL) to 9.7 (10.97) % (5 months) GI: 0.92 (0.75) (BL) to 0.34 (0.38) (5 months) PD: 2.97 (0.68) (BL) to 2.34 (0.54) mm (5 months) Control (subject level) BOP: 29.2 (29.44) (BL) to 14.3 (22.47) % (5 months) GI: 0.82 (0.8) (BL) to 0.57 (0.6) (5 months) PD: 2.83 (0.57) (BL) to 2.48 (0.49) mm (5 months) Sign. between group difference in mean GI values and colony-forming units at 5 months
Porras et al. [20]	RCT, parallel	16 patients 28 implants 3 implant types (plasma-sprayed Ti/cp Ti (HA-coated Ti)	Supra- and subgingival plaque PD ≤5 mm BOP + "incipient" radiographic lesion	3 months	OHI + mechanical cleansing (plastic scaler, rubber cups, polishing paste) + local irrigation CHX (0.12 %) and topical CHX gel application + 0.12 % CHX mouthrinse twice for 10 days	OHI + mechanical cleansing (plastic scaler, rubber cups, polishing paste)	mBI and BOP (%) scores: no sign. differences between groups at 1 and 3 months PD values: Test: 3.27 (0.81) (BL) to 2.71 (0.70) mm (3 months) Control: 3.48 (0.61) (BL) to 2.55 (0.72) mm (3 months) Changes in mean PD between test and control groups at 3 months were statistically significant (0.56 vs. 0.93 mm) Microbiological improvements in both groups

Table 4 Included studies—nonsurgical treatment of peri-implant mucositis: adjunctive antiseptic therapy (Continued)

Thone-Mühling et al. [17]	RCT, parallel	11 patients	BOP + and/or GI ≥ 1 absence of radiographic bone loss during the last 2 years	8 months	OHI + mechanical cleansing (plastic scaler and polyetheretherketone-coated ultrasonic instruments) + topical CHX gel application once + full mouth disinfection (deep scaling in one session + CHX disinfection of tongue and tonsils) + 0.2 % CHX mouthrinse 2x/day and tonsil spraying 1x/day for 14 days	OHI + mechanical cleansing (plastic scaler and polyetheretherketone-coated ultrasonic instruments) + full mouth scaling in one session	Test
		36 implants					BOP: 0.22 (0.11) (BL) to 0.16 (0.09) % (8 months)
		2 implant types					GI: 0.6 (0.24) (BL) to 0.44 (0.23) (8 months)
							PD: 3.4 (0.68) (BL) to 2.82 (0.59) mm (8 months)
							Control
							BOP: 0.17 (0.19) (BL) to 0.17 (0.11) % (8 months)
							GI: 0.62 (0.36) (BL) to 0.43 (0.37) (8 months)
							PD: 3.49 (0.78) (BL) to 2.84 (0.64) mm (8 months)
							Bacterial recolonization over time

BL baseline, BOP bleeding on probing, GI modified gingival index, mBI modified bleeding index, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

Table 5 Included studies—nonsurgical treatment of peri-implant mucositis: adjunctive antibiotic therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Schenk et al. [16]	RCT Split-mouth design	8 patients 24 implants 1 implant type (endosseous part: titanium and zirconoxide/transmucosal part: titanium oxinitride)	PD >4 mm BOP on at least 1 site per implant ± mucosal hyperplasia no radiographic bone loss	3 months	Supra-/subgingival scaling (steel curettes) + polishing (rubber cup) + locally delivered tetracycline HCl (25 %) fibre for 10 days +0.2 % CHX mouthrinse twice for 10 days	Supra-/subgingival scaling (steel curettes) + polishing (rubber cup) + +0.2 % CHX mouthrinse twice for 10 days	<p>ΔBOP (3 months, subject level)</p> <p>Test: -17 ± 25 %</p> <p>Control: 15 ± 37 %</p> <p>PD/CAL values without significant changes in both groups</p> <p>No adverse events</p> <p>Partial/complete fibre loss at three sites</p>
Hallström et al. [19]	RCT, parallel	45 patients 3 implant systems	PD ≥4 mm BOP + and/or pus Radiographic bone loss ≤2 mm	6 months	OHI + mechanical cleansing (titanium curettes + rubber cups + polishing paste) + Azithromycin® 500 mg day 1 and 250 mg days 2–4	OHI + mechanical cleansing (titanium curettes + rubber cups + polishing paste)	<p>Test</p> <p>BOP: 82.6 (24.4) (BL) to 27.3 (18.8) % (6 months, subject level)</p> <p>PD at worst site: 5.5 (0.8) (BL) to 4.1 (1.2) mm (6 months, subject level)</p> <p>Control</p> <p>BOP: 80.0 (25.0) (BL) to 47.5 (32.3) % (6 months, subject level)</p> <p>PD at worst site: 5.7 (0.8) (BL) to 4.9 (1.1) mm (6 months, subject level)</p> <p>Odds ratio of a positive treatment outcome (PD ≤ 4.0 mm and BOP ≤ 1) was 4.5:1 (test vs. control)</p> <p>Comparable reductions in bacterial counts</p>

BL baseline, BOP bleeding on probing, CAL clinical attachment level, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

Table 6 Included studies—nonsurgical treatment of peri-implantitis: alternative measures for biofilm removal

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Karring et al. [28]		11 patients 22 implants machined and medium-rough surfaces	PD \geq 5 mm, BOP + bone loss >1.5 mm and exposed threads	3 months	OHI + ultrasonic device with hydroxyapatite fluid polish	OHI + mechanical debridement (carbon fibre curettes)	Test BOP: 63.6 (BL) to 36.4 % (3 months, subject level) PD: 5.8 (1.1) (BL) to 5.8 (1.2) mm (3 months, subject level) Radiographic bone level changes: 0.1 (0.5) mm (3 months, subject level) Control BOP: 72.7 (BL) to 81.8 % (3 months, subject level) PD: 6.2 (1.6) (BL) to 6.3 (2.2) mm (3 months, subject level) Radiographic bone level changes: -0.2 (1.2) mm (3 months, subject level) Absence of BOP at 7/11 (test) and 2/11 (control) sites
Schwarz et al. [25]	RCT, parallel	20 patients 32 implants rough and medium-rough surfaces	PD \geq 4 mm, BOP + and pus Radiographic bone loss	6 months	OHI + Er:YAG laser device (cone-shaped glass fibre tip) at 12.7 J/cm ²	OHI + mechanical debridement (plastic curettes), 0.2 % CHX pocket irrigation and 0.2 % CHX gel	Test BOP: 83.2 (17.2) (BL) to 31.1 (10.1) % (6 months, subject level) PD: 5.4 (1.2) (BL) to 4.6 (1.1) mm (6 months, subject level) Control BOP: 81.3 (19.0) (BL) to 58.3 (16.9) % (6 months, subject level) PD: 5.5 (1.5) (BL) to 4.8 (1.4) mm (6 months, subject level) BOP scores at 6 months were significantly lower in the test group

Table 6 Included studies—nonsurgical treatment of peri-implantitis: alternative measures for biofilm removal (*Continued*)

Schwarz et al. [24]	RCT, parallel	20 patients	PD \geq 4 mm, BOP + and pus	12 months	OHI + Er:YAG laser device (cone-shaped glass fibre tip) at 12.7 J/cm ²	OHI + mechanical debridement (plastic curettes), 0.2 % CHX pocket irrigation and 0.2 % CHX gel	Test
		40 implants rough and medium-rough surfaces	Radiographic bone loss				Moderately deep sites
							BOP: 81.7 (6.7) (BL) to 35.0 (6.3) % (12 months, subject level)
							PD: 4.5 (1.4) (BL) to 4.0 (0.1) mm (12 months, subject level)
							Deep sites
							BOP: 79.9 (4.8) (BL) to 55.0 (6.5) % (12 months, subject level)
							PD: 5.9 (0.1) (BL) to 5.4 (0.1) mm (12 months, subject level)
							Control
							Moderately deep sites
							BOP: 81.6 (5.2) (BL) to 53.3 (7.3) % (12 months, subject level)
							PD: 4.4 (0.2) (BL) to 4.3 (0.1) mm (12 months, subject level)
							Deep sites
							BOP: 88.3 (3.5) (BL) to 66.6 (5.5) % (12 months, subject level)
							PD: 5.9 (0.3) (BL) to 5.5 (0.2) mm (12 months, subject level)
							No significant differences between groups at 12 months
Renvert et al. [31]	RCT, parallel	31 patients	PD \geq 4 mm, BOP + and/or pus	6 months	OHI + ultrasonic device with hydroxyapatite fluid polish	OHI + mechanical debridement (titanium curettes)	Test
		31 implants machined and medium-rough surfaces	Bone loss <2.5 mm				Bl: 1.7 (0.6) (BL) to 1.2 (0.7) (6 months, subject level)
							PD: 4.3 (0.6) (BL) to 3.9 (0.8) mm (6 months, subject level)
							Control
							Bl: 1.7 (0.9) (BL) to 1.4 (1.0) (6 months, subject level)

Table 6 Included studies—nonsurgical treatment of peri-implantitis: alternative measures for biofilm removal (Continued)

							PD: 6.2 (1.6) (BL) to 6.3 (2.2) mm (6 months, subject level)
							No significant differences between groups
Renvert et al. [30]	RCT, parallel	42 patients	PD \geq 5 mm, BOP + and/or pus	6 months	OHI + air abrasive device, glycine powder	OHI + Er:YAG laser device (cone-shaped glass fibre tip, 12.7 J/cm ²)	Test
		90 implants machined and medium-rough surfaces	Bone loss >3 mm				PD changes: 0.9 (0.8) mm (6 months, implant level)
							Radiographic bone level change: -0.3(0.9) mm (6 months, subject level)
							Positive treatment outcome: 47 %
							Control
							PD changes: 0.8 (0.5) mm (6 months, implant level)
							Radiographic bone level change: -0.1(0.8) mm (6 months, subject level)
							Positive treatment outcome: 44 %
							No significant differences between groups
Sahm et al.; John et al. [27, 33]	RCT, parallel	32 patients (BL)	PD \geq 4 mm, BOP + with suppuration	12 months	OHI + air abrasive device, glycine powder	OHI + mechanical debridement (carbon currettes + 0.1 % CHX)	Test
		25 patients (12 months)	Bone loss \leq 33 %				BOP: 99.0 (4.1) (BL) to 57.8 (30.7) % (12 months, subject level)
		36 implants					PD: 3.7 (1.0) (BL) to 3.2 (1.1) mm (12 months, subject level)
		8 implant systems					Control
							BOP: 94.7 (13.7) (BL) to 78.1 (30.0) % (12 months, subject level)
							PD: 3.9 (1.1) (BL) to 3.5 (1.2) mm (12 months, subject level)
							BOP: significant difference between groups at 3, 6 and 12 months

