

# The Therapy of Peri-implantitis: A Systematic Review

Lisa J. A. Heitz-Mayfield, BDS, MDS, Odont Dr<sup>1</sup>/Andrea Mombelli, Prof Dr Med Dent<sup>2</sup>

**Purpose:** To evaluate the success of treatments aimed at the resolution of peri-implantitis in patients with osseointegrated implants. **Materials and Methods:** The potentially relevant literature was assessed independently by two reviewers to identify case series and comparative studies describing the treatment of peri-implantitis with a follow-up of at least 3 months. Medline, Embase, and The Cochrane Library were searched. For the purposes of this review, a composite criterion for successful treatment outcome was used which comprised implant survival with mean probing depth < 5 mm and no further bone loss. **Results:** A total of 43 publications were included: 4 papers describing 3 nonsurgical case series, 13 papers describing 10 comparative studies of nonsurgical interventions, 15 papers describing 14 surgical case series, and 11 papers describing 6 comparative studies of surgical interventions. No trials comparing nonsurgical with surgical interventions were found. The length of follow-up varied from 3 months to 7.5 years. Due to the heterogeneity of study designs, peri-implantitis case definitions, outcome variables, and reporting, no meta-analysis was performed. Eleven studies could be evaluated according to a composite success criterion. Successful treatment outcomes at 12 months were reported in 0% to 100% of patients treated in 9 studies and in 75% to 93% of implants treated in 2 studies. Commonalities in treatment approaches between studies included (1) a pretreatment phase, (2) cause-related therapy, and (3) a maintenance care phase. **Conclusions:** While the available evidence does not allow any specific recommendations for the therapy of peri-implantitis, successful treatment outcomes at 12 months were reported in a majority of patients in 7 studies. Although favorable short-term outcomes were reported in many studies, lack of disease resolution as well as progression or recurrence of disease and implant loss despite treatment were also reported. The reported outcomes must be viewed in the context of the varied peri-implantitis case definitions and severity of disease included as well as the heterogeneity in study design, length of follow-up, and exclusion/inclusion criteria. *INT J ORAL MAXILLOFAC IMPLANTS* 2014;29(SUPPL):325–345. doi: 10.11607/jomi.2014suppl.g5.3

**Key words:** peri-implantitis, systematic review, treatment, therapy

Peri-implantitis—an infectious condition of the tissues around osseointegrated implants with loss of supporting bone and clinical signs of inflammation (bleeding and/or suppuration on probing)—has a prevalence on the order of 10% of implants and 20% of patients 5 to 10 years after implant placement.<sup>1</sup> The numbers of patients with a history of periodontitis and those who are smokers in a cohort, as well as the type

and frequency of aftercare, are factors that influence these prevalence data. Furthermore, the prevalence of peri-implantitis will vary depending on the bone loss threshold and/or probing depth threshold used for case definition. Various clinical protocols for prevention and treatment of peri-implantitis have been proposed, including mechanical debridement, the use of antiseptics and local or systemic antibiotics, as well as surgical access and regenerative procedures. Several attempts to combine the data of the available literature in a meta-analysis have failed in the past due to insufficient data.<sup>2–6</sup> In a recent review on a part of this literature,<sup>7</sup> it was noted that almost all reports on the treatment of naturally occurring peri-implantitis in humans do in fact not satisfy the strict criteria for a randomized controlled trial (RCT). The absence of a true control group (no treatment or placebo) was a common limitation. Trials at the highest level of evidence compared test procedures, both of which had an unclear outcome. As it is difficult to recruit sufficient numbers of patients with peri-implantitis to take part in a true randomized trial, some studies may have

<sup>1</sup>Professor, International Research Collaborative, The University of Western Australia, Nedlands, Western Australia, Australia.

<sup>2</sup>Professor and Chairman, School of Dental Medicine, Division of Periodontology and Oral Pathophysiology, University of Geneva, Geneva, Switzerland.

**Correspondence to:** Professor Lisa J. A. Heitz-Mayfield, International Research Collaborative, The University of Western Australia, 35 Stirling Highway, Nedlands 6009, Western Australia, Australia. Fax: + 61 893212741  
Email: heitz.mayfield@iinet.net.au

©2014 by Quintessence Publishing Co Inc.

been underpowered. With regard to outcomes, there is inconsistency about primary treatment goals and minimally required observation periods.