BI bleeding index, BL baseline, BOP bleeding on probing, CHX chlorhexidine digluconate, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

Table 7 Included studies—nonsurgical treatment of peri-implantitis: adjunctive antiseptic therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Machtei et al. [23]	Multicentre RCT, parallel	60 patients	PD = 6–10 mm and BOP + radiographic bone loss	6 months	OHI + ultrasonic debridement + matrix containing 2.5-mg CHX chips (i.e. up to 4 per implant site)	OHI + ultrasonic debridement + biodegradable crosslinked gelatin matrix chip	Test
		77 implants			Repeated application at sites with PD \geq 6 mm at 2, 4, 6, 8, 12 and 18 weeks	Repeated application at sites with PD \geq 6 mm at 2, 4, 6, 8, 12 and 18 weeks	BOP: 100 (0.0) (BL) to 42.5 (50.0) % (6 months, subject level) PD: 7.6 (1.1) (0.0) to 5.47 (1.86) mm (6 months, subject level) Control BOP: 100 (0.0) (BL) to 54.5 (50.5) % (6 months, subject level) PD: 7.21 (1.08) (BL) to 5.48 (1.25) mm (6 months, subject level) BOP and PD reductions at 6 months not sign. different between groups

BL baseline, BOP bleeding on probing, CHX chlorhexidine digluconate, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

when compared with mechanical debridement + local antiseptic therapy using CHX. The application of this specific air abrasive device was not associated with any emphysema formation or complications in peri-implant wound healing [27, 33]. At more advanced sites, Er:YAG laser monotherapy and glycine powder air polishing resulted in comparable BOP/PD reductions and crestal bone level changes, but failed to reduce bacterial load [36] (Table 6).

Adjunctive antiseptic therapy One multicenter RCT reported on the adjunctive antiseptic therapy to ultrasonic debridement (Table 7). In particular, a CHX containing matrix was repeatedly applied at 2, 4, 6, 8, 12 and 18 weeks until PD was reduced to \leq 5 mm. At 6 months, CHX chips resulted in a significantly higher PD reduction than the placebo chips [23].

Adjunctive antibiotic therapy Three RCTs reported on the adjunctive local antibiotic therapy to mechanical debridement (Table 8). In particular, minocycline microspheres were either applied once [32] at baseline or repeatedly [29] at 30 and 90 days and compared with local antiseptic therapy using CHX gel (1.0 %). At 12 months, minocycline was associated with significantly

higher BOP (refers to a repeated application) and PD (refers to a single application) reductions when compared with the control group. The radiographic (refers to a repeated application) and microbiological analyses failed to reveal any significant differences between both groups. Similar clinical outcomes were also noted when doxycycline hyclate was used as an adjunct to mechanical debridement [26].

In one RCT, adjunctive local antibiotic therapy (minocycline microspheres) was compared to adjunctive antimicrobial photodynamic therapy. At 12 months, both test and control groups were associated with significant but comparable clinical, microbiological and immunological improvements [34, 37] (Table 8).

The weighted mean (WM) BOP and PD reductions following conventional nonsurgical treatment (referring to the control groups in respective studies) [23–27] amounted to 31.12 % [SE = 9.14; 95 % CI (12.20, 49.05)] and 0.71 mm [SE = 0.32; 95 % CI (0.07, 1.35)], respectively. The weighted mean (WM) BOP and PD reductions for alternative/adjunctive measures (i.e. air polishing, aPDT, CHX chip, doxycycline, Er:YAG laser) [23–27] amounted to 42.85 % [SE = 9.24; 95 % CI (24.70, 60.97)] and 0.87 mm [SE = 0.29; 95 % CI (0.29, 1.44)], respectively.

Table 8 Included studies—nonsurgical treatment of peri-implantitis: adjunctive antibiotic therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Büchter et al. [26]	RCT, parallel	28 patients 48 implants medium-rough surfaces	PD >5 mm Bone loss >50 %	18 weeks	OHI + mechanical debridement (plastic curettes) + 0.2 % CHX pocket irrigation + 8 % doxycycline hyclate	OHI + mechanical debridement (plastic curettes) + 0.2 % CHX pocket irrigation	Test BOP: 0.54 (0.07) (BL) to 0.27 (0.06) % (18 weeks, subject level) PD: 5.64 (0.32) (BL) to 4.49 (0.29) mm (18 weeks, subject level) Control BOP: 0.63 (0.06) (BL) to 0.50 (0.07) % (18 weeks, subject level) PD: 5.68 (0.28) (BL) to 5.4 (0.34) mm (18 weeks, subject level) BOP and PD reductions sign. higher in the test group
Renvert et al. [32]	RCT, parallel	32 patients 1–5 (test)/1–6 (control) implants per patient machined surfaces	PD ≥4 mm, BOP + with suppuration Bone loss ≤3 threads Presence of anaerobic bacteria	12 months	OHI + mechanical debridement (scalers + rubber cup + polishing) + 1 mg minocycline microspheres	OHI + mechanical debridement (scalers + rubber cup + polishing) + 1.0 % chlorhexidine gel	Test BOP: 88 (12) (BL) to 71 (22) % (12 months, subject level) PD: 3.9 (0.7) (BL) to 3.6 (0.6) mm (12 months, subject level) Control BOP: 86 (14) (BL) to 78 (13) % (12 months, subject level) PD: 3.9 (0.3) (BL) to 3.9 (0.4) mm (12 months, subject level) PD reductions at 12 months sign. higher in the test group Comparable microbiological improvements in both groups
Renvert et al. [29]	RCT, parallel	32 patients 95 implants machined surfaces	PD ≥4 mm, BOP + with suppuration Bone loss ≤3 threads Presence of anaerobic bacteria	12 months	OHI + mechanical debridement + 1 mg minocycline microspheres Treatment was repeated at days 30 and 90	OHI + mechanical debridement + 0.5 ml of 1.0 % CHXgel Treatment was repeated at days 30 and 90	Test BOP: 86.5 (20.1) (BL) to 48.1 (20.7) % (12 months, implant level) PD: 3.85 (1.04) (BL) to 3.55 (0.98) mm (12 months, implant level)

Table 8 Included studies—nonsurgical treatment of peri-implantitis: adjunctive antibiotic therapy (Continued)

Schär et al.; Bassetti et al. [34, 37]	RCT, parallel	40 patients	PD = 4–6 mm, BOP + bone loss = 0.5–2 mm	12 months	OHI + mechanical debridement (titanium curettes + glycin powder air polishing, pocket irrigation using 3 % hydrogen peroxide) + aPDT (660 nm, phenothiazine chloride dye)	OHI + mechanical debridement (titanium curettes + glycin powder air polishing, pocket irrigation using 3 % hydrogen peroxide) + minocycline microspheres	<p>Radiographic bone levels: 0.77 (0.85) (BL) to 0.7 (0.85) mm (12 months, implant level)</p> <p>Control</p> <p>BOP: 89.2 (17.2) (BL) to 63.5 (19.2) % (12 months, implant level)</p> <p>PD: 3.87 (1.16) (BL) to 3.72 (1.02) mm (12 months, implant level)</p> <p>Radiographic bone levels: 0.41 (0.7) (BL) to 0.46 (0.76) mm (12 months, implant level)</p> <p>BOP reductions at 12 months sign. higher in the test group</p> <p>Comparable microbiological improvements in both groups</p> <p>Test</p> <p>BOP change: 57 % (12 months, subject level)</p> <p>PD changes: 0.56 mm (12 months, subject level)</p> <p>Complete resolution of mucosal inflammation: 31.6 %</p> <p>Control</p> <p>BOP change: 65 % (12 months, subject level)</p> <p>PD changes: 0.11 mm (12 months, subject level)</p> <p>Complete resolution of mucosal inflammation: 35.0 %</p> <p>No significant differences in clinical, microbiological and immunological parameters between groups</p>
		40 implants medium- rough surfaces					

aPDT antimicrobial photodynamic therapy, BL baseline, BOP bleeding on probing, CHX chlorhexidine digluconate, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study

Table 9 Included studies—surgical treatment of peri-implantitis: alternative measures for surface decontamination

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Deppe et al. [40]	CCT, parallel	32 patients 73 implants machined, rough- and medium-rough surfaces	PD \geq 5 mm, BOP + progressive vertical bone loss	5 years	OHI + open flap ^a surgery + air polishing + carbon dioxide laser (cw mode, 2.5 W, 12 \times 5 s) decontamination + soft tissue resection	OHI + open flap ^b surgery + air polishing + soft tissue resection	Test SBI: 0.6 (0.3) (BL) to 1.8 (1.1) (48 months, implant level) PD: 6.1 (1.6) (BL) to 3.4 (1.5) mm (48 months, implant level) Control SBI: 0.7 (0.8) (BL) to 1.1 (1.2) (48 months, implant level) PD: 5.1 (1.3) (BL) to 4.3 (1.2) mm (48 months, implant level) Comparable outcomes in both groups
De Waal et al. [38]	RCT, parallel	30 patients 79 implants machined, rough- and medium-rough surfaces	PD \geq 5 mm, BOP + and/or suppuration Bone loss \geq 2 mm	12 months	OHI/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + surface debridement using surgical gauzes soaked in saline + decontamination using 0.12 % CHX + 0.05 % cetylpyridinium chloride CPC	OHI/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + surface debridement using surgical gauzes soaked in saline + decontamination using placebo solution	Test BOP: 80.4 (26.5) (BL) to 60.5 (30.1) % (12 months, implant level) PD: 6.6 (1.6) (BL) to 4.3 (2.1) mm (12 months, implant level) MBL: 4.3 (2.1) (BL) to 5.0 (2.5) mm (12 months, implant level) Control BOP: 79.7 (28.1) (BL) to 57.2 (29.0) % (12 months, implant level) PD: 5.5 (1.4) (BL) to 3.7 (0.8) mm (12 months, implant level)