A recent Cochrane systematic review included nine randomized controlled trials in an attempt to identify the most effective interventions for treating peri-implantitis around osseointegrated oral implants.<sup>8</sup> The authors concluded that there is no reliable evidence suggesting which could be the most effective interventions for treating peri-implantitis.<sup>8</sup>

Due to the above observations, the authors of the present review decided to take a broader approach to evaluate the effect of treatment, feeling that it was currently not suitable to restrict a review on the therapy of peri-implantitis to randomized trials. This report aims to evaluate the results of treatment of peri-implantitis in humans in a broader way than done previously.

An ideal goal of peri-implantitis therapy would be the resolution of disease (ie, no suppuration or bleeding on probing, no further bone loss) and the establishment and maintenance of healthy hard and soft peri-implant tissues. If this goal were not achievable, a reduction in clinical inflammation, ie, a reduction in peri-implant probing depths and bleeding on probing, as well as the establishment of a local environment conducive to biofilm control would be desirable.

The authors of this systematic review considered a composite outcome for successful peri-implantitis therapy would ideally be: implant survival with the absence of peri-implant probing depths (PD)  $\geq$  5 mm, with concomitant bleeding on probing (BoP) with light pressure and no suppuration, in addition to no further bone loss. If these criteria were met, it can be assumed that no further intervention other than nonsurgical maintenance care would be required, and the treatment outcome would therefore be regarded as successful.

Therefore, the focus question for this systematic review was "In patients with osseointegrated implants diagnosed with peri-implantitis, how successful is treatment aimed at resolution of the disease?"

## MATERIALS AND METHODS

### Search Strategy

On August 15, 2012, the authors searched the following medical databases to identify the literature on the treatment of peri-implantitis in humans: Medline via OVID, PubMed (NLM), Embase via OVID, The Cochrane Central Register of Controlled Trials (The Cochrane Library). The Boolean search algorithm employed to find the potentially relevant literature was developed on the basis of preliminary scoping searches and the experience of previous reviews conducted by these authors on the same subject<sup>7,9</sup> and included the following terms:

"peri-implant disease" OR "periimplant disease" OR "peri-implant complication" OR periimplant complication OR peri-implant infection OR periimplant infection OR peri-implant" OR "periimplant" OR "peri-implantitis" OR "periimplantitis" OR ("implant" AND "failure" OR "failing" OR "ailing")

together with (AND)

"treatment" OR "therapy" OR "management"

In addition, previous review articles on the subject were searched, as well as the reference lists of the articles already identified for further potentially relevant publications. Although there was no language restriction, the minimum requirement was access to an English version of title and abstract (Table 1).

### Study Selection Criteria

To be eligible for inclusion in this review, reports had to provide treatment outcomes evaluating nonsurgical or surgical interventions to treat peri-implantitis in humans. The study selection criteria were:

- Include patients with at least one dental osseointegrated implant affected by peri-implantitis
- Describe a pathological condition compatible with the definition of "peri-implantitis"
- Describe a clinical intervention aiming at the treatment of the condition
- Include at least five comparable cases treated with the same procedure, followed up for at least 3 months after therapy.

The authors independently screened titles and abstracts of the search results. The full text of all studies of possible relevance was obtained for assessment against the stated inclusion criteria. Any disagreement regarding inclusion was resolved by discussion.

### Data Extraction

The following information was sought and recorded by the two authors independently on data extraction forms: study design, year of publication, number of patients and implants with peri-implantitis, implant type, disease definition, treatment procedures (pre-treatment phase, procedure to gain access, implant surface treatment, antimicrobial agents, regenerative materials, postsurgical care), length of follow-up, and outcomes.

The following treatment outcomes, when reported, were recorded: (1) implant failure leading to loss or removal of the implant; (2) persistence or recurrence of peri-implantitis, ie, suppuration from the peri-implant sulcus, continued bone loss; (3) complications and side

**Table 1 Systematic Search Strategy**

**Focus question** In patients with osseointegrated implants diagnosed with peri-implantitis, how successful is treatment aimed at resolution of the disease?