Table 9 Included studies—surgical treatment of peri-implantitis: alternative measures for surface decontamination (Continued)

							MBL: 3.6 (1.9) (BL) to 3.9 (2.0) mm (12 months, implant level)
							No sign. differences in BOP and PD reductions between groups
De Waal et al. [39]	RCT, parallel	44 patients	PD \geq 5 mm, BOP + and/or suppuration	12 months	OHI/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + surface debridement using surgical gauzes soaked in saline + decontamination using 0.12 % CHX + 0.05 % cetylpyridinium chloride	OHI/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + surface debridement using surgical gauzes soaked in saline + decontamination using 2.0 % CHX	Test
		108 implants machined, rough- and medium-rough surfaces	Bone loss \geq 2 mm				BOP: 82.1 (23.9) (BL) to 42.7 (34.2) % (12 months, implant level)
							PD: 4.7 (1.0) (BL) to 3.0 (0.7) mm (12 months, implant level)
							MBL: 4.0 (1.5) (BL) to 4.3 (1.7) mm (12 months, implant level)
							Control
							BOP: 74.2 (27.8) (BL) to 37.0 (35.5) % (12 months, implant level)
							PD: 5.0 (1.2) (BL) to 2.9 (0.7) mm (12 months, implant level)
							MBL: 4.1 (1.6) (BL) to 4.1 (1.7) mm (12 months, implant level)
							No sign. differences in BOP and PD reductions between groups

Table 9 Included studies—surgical treatment of peri-implantitis: alternative measures for surface decontamination (Continued)

Papadopoulos et al. [41]	RCT, parallel	16 patients	PD \geq 6 mm, BOP + and/or suppuration	6 months	Mechanical debridement + open flap surgery + mechanical debridement (plastic curettes) and cotton swabs soaked in saline	Mechanical debridement + open flap surgery + mechanical debridement (plastic curettes) and cotton swabs soaked in saline + 980 nm diode laser application	Test
		16 implants	Radiographic bone loss \geq 2 mm				<p>BOP: 81.2 (BL) to 23.8 % (6 months, implant level)</p> <p>PD: 5.92 (BL) to 4.44 mm (6 months, implant level)</p> <p>Control</p> <p>BOP: 81.2 (BL) to 23.8 % (6 months, implant level)</p> <p>PD: 5.52 (BL) to 4.31 mm (6 months, implant level)</p> <p>Sign. BOP and PD reductions in both groups at 6 months</p>

BL baseline, BOP bleeding on probing, CCT non-randomized controlled clinical study, CHX chlorhexidine digluconate, MBL marginal bone level, OHI oral hygiene instructions, PD probing pocket depth, RCT randomized controlled clinical study, SBI sulcus bleeding index

^aSubgroup analysis of $n = 17$ implants

^bSubgroup analysis of $n = 16$ implants

Table 10 Included studies—surgical treatment of peri-implantitis: adjunctive resective therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Romeo et al. [42, 57]	RCT, parallel	17 patients	Suppuration or sulcus bleeding, PD >4 mm horizontal peri-implant translucency	36 months	Full mouth disinfection/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + decontamination using metronidazole + tetracycline hydrochloride (3 min) + implantoplasty using diamond and arkansas burs/silicone polishers	Full mouth disinfection/mechanical debridement + resective therapy (apical re-positioned flap + bone re-contouring) + decontamination using metronidazole + tetracycline hydrochloride (3 min)	Test BOP: 2.83 (0.47) (BL) to 0.5 (0.69) (24 months ^a , implant level)PD: 5.79 (1.69) (BL) to 3.58 (1.06) mm (24 months ^a , implant level) MBL: 0.0–0.01 mm (36 months, implant level) Control BOP: 2.86 (0.35) (BL) to 2.33 (0.74) (24 months ^a , implant level) PD: 6.52 (1.62) (BL) to 5.5 (1.47) mm (24 months ^a , implant level) MBL: 1.44–1.54 mm (36 months, implant level)

22 implants rough surfaces

BL baseline, BOP bleeding on probing, MBL marginal bone loss, PD probing pocket depth, RCT randomized controlled clinical study
^aAll patients of the control group were discontinued from the study due to persistent clinical signs of inflammation

Surgical treatment of peri-implantitis

Twelve studies (18 publications) reported on the surgical treatment of peri-implantitis, employing either alternative measures for surface decontamination (3 RCTs and 1 CCT) [38–41], adjunctive resective (1 RCT) [42] or augmentative (4 RCTs and 4 CCTs) [40, 43–55] therapy. In these studies, peri-implantitis was commonly defined by BOP and a radiographic bone level changes. However, the thresholds used to assess bone loss revealed large variations and defect configurations (i.e. supra-/intra-bony defects) [56] were rarely reported (Tables 9, 10 and 11).

Alternative measures for surface decontamination In one CCT, Deppe et al. [40] assessed the clinical efficacy of carbon dioxide laser decontamination used as an

adjunct to resective flap surgery + air polishing (control). While the test treatment improved the clinical outcomes over the control measure at 4 months, mean SBI and PD values were comparable in both groups at about 5 years (Table 9).

In further two studies, De Waal et al. [38, 39] employed an open flap debridement using gauzes soaked in sterile saline + bone re-contouring + apical flap re-positioning and compared one test (0.12 % CHX + 0.05 % cetylpyridinium chloride) and two control (placebo solution or 2.0 % CHX) measures for surface decontamination. At 12 months, the test and both control procedures were associated with marked but comparable reductions in mean BOP and PD scores, respectively. Furthermore, between group comparisons

Table 11 Included studies—surgical treatment of peri-implantitis: adjunctive augmentative therapy

Publication	Design	Population	Case definition	Period	Test	Control	Mean (SD) outcome
Schwarz et al. [48, 51, 54]	RCT, parallel	20 patients	PD >6 mm, BOP + and/or pus	4 years nonsubmerged healing	OHI + initial nonsurgical therapy	OHI + initial nonsurgical therapy	Test
		21 implants machined and medium-rough surfaces	Intrabony defect >3 mm				Open flap surgery + mechanical debridement (plastic curettes) + nanocrystalline hydroxyapatite paste
							PD reduction: 2.5 (0.9) mm (4 years, subject level)
							Control
							BOP reduction: 51 % (4 years, subject level)
							PD reduction: 1.1 (0.3) mm (4 years, subject level)
							BOP and PD reductions sign. higher at control sites
Deppe et al. [40]	CCT, parallel	32 patients	PD ≥5 mm, BOP + progressive vertical bone loss	5 years	Group 2 OHI + open flap ^a surgery + air polishing + carbon dioxide laser (cw mode, 2.5 W, 12 × 5 s) decontamination + beta tricalcium phosphate + cortical bone chips harvested from the retromolar area (50:50) + nonresorbable synthetic barrier membrane	Group 4 OHI + open flap ^b surgery + air polishing + beta tricalcium phosphate + cortical bone chips harvested from the retromolar area (50:50) + nonresorbable synthetic barrier membrane	Test
		73 implants machined, rough- and medium-rough surfaces					
							PD: 4.8 (1.4) (BL) to 2.5 (1.1) mm (48 months, implant level)
							Control
							SBI: 1.2 (0.6) (BL) to 1.9 (1.0) (48 months, implant level)
							PD: 5.7 (1.4) (BL) to 2.5 (1.4) mm (48 months, implant level)

Table 11 Included studies—surgical treatment of peri-implantitis: adjunctive augmentative therapy (Continued)

							Comparable outcomes in both groups
Roos-Jansaker et al. [45–47]	CCT, parallel	25 patients	BOP + and/or pus	5 years transmucosal healing systemic antibiotic medication (amoxicillin + metronidazole for 10 days)	Removal of the suprastructure	Removal of the suprastructure	Test
		45 implants machined and medium-rough surfaces	Bone loss ≥ 3 threads one- to four-wall defects		Open flap surgery + debridement + decontamination using hydrogen peroxide 3 % algae derived xenograft + resorbable synthetic barrier membrane	Open flap surgery + debridement + decontamination using hydrogen peroxide 3 % algae derived xenograft +	PD reduction: 3.0 (2.4) mm (5 years, implant level)
							Radiographic defect fill: 0.1 (0.5) mm (5 years, implant level)
							Control
							PD reduction: 3.3 (2.0) mm (5 years, implant level)
							Radiographic defect fill: 0.1 (0.5) mm (5 years, implant level)
							Comparable defect fill and BOP reductions in both groups
Schwarz et al. [53]	CCT, parallel	27 patients	PD >6 mm, BOP + and/or pus	12 months nonsubmerged healing	Circumferential-type (Ie) defects OHI + initial nonsurgical therapy	Buccal dehiscence-type defects with a semicircular (Ib) or circular component (Ic)	Test Ib
		27 implants machined and medium-rough surfaces	Intrabony defect >3 mm		Open flap surgery + mechanical debridement (carbon curettes) + decontamination (cotton pellets soaked in saline)	OHI + initial nonsurgical therapy Open flap surgery + Mechanical debridement (carbon curettes) + decontamination (cotton pellets soaked in saline)	BOP reduction: 38.9 (16.6) % (12 months, subject level)
			Supracrestal component ≤ 1 mm		Bovine-derived xenograft + native collagen barrier membrane	Bovine-derived xenograft + native collagen barrier membrane	PD reduction: 1.6 (0.9) mm (12 months, subject level)
							Test Ic
							BOP reduction: 25.9 (14.7) % (12 months, subject level)
							PD reduction: 1.6 (0.7) mm (12 months, subject level)
							Control Ie
							BOP reduction: 61.1 (16.7) % (12 months, subject level)

Table 11 Included studies—surgical treatment of peri-implantitis: adjunctive augmentative therapy (Continued)