**Search strategy**

Population	Patients diagnosed with peri-implantitis
Intervention or exposure	Treatment
Comparison	Include both nonsurgical and surgical treatment
Outcome	Resolution of disease: implant survival and absence of PD $\geq$ 5 mm with suppuration/BoP and no further bone loss
Search combination	"peri-implant disease" OR "periimplant disease" OR "peri-implant complication" OR "periimplant complication" OR "peri-implant infection" OR "periimplant infection" OR "peri-implant" OR "peri-implant" OR "peri-implantitis" OR "peri-implantitis" OR ("implant" AND "failure" OR "failing" OR "ailing") together with (AND) "treatment" OR "therapy" OR "management"

**Database search**

Electronic	Medline via OVID, Pubmed (NLM), Embase via OVID, The Cochrane Central Register of Controlled Trials (The Cochrane Library)
Journals	All journals

**Selection criteria**

Inclusion criteria	Include patients with at least one dental osseointegrated implant affected by peri-implantitis Describe a pathological condition compatible with the definition of peri-implantitis Describe a clinical intervention aiming at the treatment of the condition Include at least five comparable cases treated with the same procedure, followed up for at least 3 months after therapy
Exclusion criteria	No access to an English version of title and abstract

effects; (4) change in peri-implant probing depth; (5) change in bleeding on probing; (6) change in peri-implant mucosal recession; and (7) change in radiographic marginal bone level.

While the ideal composite criterion for successful treatment outcome, as outlined in the introduction, would have included the absence of peri-implant probing depths  $\geq$  5 mm with concomitant BoP, this data could not be extracted from the available studies. Therefore, for the purposes of this review, the following composite criterion for a successful treatment outcome was used: implant survival with mean PD < 5 mm and no further bone loss.

**Assessment of Case Definition**

The authors of this review classified the case definition of peri-implantitis of each study as follows:

- *Clear:* (1) A clear threshold of loss of supporting bone (eg, bone loss > 1.8 mm, (2) presence of bleeding on probing and/or suppuration on probing.
- *Unclear:* (1) Bone loss with no threshold given or where the threshold could indicate peri-implant mucositis rather than peri-implantitis (eg, bone loss < 1.8 mm, or < 30% implant length); (2) presence of bleeding on probing and/or suppuration on probing.

- *Inadequate:* Bone loss without information on bleeding and/or suppuration on probing.

**Quality Assessment and Risk of Bias Assessment**

Quality assessment and assessment of risk of bias were undertaken independently, and in duplicate by the two authors as part of the data extraction process. For the included randomized controlled trials, this was conducted using the Cochrane Collaboration's tool for assessing risk of bias.<sup>10</sup>

The following possible sources of bias were addressed: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias and detection bias); incomplete outcome data (attrition bias); and selective reporting (reporting bias). The authors' judgment for each source of bias item was assigned for each trial in the data extraction table. An overall risk of bias was then assigned to each trial according to Higgins et al.<sup>10</sup>

For the included case series, the quality assessment addressed examiner blinding, examiner calibration, standardized probing force, standardized radiographic assessment, incomplete data outcome, and selective reporting.

**Table 2 Characteristics of Case Series of Nonsurgical Therapies in Peri-implantitis Patients**

Study	Patients	Implants	Implant type	Disease definition	Surface treatment
Mombelli and Lang <sup>16</sup>	9	9	Straumann: HC	PD ≥ 5 mm, marked BL, anaerobes	PS, CHX
Mombelli et al <sup>17</sup>	25	30	Straumann: HC, HS, S	PD ≥ 5 mm, circumferential BL	PS, CHX
Salvi et al <sup>18</sup> Persson et al <sup>19</sup>	25	31	NR	PD ≥ 5 mm, BL ≥ 2 mm, BoP	CFC, CHX

HC: hollow-cylinder implant; HS: hollow-screw implant; S: screw-shaped implant; NR: not reported; PD: probing depth; BL: bone loss; BoP: bleeding on probing; PS: plastic scaler; CFC: carbon fiber curette; CHX: chlorhexidine; AB: systemic antibiotic; LDD: local delivery device; FMPS: full-mouth plaque score.