Rocuzzo et al. [44]	CCT, parallel	26 patients	PD \geq 6 mm	12 months nonsubmerged healing simultaneous connective tissue graft at sites lacking keratinized mucosa systemic antibiotic medication (amoxicillin + clavulanic acid for 6 days)	SLA surfaced implants	TPS surfaced implants	PD reduction: 2.7 (0.7) mm (12 months, subject level) Sign. difference in BOP reductions between Ic and le
		26 implants rough and medium-rough surfaces	Crater-like (intrabony) defects		OHI	OHI	BOP reduction: 60.4 % (12 months, subject level)
				Open flap surgery + mechanical debridement (plastic curettes) + decontamination (24 % EDTA and 1 % CHX gel) + bovine-derived xenograft	Open flap surgery + mechanical debridement (plastic curettes) + decontamination (24 % EDTA and 1 % CHX gel) + bovine-derived xenograft	PD reduction: 3.4 (1.7) mm (12 months, subject level)	
							Radiographic defect fill: 1.9 (1.3) mm (12 months, subject level) Control BOP reduction: 33.9 % (12 months, subject level) PD reduction: 2.1 (1.2) mm (12 months, subject level) Radiographic defect fill: 1.6 (0.7) mm (12 months, subject level) BOP and PD reductions sign. higher in the test group

Table 11 Included studies—surgical treatment of peri-implantitis: adjunctive augmentative therapy (Continued)

Author	Study Design	Patients	PD	Healing Time	Intervention	Control	Outcomes
Schwarz et al. [49, 50, 52]	RCT, parallel	17 patients	PD >6 mm, BOP + and/or pus	4 years nonsubmerged healing	OHI + initial nonsurgical therapy	OHI + initial nonsurgical therapy	Test
		17 implants machined and medium-rough surfaces	Intrabony defect >3 mm Supracrestal component >1 mm	Open flap surgery + debridement + decontamination using an Er:YAG laser device (cone-shaped glass fibre tip) at 11.4 J/cm ² implantoplasty at buccally and supracrestally exposed implant parts Bovine-derived xenograft + native collagen barrier membrane at intrabony components	Open flap surgery + Mechanical debridement (plastic curettes) + decontamination (cotton pellets soaked in saline) implantoplasty at buccally and supracrestally exposed implant parts Bovine-derived xenograft + native collagen barrier membrane at intrabony components	BOP reduction: 71.6 (24.9) % (4 years, subject level) PD reduction: 1.3 (1.8) mm (4 years, subject level) Control BOP reduction: 85.2 (16.4) % (4 years, subject level) PD reduction: 1.2 (1.9) mm (4 years, subject level) BOP and PD reductions comparable in both groups	
Aghanzadeh et al. [43]	RCT, parallel	45 patients	PD ≥2 mm, BOP + and pus	12 months nonsubmerged healing systemic antibiotic medication (Azithromycin for 4 days)	Open flap surgery + mechanical debridement (titanium instruments) + decontamination using hydrogen peroxide 3 % cortical bone chips harvested from the mandibular ramus + resorbable synthetic barrier membrane	Open flap surgery + mechanical debridement (titanium instruments) + decontamination using hydrogen peroxide 3 % bovine-derived xenograft + resorbable synthetic barrier membrane	Test
		75 implants medium-rough surfaces	Bone loss ≥2 mm Angular defects ≥3 mm in depth				BOP reduction: 44.8 (6.3) % (12 months, implant level) PD reduction: 2.0 (0.3) mm (12 months, implant level) Radiographic bone level gain: 0.2 (0.3) mm (12 months, implant level) Control BOP reduction: 50.4 (5.3) % (12 months, implant level) PD reduction: 3.1 (0.2)mm (12 months, implant level)

Table 11 Included studies—surgical treatment of peri-implantitis: adjunctive augmentative therapy (Continued)

							Radiographic bone level gain: 0.8 (0.4) mm (12 months, implant level)
							PD reductions and bone level gains were significantly higher at control sites
Wohlfahrt et al. [55, 58]	RCT, parallel	33 patients	PD \geq 5 mm, BOP + intrabony defects \geq 4 mm	12 months submerged healing for 6 months	Open flap surgery + mechanical debridement (titanium curettes) + conditioning using 24 % ethylenediaminetetraacetic acid gel (2 min) + augmentation of intrabony defect components using porous titanium granules	Open flap surgery + mechanical debridement (titanium curettes) + conditioning using 24 % ethylenediaminetetraacetic acid gel (2 min)	Test
		33 implants medium-rough surfaces					BOP reduction: 0.38 (2.1) % (12 months, implant level)
							PD reduction: 1.7 (1.7) mm (12 months, implant level)
							Radiographic defect fill: 57.0 (45.1) % (12 months, implant level)
							Control
							BOP reduction: 0.56 (2.9) % (12 months, implant level)
							PD reduction: 2.0 (2.3) mm (12 months, implant level)
							Radiographic defect fill: -14.8 (83.4) % (12 months, implant level) no sign. reductions in BOP scores in both groups comparable reductions in MMP-8 and bone level markers

BL baseline, BOP bleeding on probing, CCT non-randomized controlled clinical study, CHX chlorhexidine digluconate, MMP-8 matrixmetalloproteinase-8, PD probing pocket depth, RCT randomized controlled clinical study, SBI sulcus bleeding index, SLA sand blasted and acid etched, TPS titanium plasma flamed

^aSubgroup analysis of $n = 11$ implants

^bSubgroup analysis of $n = 13$ implants

failed to reveal any significant differences in mean marginal bone loss after therapy [38, 39]. Similarly, Papadopoulos et al. [41] also failed to reveal any significant clinical improvements in mean BOP and PD scores at 6 months, when a 980-nm diode laser was used as an adjunct to mechanical open flap debridement (Table 9).

Adjunctive resective therapy One study assessed the clinical efficacy of an implantoplasty (diamond/arkansas burs + silicone polishers) when used as an adjunct to open flap debridement + bone re-contouring + apical flap re-positioning [42]. At 24 months, all patients from the control group had to be discontinued from the study due to persistent active signs of peri-implant inflammation. This was associated with elevated mBI and PD scores when compared with the test group. On the contrary, resective therapy resulted in significantly higher mean mucosal recessions (1.64 ± 1.29 vs. 2.3 ± 1.45 mm) but no pseudopocket formation [42], while test sites were associated with stable radiographic bone levels at 3 years, the interproximal bone loss at control sites amounted to 1.45–1.54 mm [57] (Table 10).

The calculated WM BOP [38, 39, 55] and PD [38–40, 55] reductions following surgical treatment (i.e. open flap with and without soft tissue resection) amounted to 34.81 % [SE = 8.95; 95 % CI (17.25, 52.37)] and 1.75 mm [SE = 0.34; 95 % CI (1.08, 2.42)].

Adjunctive augmentative therapy The clinical efficacy of adjunctive augmentative therapy to open flap debridement (titanium curettes + conditioning using 24 % ethylenediaminetetraacetic acid gel + submerged healing for 6 months) was merely assessed in one study [55]. Notably, 12/16 control and 13/16 test sites revealed a premature exposure during the submerged healing phase of 6 months. At 12 months after therapy, the application of porous titanium granules to the intrabony defect components resulted in a significantly higher percentage of radiographic defect fill when compared with open flap surgery alone. Moreover, the test group was associated with an increase in implant stability quotient, whereas these values further decreased at control sites. However, both groups revealed comparable PD reductions and only minor improvements in mean BOP scores [55]. The immunological analysis did not reveal any significant between differences in the reduction of MMP-8 levels or bone level markers [58] (Table 11). Four RCTs and four CCTs compared different augmentation protocols employing various methods for surface decontamination, bone fillers (i.e. alloplastic, xenogenic, autogenous) and barrier membranes (synthetic, native collagen) over a period of up to 5 years [40, 43–55]. The majority of these studies

considered PD and BOP reductions as primary outcomes but also reported on radiographic defect fill (Table 11).

WM BOP [43, 49, 51, 53, 55] and PD [40, 43–55] reductions following adjunctive augmentative therapy amounted to 50.73 % [SE = 3.5; 95 % CI (43.87, 57.59)] and 2.20 mm [SE = 0.22; 95 % CI (1.76, 2.64)], respectively. The outcomes of therapy was mainly influenced by the type of bone filler (i.e. a slowly resorbing bovine-derived mineral was superior to autogenous bone and an alloplastic material), defect characteristics (i.e. circumferential-type defects were superior to dehiscence-type defects) and implant surface characteristics (i.e. moderately rough surfaces were superior to rough surfaces) (Table 11).

Meta-analysis

Meta-analysis to estimate the weighted mean difference (WMD) between test and control treatments was conducted on RCTs reporting on similar assessments of either absolute BOP or PD scores.

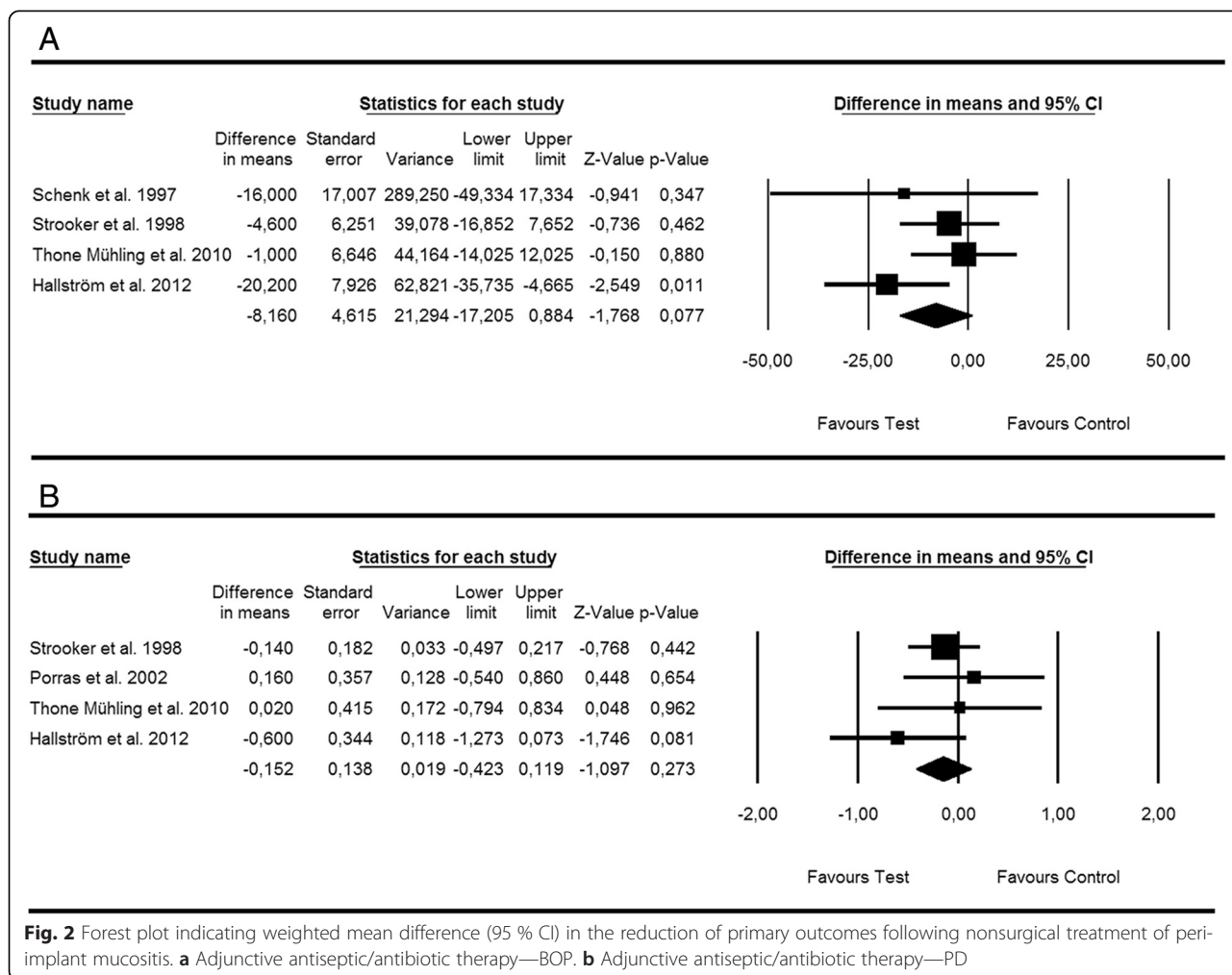
Nonsurgical treatment of peri-implant mucositis—

adjunctive antiseptics/antibiotics Based on four and four studies, WMD in BOP [16, 17, 19, 22] and PD [17, 19, 20, 22] scores amounted to -8.16 % [SE = 4.61; $p > 0.05$; 95 % CI (-17.20 , 0.88)] and -0.15 mm [SE = 0.13; $p > 0.05$; 95 % CI (-0.42 , 0.11)], not favouring local antiseptic or antibiotic (i.e. local and systemic) therapy as an adjunct to mechanical debridement (p value for heterogeneity: 0.42, $I^2 = 0.0$ % = low heterogeneity; p value for heterogeneity: 0.45, $I^2 = 0.0$ % = low heterogeneity, respectively) (Fig. 2a, b).

Egger's linear regression method revealed symmetrical plots for changes in BOP ($p = 0.51$) and PD ($p = 0.69$) thus suggesting the absence of publication bias.

Nonsurgical treatment of peri-implantitis—alternative methods for biofilm removal

Based on three studies [24, 25, 27], WMD in BOP scores between test and control groups amounted to -23.12 % [SE = 4.81; $p < 0.001$; 95 % CI (-32.56 , -13.69)] favouring alternative methods (i.e. Er:YAG laser, glycine air polishing,) for biofilm removal over mechanical debridement (p value for heterogeneity: 0.55, $I^2 = 0.0$ % = low heterogeneity; 0.39) (Fig. 3a). Based on five studies [24, 25, 27, 28, 31], WMD in PD scores between test and control groups amounted to -0.49 mm [SE = 0.21; $p < 0.05$; 95 % CI (-0.91 , -0.08)] not favouring alternative methods (i.e. Er:YAG laser, glycine air polishing, ultrasonic system) for biofilm removal over mechanical debridement (p value for heterogeneity: 0.029, $I^2 = 62.8$ % = substantial heterogeneity; 0.39) (Fig. 3b).



Egger’s linear regression method revealed symmetrical plots for changes in BOP ($p = 0.41$) and PD ($p = 0.39$) thus suggesting the absence of any publication bias.

Nonsurgical treatment of peri-implantitis—adjunctive antiseptic/antibiotic therapy Based on four studies [23, 26, 29, 32], WMD in BOP scores between test and control groups amounted to -16.53% [SE = 4.41; $p < 0.001$; 95 % CI (-25.18, -7.89)] favouring local antibiotic therapy as an adjunct to mechanical debridement (p value for heterogeneity: 0.113, $I^2 = 49.77\%$ = moderate heterogeneity) (Fig. 3c). WMD in PD scores between test and control groups amounted to -0.829 mm [SE = 0.51; $p > 0.05$; 95 % CI (-1.84, 0.18)] not favouring antiseptic/antibiotic therapy as an adjunct to mechanical debridement (p value for heterogeneity: 0.000, $I^2 = 87.37\%$ = considerable heterogeneity) (Fig. 3d).

Egger’s linear regression method revealed symmetrical plots for changes in BOP ($p = 0.17$) and PD ($p = 0.07$) thus suggesting the absence of any publication bias.

Surgical treatment of peri-implantitis - alternative measures for surface decontamination Based on two studies [38, 39], WMD in BOP and PD scores between test and control groups amounted to 5.61 % [SE = 7.68; $p > 0.05$; 95 % CI (-9.44, 20.68)] and 0.22 mm [SE = 0.22; $p > 0.05$; 95 % CI (-0.20, 0.65)] not favouring alternative (i.e. CHX + CPC) over conventional (i.e. CHX) measures for surface decontamination (p value for heterogeneity: 0.76, $I^2 = 0.0\%$ = low heterogeneity; 0.60, $I^2 = 0.0\%$ = low heterogeneity, respectively) (Fig. 4a, b).

Discussion

The present systematic review and meta-analysis was conducted to address the following focused question: “In patients with peri-implant mucositis and peri-implantitis, what is the efficacy of nonsurgical (i.e. referring to peri-implant mucositis and peri-implantitis) and surgical (i.e. referring to peri-implantitis) treatments with alternative or adjunctive measures on changing signs of inflammation compared with conventional nonsurgical and surgical treatments alone?”.

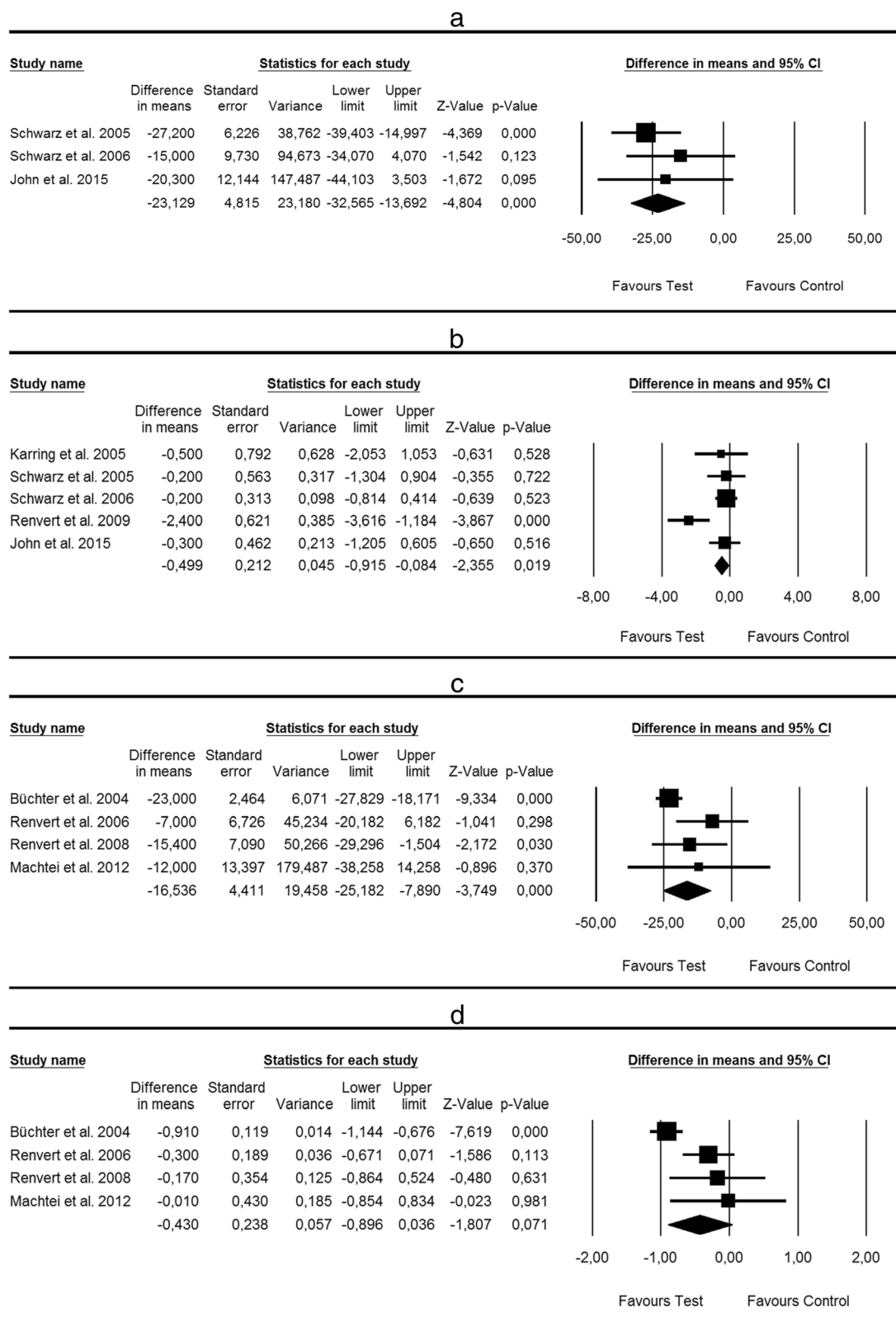
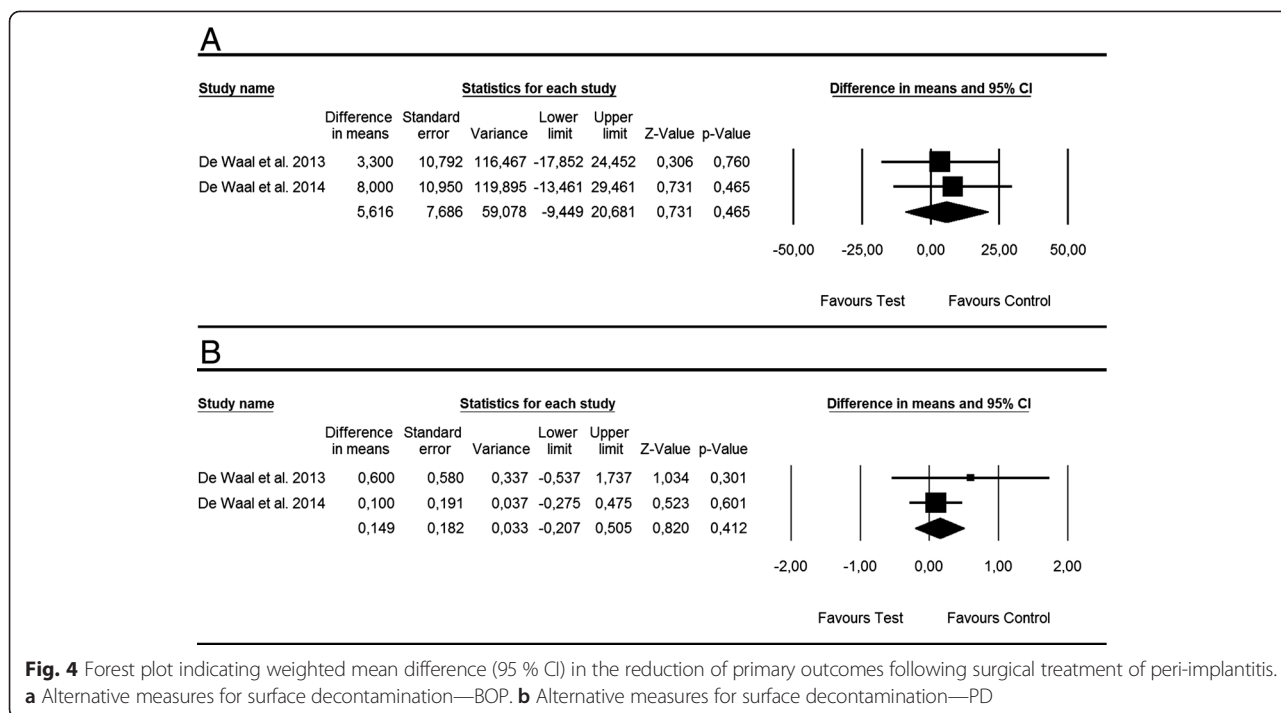


Fig. 3 Forest plot indicating weighted mean difference (95 % CI) in the reduction of primary outcomes following nonsurgical treatment of peri-implantitis. **a** Alternative measures for biofilm removal—BOP. **b** Alternative measures for biofilm removal—PD. **c** Adjunctive antibiotic therapy—BOP. **d** Adjunctive antiseptic/antibiotic therapy—PD



Basically, the literature search revealed that only a few studies considered appropriate test and control treatments needed to address the aforementioned focused question. In particular, this was true for 8 (7 RCTs and 1 CCT) [15–22] and 9 (9 RCTs) [23–26, 28, 29, 31–33] studies reporting on the nonsurgical treatment of peri-implant mucositis and peri-implantitis, as well as 5 RCTs [38, 39, 41, 42, 55] reporting on the surgical treatment of peri-implantitis. In addition, 5 RCTs and 4 CCTs not implementing appropriate control measures (i.e. mechanical/ultrasonic debridement or open flap debridement alone) but reporting on changes in primary outcomes were included for the estimation of the overall efficacy (referring to WM changes in BOP and PD scores) of nonsurgical [30, 34] and surgical [40, 43, 44, 46, 48, 52, 53] treatments of peri-implantitis. Moreover, it must be emphasized that the percentage across all included studies for high risk of bias items was 34.1 %, thus pointing to a need to improve the quality of reporting in future studies.

Within these limitations, the current data synthesis revealed that for the nonsurgical treatment of peri-implant mucositis, WMD in BOP [16, 17, 19, 22] and PD [15, 17, 19, 20, 22] scores amounted to -8.16 % and -0.15 mm, not favouring local antiseptic or antibiotic (i.e. local and systemic) therapy as an adjunct to mechanical debridement alone. Basically, these data corroborate the findings of a recent systematic review and meta-analysis, also indicating that adjunctive therapy

may not improve the efficacy of professionally administered plaque removal in reducing BOP (i.e. local antiseptic or local/systemic antibiotics), GI and PD (i.e. local antiseptics, systemic antibiotics, air abrasive device) scores at mucositis sites [9]. When considering the present narrative data synthesis on the adjunctive [15] or alternative use of glycine powder air polishing [21], it was also noted that this device did not reveal any major improvements in BI/BOP scores or disease resolution over the respective control measures. In this context, it must be emphasized that BOP is the key parameter for the diagnosis of peri-implant mucositis [1], and the “resolution of peri-implant mucosal inflammation as evidenced by the absence of BOP” was the suggested endpoint following nonsurgical treatment of mucositis lesions [13]. All these data, taken together with the present findings support the view that OHI and mechanical debridement with or without polishing tools may be defined as a current standard of care for the management of peri-implant mucositis [6].

In contrast, for the nonsurgical treatment of peri-implantitis, WMD in BOP scores amounted to -16.53 % [23, 26, 29, 32] and 23.12 % [24, 25, 27], thus favouring either adjunctive local antibiotic therapy or alternative measures for plaque removal (i.e. Er:YAG laser or glycine powder air polishing) over respective control treatments. However, these improvements were not observed when analysing WMD in PD scores between test and control groups. Basically, these observations were also supported by the differences in the estimated WM BOP (31.12 vs.

42.85 %) and PD (0.71 vs. 0.87 mm) reductions noted following nonsurgical treatment of peri-implantitis using either conventional [23–27] or alternative/adjunctive measures (i.e. air polishing, aPDT, CHX chip, doxycycline, Er:YAG laser) [23–27], respectively.

Since the suggested endpoint following nonsurgical treatment of peri-implantitis is a “composite outcome of disease resolution including the absence of deep PD with bleeding and suppuration” [13], one has to critically emphasize the limited efficacy at “deep sites”. In particular, several studies reported on increasing BOP scores between 3 and 12 months following nonsurgical treatment of “severe” peri-implantitis sites using either mechanical debridement, adjunctive aPDT, Er:YAG laser monotherapy or glycine powder air polishing. The efficacy of all treatment procedures investigated was higher at “moderately” deep sites [24, 27, 33, 59]. In this context, however, one also has to realize that PD scores at implant sites may be influenced by a variety of different local factors, including the soft tissue thickness, vertical implant positioning, or a specific design of the implant-abutment connection (e.g. platform-switching). Accordingly, the classification of a “deep” pocket needs to be accomplished on an individual basis and disease severity should also consider “proportions of affected implants per patient in the presence of multiple implants” [6].

When further analysing the present results, it was also noted that nonsurgical treatment of peri-implantitis commonly failed to result in major microbiological improvements [32, 34–37], thus potentially explaining the frequency of residual BOP scores at respective sites.

At the time being, there is a lack of clinical studies aimed at comparing the efficacy of nonsurgical and surgical treatments of peri-implantitis. However, a preclinical study employing the ligature model has indicated that open flap debridement was associated with significant histological improvements in osseous defect fill and establishment of a new bone-to-implant when compared with nonsurgical treatments. The latter outcome was mainly influenced by the method of surface decontamination [60]. Accordingly, a “proven method of decontaminating the implant surface” has been defined as a critical component in surgical therapy [13]. However, the present qualitative and quantitative analysis has indicated that the clinical, radiographical and microbiological outcomes following either open flap debridement or surgical augmentative therapy were not influenced by the decontamination protocol, including chemical or photothermal (i.e. carbon dioxide, diode- or Er:YAG laser radiation) approaches [38–41, 49, 50, 52]. Moreover, two RCTs [38, 39] reported on an additional bone loss at 6 and 12 months after open flap debridement, thus indicating that disease resolution (i.e. “absence of deep probing pocket depths with bleeding and suppuration and no additional bone loss”) [13] was commonly not achieved.

The present data synthesis also revealed a lack of RCTs/CCTs implementing appropriate test and control groups to assess the efficacy of adjunctive resective or augmentative measures over open flap debridement alone. The available studies have indicated that resective surgery (i.e. apical re-positioned flap + bone contouring) + implantoplasty was more effective in obtaining and maintaining disease resolution over resective surgery alone [42, 57]. In contrast, surgical augmentative therapy of the intrabony defect component using porous titanium granules was associated with a significantly higher radiographic defect fill, but failed to improve a reduction in mean BOP and PD scores over the control treatment [55]. When considering the estimated WM BOP (50.73 vs. 34.81 %) [38, 39, 43, 49, 51, 53, 55] and PD (2.20 vs. 1.75 mm) [38–40, 43–55] reductions, the clinical outcomes obtained following adjunctive augmentative therapy tended to be improved when compared with surgical measures alone. However, it has to be realized that for the data synthesis in the latter group, surgical procedures with and without soft tissue resection were combined, and therefore, the interpretation of the overall performance of surgical measures without augmentative measures on PD reductions is difficult. Moreover, obvious variations in the surgical procedures, including different decontamination protocols, administration of prophylactic systemic antibiotics, and modes of healing (i.e. open vs. submerged) may not allow for a direct comparison of these estimated outcomes. Basically, the estimated WM BOP and PD reductions corroborate those calculations reported in a recent systematic review on reconstructive procedures for the management of peri-implantitis. When also case series were included in the meta-analysis, these values amounted to 45.8 and 2.97 mm [61]. Furthermore, the present qualitative analysis of the available data on surgical augmentative therapy have indicated, that the outcomes of therapy may be influenced by several local factors, mainly including the physicochemical properties of the bone filler [43, 48, 51, 54], the defect configuration [53], as well as implant surface characteristics [44]. Any beneficial effect of a resorbable synthetic barrier membrane could not be identified [45–47]. Nevertheless, the available evidence did not allow for any conclusive statements on the potential superiority of any particular augmentation protocol.

Finally, it must be emphasized that laser therapy, the application of bone grafts and barrier membranes were reported to be associated with the highest cost-effectiveness ratio (i.e. costs and proportions of lost implants) among 11 treatment procedures investigated [62].

Conclusions

While OHI + mechanical debridement alone was found to be effective for the management of peri-implant mucositis,

alternative/adjunctive measures may improve the efficacy over/of conventional treatments at peri-implantitis sites. Adjunctive resective and/or augmentative measures are promising; however, their beneficial effect on the clinical outcome of surgical treatments needs to be further investigated.

Abbreviations

aPDT: antimicrobial photodynamic therapy; BOP: bleeding on probing; CAL: clinical attachment level; CCD: controlled clinical study; CHX: chlorhexidine digluconate; Er:YAG laser: erbium-doped yttrium aluminum garnet laser; GI: gingival index; mBI: (modified) bleeding index; MMP: matrix metalloproteinase; MR: mucosal recession; OHI: oral hygiene instructions; PD: probing pocket depth; RCT: randomized controlled clinical study; WM: weighted mean changes; WMD: weighted mean differences.

Competing interests

Frank Schwarz and Jürgen Becker received lecture fees and/or unrestricted research grants from Geistlich Biomaterials, Rooth, Switzerland; Osteology Foundation, Lucerne, Switzerland; EMS, Nyon, Switzerland. Frank Schwarz, Andrea Schmucker and Jürgen Becker declare that they have no competing interests related to this systematic review.

Authors' contributions

FS and JB have made substantial contributions to study conception and interpretation of data as well as manuscript preparation. AS and FS were involved in the literature search and data management as well as the statistical analysis. All authors read and approved the final manuscript.

Acknowledgements

The authors appreciate the additional information provided during the process of "contact" with the following authors: Herbert Deppe, Department of Oral and Maxillofacial Surgery at the Klinikum Rechts Der Isar, Technische Universität München, Munich, Germany; Eli Machtei, Department of Periodontology, School of Graduate Dentistry, Rambam HCC, Technion - Israeli Institute of Technology, Haifa, Israel; Giovanni Salvi, Department of Periodontology, School of Dental Medicine, University of Bern, Bern, Switzerland; Yvonne de Waal, Center for Dentistry and Oral Hygiene, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

Received: 3 June 2015 Accepted: 28 July 2015

Published online: 13 August 2015

References

- Lang NP, Berglundh T. Periimplant diseases: where are we now? Consensus of the Seventh European Workshop on Periodontology. *J Clin Periodontol.* 2011;38 Suppl 11:178–81.
- Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. *J Clin Periodontol.* 2015;42 Suppl 16:158–71.
- Renvert S, Polyzois I. Risk indicators for peri-implant mucositis: a systematic literature review. *J Clin Periodontol.* 2015;42 Suppl 16:172–86.
- Schwarz F, Mihatovic I, Golubovich V, Eick S, Iglhaut T, Becker J. Experimental peri-implant mucositis at different implant surfaces. *J Clin Periodontol.* 2014;41:513–20.
- Costa FO, Takenaka-Martinez S, Cota LO, Ferreira SD, Silva GL, Costa JE. Peri-implant disease in subjects with and without preventive maintenance: a 5-year follow-up. *J Clin Periodontol.* 2012;39:173–81.
- Jepsen S, Berglundh T, Genco R, Aass AM, Demirel K, Derks J, et al. Primary prevention of peri-implantitis: managing peri-implant mucositis. *J Clin Periodontol.* 2015;42 Suppl 16:152–7.
- Heitz-Mayfield LJ, Mombelli A. The therapy of peri-implantitis: a systematic review. *Int J Oral Maxillofac Implants.* 2014;29(Suppl):325–45.
- Klinge B, Meyle J. Working G. Peri-implant tissue destruction. The Third EAO Consensus Conference 2012. *Clin Oral Implants Res.* 2012;23 Suppl 6:108–10.
- Schwarz F, Becker K, Sager M. Efficacy of professionally administered plaque removal with or without adjunctive measures for the treatment of peri-implant mucositis. A systematic review and meta-analysis. *J Clin Periodontol.* 2015;42 Suppl 16:202–13.
- Claffey N, Clarke E, Polyzois I, Renvert S. Surgical treatment of peri-implantitis. *J Clin Periodontol.* 2008;35:316–32.
- Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.
- Miller SA, Forrest JL. Enhancing your practice through evidence-based decision making: PICO, learning how to ask good questions. *J Evid Base Dent Pract.* 2001;1:136–41.
- Sanz M, Chapple IL, Working Group 4 of the VEWoP. Clinical research on peri-implant diseases: consensus report of Working Group 4. *J Clin Periodontol.* 2012;39 Suppl 12:202–6.
- Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from <http://www.cochrane-handbook.org>. 2011.
- Ji YJ, Tang ZH, Wang R, Cao J, Cao CF, Jin LJ. Effect of glycine powder air-polishing as an adjunct in the treatment of peri-implant mucositis: a pilot clinical trial. *Clin Oral Implants Res.* 2014;25:683–9.
- Schenk G, Flemmig TF, Betz T, Reuther J, Klaiber B. Controlled local delivery of tetracycline HCl in the treatment of periimplant mucosal hyperplasia and mucositis. A controlled case series. *Clin Oral Implants Res.* 1997;8:427–33.
- Thone-Mühlhling M, Swierkot K, Nonnenmacher C, Mutters R, Flores-de-Jacoby L, Mengel R. Comparison of two full-mouth approaches in the treatment of peri-implant mucositis: a pilot study. *Clin Oral Implants Res.* 2010;21:504–12.
- De Siena F, Corbella S, Taschieri S, Del Fabbro M, Francetti L. Adjunctive glycine powder air-polishing for the treatment of peri-implant mucositis: an observational clinical trial. *Int J Dent Hyg.* 2014;14. doi:10.1111/ijdh.12114.
- Hallström H, Persson GR, Lindgren S, Olofsson M, Renvert S. Systemic antibiotics and debridement of peri-implant mucositis. A randomized clinical trial. *J Clin Periodontol.* 2012;39:574–81.
- Porras R, Anderson GB, Caffesse R, Narendran S, Trejo PM. Clinical response to 2 different therapeutic regimens to treat peri-implant mucositis. *J Periodontol.* 2002;73:1118–25.
- Riben Grundström C, Norderyd O, Andre U, Renvert S. Treatment of peri-implant mucositis using a glycine powder air-polishing or ultrasonic device. A randomized clinical trial. *J Clin Periodontol.* 2015;42:462–9.
- Strooker H, Rohn S, Van Winkelhoff AJ. Clinical and microbiologic effects of chemical versus mechanical cleansing in professional supportive implant therapy. *Int J Oral Maxillofac Implants.* 1998;13:845–50.
- Machtei EE, Frankenthal S, Levi G, Elimelech R, Shoshani E, Rosenfeld O, et al. Treatment of peri-implantitis using multiple applications of chlorhexidine chips: a double-blind, randomized multi-centre clinical trial. *J Clin Periodontol.* 2012;39:1198–205.
- Schwarz F, Bieling K, Bonsmann M, Latz T, Becker J. Nonsurgical treatment of moderate and advanced periimplantitis lesions: a controlled clinical study. *Clin Oral Invest.* 2006;10:279–88.
- Schwarz F, Sculean A, Rothamel D, Schwenzer K, Georg T, Becker J. Clinical evaluation of an Er : YAG laser for nonsurgical treatment of peri-implantitis: a pilot study. *Clin Oral Implants Res.* 2005;16:44–52.
- Büchter A, Meyer U, Kruse-Losler B, Joos U, Kleinheinz J. Sustained release of doxycycline for the treatment of peri-implantitis: randomised controlled trial. *Br J Oral Maxillofac Surg.* 2004;42:439–44.
- John G, Sahn N, Becker J, Schwarz F. Nonsurgical treatment of peri-implantitis using an air-abrasive device or mechanical debridement and local application of chlorhexidine. Twelve-month follow-up of a prospective, randomized, controlled clinical study. *Clin Oral Invest.* 2015. doi:10.1007/s00784-015-1406-7.
- Karring ES, Stavropoulos A, Ellegaard B, Karring T. Treatment of peri-implantitis by the VectorR system. A pilot study. *Clin Oral Implants Res.* 2005;16:288–93.
- Renvert S, Lessem J, Dahlen G, Renvert H, Lindahl C. Mechanical and repeated antimicrobial therapy using a local drug delivery system in the treatment of peri-implantitis: a randomized clinical trial. *J Periodontol.* 2008;79:836–44.
- Renvert S, Lindahl C, Roos Jansker A-M, Persson GR. Treatment of peri-implantitis using an Er:YAG laser or an air-abrasive device: a randomized clinical trial. *J Clin Periodontol.* 2011;38:65–73.
- Renvert S, Samuelsson E, Lindahl CPersson GR. Mechanical non-surgical treatment of peri-implantitis: a double-blind randomized longitudinal clinical study. I: clinical results. *J Clin Periodontol.* 2009;36:604–9.
- Renvert S, Lessem J, Dahlen G, Lindahl C, Svensson M. Topical minocycline microspheres versus topical chlorhexidine gel as an adjunct to mechanical

- debridement of incipient peri-implant infections: a randomized clinical trial. *J Clin Periodontol.* 2006;33:362–9.
33. Sahn N, Becker J, Santel T, Schwarz F. Non-surgical treatment of peri-implantitis using an air-abrasive device or mechanical debridement and local application of chlorhexidine: a prospective, randomized, controlled clinical study. *J Clin Periodontol.* 2011;38:872–8.
 34. Schär D, Ramseier CA, Eick S, Arweiler NB, Sculean A, Salvi GE. Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: six-month outcomes of a prospective randomized clinical trial. *Clin Oral Implants Res.* 2013;24:104–10.
 35. Persson GR, Samuelsson E, Lindahl C, Renvert S. Mechanical non-surgical treatment of peri-implantitis: a single-blinded randomized longitudinal clinical study. II Microbiological results. *J Clin Periodontol.* 2010;37:563–73.
 36. Persson GR, Roos-Jansker AM, Lindahl C, Renvert S. Microbiologic results after non-surgical erbium-doped:yttrium, aluminum, and garnet laser or air-abrasive treatment of peri-implantitis: a randomized clinical trial. *J Periodontol.* 2011;82:1267–78.
 37. Bassetti M, Schär D, Wicki B, Eick S, Ramseier CA, Arweiler NB, et al. Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: 12-month outcomes of a randomized controlled clinical trial. *Clin Oral Implants Res.* 2013;25:279–87.
 38. de Waal YC, Raghoobar GM, Huddleston Slater JJ, Meijer HJ, Winkel EG, van Winkelhoff AJ. Implant decontamination during surgical peri-implantitis treatment: a randomized, double-blind, placebo-controlled trial. *J Clin Periodontol.* 2013;40:186–95.
 39. de Waal YC, Raghoobar GM, Meijer HJ, Winkel EG, van Winkelhoff AJ. Implant decontamination with 2% chlorhexidine during surgical peri-implantitis treatment: a randomized, double-blind, controlled trial. *Clin Oral Implants Res.* 2014. doi:10.1111/clr.12419.
 40. Deppe H, Horch HH, Neff A. Conventional versus CO₂ laser-assisted treatment of peri-implant defects with the concomitant use of pure-phase beta-tricalcium phosphate: a 5-year clinical report. *Int J Oral Maxillofac Implants.* 2007;22:79–86.
 41. Papadopoulos CA, Vouros I, Menexes G, Konstantinidis A. The utilization of a diode laser in the surgical treatment of peri-implantitis. A randomized clinical trial. *Clin Oral Investig.* 2015. doi:10.1007/s00784-014-1397-9.
 42. Romeo E, Ghisolfi M, Murgolo N, Chiapasco M, Lops D, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part I: clinical outcome. *Clin Oral Implants Res.* 2005;16:9–18.
 43. Aghazadeh A, Persson GR, Renvert S. A single-centre randomized controlled clinical trial on the adjunct treatment of intra-bony defects with autogenous bone or a xenograft: results after 12 months. *J Clin Periodontol.* 2012;39(7):666–73.
 44. Rocuzzo M, Bonino F, Bonino L, Dalmaso P. Surgical therapy of peri-implantitis lesions by means of a bovine-derived xenograft: comparative results of a prospective study on two different implant surfaces. *Surgical treatment of peri-implantitis.* *J Clin Periodontol.* 2011;38(8):738–45.
 45. Roos-Jansaker AM, Persson GR, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up. *J Clin Periodontol.* 2014;41:1108–14.
 46. Roos-Jansaker AM, Renvert H, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a prospective cohort study. *J Clin Periodontol.* 2007;34:625–32.
 47. Roos-Jansker A-M, Lindahl C, Persson GR, Renvert S. Long-term stability of surgical bone regenerative procedures of peri-implantitis lesions in a prospective case-control study over 3 years. *J Clin Periodontol.* 2011;38:590–7.
 48. Schwarz F, Bieling K, Latz T, Nuesry E, Becker J. Healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite (Ostim) or a bovine-derived xenograft (Bio-Oss) in combination with a collagen membrane (Bio-Gide). A case series. *J Clin Periodontol.* 2006;33:491–9.
 49. Schwarz F, Hegewald A, John G, Sahn N, Becker J. Four-year follow-up of combined surgical therapy of advanced peri-implantitis evaluating two methods of surface decontamination. *J Clin Periodontol.* 2013;40:962–7.
 50. Schwarz F, John G, Mainusch S, Sahn N, Becker J. Combined surgical therapy of peri-implantitis evaluating two methods of surface debridement and decontamination. A two-year clinical follow up report. *J Clin Periodontol.* 2012;39:789–97.
 51. Schwarz F, Sahn N, Bieling K, Becker J. Surgical regenerative treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane: a four-year clinical follow-up report. *J Clin Periodontol.* 2009;36:807–14.
 52. Schwarz F, Sahn N, Iglhaut G, Becker J. Impact of the method of surface debridement and decontamination on the clinical outcome following combined surgical therapy of peri-implantitis: a randomized controlled clinical study. *J Clin Periodontol.* 2011;38:276–84.
 53. Schwarz F, Sahn N, Schwarz K, Becker J. Impact of defect configuration on the clinical outcome following surgical regenerative therapy of peri-implantitis. *J Clin Periodontol.* 2010;37:449–55.
 54. Schwarz F, Sculean A, Bieling K, Ferrari D, Rothamel D, Becker J. Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. *J Clin Periodontol.* 2008;35:80–7.
 55. Wohlfahrt JC, Lyngstadaas SP, Ronold HJ, Saxegaard E, Ellingsen JE, Karlsson S, et al. Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial. *Int J Oral Maxillofac Implants.* 2012;27:401–10.
 56. Schwarz F, Hertzen M, Sager M, Bieling K, Sculean A, Becker J. Comparison of naturally occurring and ligature-induced peri-implantitis bone defects in humans and dogs. *Clin Oral Implants Res.* 2007;18:161–70.
 57. Romeo E, Lops D, Chiapasco M, Ghisolfi M, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part II: radiographic outcome. *Clin Oral Implants Res.* 2007;18:179–87.
 58. Wohlfahrt JC, Aass AM, Granfeldt F, Lyngstadaas SP, Reseland JE. Sulcus fluid bone marker levels and the outcome of surgical treatment of peri-implantitis. *J Clin Periodontol.* 2014;41:424–31.
 59. Deppe H, Mucke T, Wagenpfeil S, Kesting M, Sculean A. Nonsurgical antimicrobial photodynamic therapy in moderate vs severe peri-implant defects: a clinical pilot study. *Quintessence Int.* 2013;44:609–18.
 60. Schwarz F, Jepsen S, Hertzen M, Sager M, Rothamel D, Becker J. Influence of different treatment approaches on non-submerged and submerged healing of ligature induced peri-implantitis lesions: an experimental study in dogs. *J Clin Periodontol.* 2006;33:584–95.
 61. Khoshkam V, Chan HL, Lin GH, Mac Eachern MP, Monje A, Suarez F, et al. Reconstructive procedures for treating peri-implantitis: a systematic review. *J Dent Res.* 2013;92:1315–8.
 62. Schwendicke F, Tu YK, Stolpe M. Preventing and treating peri-implantitis: a cost-effectiveness analysis. *J Periodontol.* 2015;9:1–15.
 63. Lavigne SE, Krust-Bray KS, Williams KB, Killoy WJ, Theisen F. Effects of subgingival irrigation with chlorhexidine on the periodontal status of patients with HA-coated integral dental implants. *Int J Oral Maxillofac Implants.* 1994;9:156–62.
 64. Ciancio SG, Lauciello F, Shibly O, Vitello M, Mather M. The effect of an antiseptic mouthrinse on implant maintenance: plaque and peri-implant gingival tissues. *J Periodontol.* 1995;66:962–5.
 65. Felo A, Shibly O, Ciancio SG, Lauciello FR, Ho A. Effects of subgingival chlorhexidine irrigation on peri-implant maintenance. *Am J Dent.* 1997;10:107–10.
 66. Bach G, Neckel C, Mall C, Krekeler G. Conventional versus laser-assisted therapy of periimplantitis: a five-year comparative study. *Implant Dent.* 2000;9:247–51.
 67. Dörtbudak O, Haas R, Bernhart T, Mailath-Pokorny G. Lethal photosensitization for decontamination of implant surfaces in the treatment of peri-implantitis. *Clin Oral Implants Res.* 2001;12:104–8.
 68. Khoury F, Buchmann R. Surgical therapy of peri-implant disease: a 3-year follow-up study of cases treated with 3 different techniques of bone regeneration. *J Periodontol.* 2001;72:1498–508.
 69. Roos-Jansaker AM, Renvert H, Lindahl C, Renvert S. Submerged healing following surgical treatment of peri-implantitis: a case series. *J Periodontol.* 2001;72:1498–508.
 70. Duarte PM, de Mendonca AC, Maximo MB, Santos VR, Bastos MF, Nociti FH. Effect of anti-infective mechanical therapy on clinical parameters and cytokine levels in human peri-implant diseases. *J Periodontol.* 2009;80:234–43.
 71. Maximo MB, de Mendonca AC, Renata Santos V, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. *Clin Oral Implants Res.* 2009;20:99–108.
 72. Ramberg P, Lindhe J, Botticelli D, Botticelli A. The effect of a triclosan dentifrice on mucositis in subjects with dental implants: a six-month clinical study. *J Clin Dent.* 2009;20:103–7.

73. Corbella S, Del Fabbro M, Taschieri S, De Siena F, Francetti L. Clinical evaluation of an implant maintenance protocol for the prevention of peri-implant diseases in patients treated with immediately loaded full-arch rehabilitations. *Int J Dent Hyg*. 2011;9:216–22.
74. Heitz-Mayfield LJ, Salvi GE, Botticelli D, Mombelli A, Faddy M, Lang NP, et al. Anti-infective treatment of peri-implant mucositis: a randomised controlled clinical trial. *Clin Oral Implants Res*. 2011;22:237–41.
75. De Angelis N, Felice P, Grusovin MG, Camurati A, Esposito M. The effectiveness of adjunctive light-activated disinfection (LAD) in the treatment of peri-implantitis: 4-month results from a multicentre pragmatic randomised controlled trial. *Eur J Oral Implantol*. 2012;5:321–31.
76. Salvi GE, Aglietta M, Eick S, Sculean A, Lang NP, Ramseier CA. Reversibility of experimental peri-implant mucositis compared with experimental gingivitis in humans. *Clin Oral Implants Res*. 2012;23:182–90.
77. De Siena F, Francetti L, Corbella S, Taschieri S, Del Fabbro M. Topical application of 1% chlorhexidine gel versus 0.2% mouthwash in the treatment of peri-implant mucositis. An observational study. *Int J Dent Hyg*. 2013;11:41–7.
78. McKenna DF, Borzabadi-Farahani A, Lynch E. The effect of subgingival ozone and/or hydrogen peroxide on the development of peri-implant mucositis: a double-blind randomized controlled trial. *Int J Oral Maxillofac Implants*. 2013;28:1483–9.
79. Flichy-Fernandez AJ, Ata-Ali J, Alegre-Domingo T, Candel-Marti E, Ata-Ali F, Palacio JR, et al. The effect of orally administered probiotic lactobacillus reuteri-containing tablets in peri-implant mucositis: a double-blind randomized controlled trial. *J Periodontol Res*. 2015. doi:10.1111/jre.12264.

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com