**Table 3 Characteristics of Comparative Studies of Nonsurgical Therapies in Peri-implantitis Patients**

Study	Patients	Implants	Implant type	Disease definition	Pretreatment	Surface treatment
Büchter et al <sup>20</sup>	14 14	24 24	Straumann SLA	BL > 50%, implant length	FMD removal of prosthesis	PS, CHX PS, CHX
Renvert et al <sup>21</sup> Renvert et al <sup>22</sup>	16 16	NR NR	Brånemark	PD ≥ 4 mm, BoP and/or SUP, BL ≤ 1.8 mm, anaerobes	NR	PS PS
Renvert et al <sup>23</sup>	15 17	38 57	Brånemark: machined	PD ≥ 4 mm, BoP and/or SUP, BL ≤ 1.8 mm, anaerobes	NR	PS PS
Karring et al <sup>24</sup>	11	11 11	Straumann, Astra Tech, Brånemark: S	PD ≥ 5 mm, BL ≥ 1.5 mm, BoP	NR	CFC US: Vector
Renvert et al <sup>25</sup> Persson et al <sup>26</sup>	19 18	19 18	Astra Tech, Brånemark: S	PD ≥ 4 mm, BoP and/or SUP, BL < 2.5 mm	NR	TC US: Vector
Sahm et al <sup>27</sup>	16 16	23 20	S, multiple surfaces	PD ≥ 4 mm, BoP and/or SUP, BL ≤ 30% implant length	Polishing	APG CFC
Schwarz et al <sup>28</sup>	10 10	16 16	S, SLA, TPS	PD ≥ 4 mm, BL, BoP and SUP	NR	PS, CHX Er:YAG laser
Schwarz et al <sup>29</sup>	10 10	10 20	7 brands	Moderate: PD 4–6 mm, BL < 30% implant length, BoP and SUP Advanced: PD > 7 mm, BL > 30% implant length, BoP and SUP	NR	PS, CHX Er:YAG laser
Renvert et al <sup>30</sup> Persson et al <sup>31</sup>	21 21	45 55	Machined, moderately rough	PD ≥ 5 mm, BoP and/or SUP, BL > 3 mm	Removal of prosthesis	APG Er:YAG laser
Schär et al <sup>32</sup>	20 20	20 20	S, Straumann SLA	PD 4–6 mm, BoP, BL = 0.5–2.0 mm	NR	TC, APG, H <sub>2</sub> O <sub>2</sub> TC, APG, H <sub>2</sub> O <sub>2</sub>

S: screw-shaped implant; SLA: sandblasted large-grit acid-etched; TPS: titanium plasma sprayed; BL: bone loss; PD: probing depth; BoP: bleeding on probing; SUP: suppuration; FMD: full-mouth debridement; NR: not reported; PS: plastic scaler; CHX: chlorhexidine; CFC: carbon fiber curette; US: Ultrasonic device; TC: titanium curette; APG: air-powder abrasive with glycine powder; LDD: local delivery device; PDT: photodynamic therapy.

## Data Synthesis

The two reviewers extracted the pertinent information independently, and in duplicate from the selected trials into four spreadsheets, representing either case series or comparative studies, and nonsurgical protocols or surgical protocols. Due to the heterogeneity of study designs, outcome variables, and reporting, no meta-analysis was performed.

## RESULTS

The initial search yielded over 400 potentially relevant publications. A majority of them, however, failed to satisfy all inclusion criteria for this review because they did not concern patients with dental osseointegrated implants; turned out to be reviews, commentaries or editorials without original data; did not address a path-

Antimicrobial	Maintenance	Follow-up
AB: ornidazole	NR	12 mo
LDD: tetracycline fiber	NR	12 mo
LDD: minocycline	Oral hygiene instruction, FMPS $\leq$ 20%	12 mo

Antimicrobial	Maintenance	Follow-up
LDD: doxycycline	Oral hygiene instruction	4.5 mo
CHX LDD: minocycline	Oral hygiene instruction	12 mo
CHX: repeated 3 times LD: minocycline repeated 3 times	Oral hygiene instruction	12 mo
	Retreated at 3 mo	6 mo
	Oral hygiene instruction	6 mo
CHX	Supramucosal prophylaxis, oral hygiene instruction	6 mo
CHX rinsing	4, 12, 24 wk supragingival/ mucosal polishing	6 mo
CHX rinsing	1, 3, 6, 12 mo supragingival/ mucosal polishing	12 mo
	NR	6 mo
LDD: minocycline PDT	Oral hygiene instruction: wk 1, 2, 4, 8	6 mo

ological condition compatible with the definition of peri-implantitis; and/or did not report the same treatment in at least five cases with a follow-up of at least 3 months. This left 48 papers for which the full text was sought for further evaluation. After further evaluation, an additional 5 papers were excluded due to the following reasons: insufficient information<sup>11-13</sup> and paper unavailable,<sup>14,15</sup> leaving a total of 43 papers.

The 43 papers fulfilling all study selection criteria were subdivided into four categories. Table 2 lists the details of 4 papers concerning 3 studies describing a series of at least 5 patients treated with the same nonsurgical protocol. Table 3 lists the characteristics of the 13 papers concerning 10 studies presenting a comparison of nonsurgical treatment groups. Table 4 lists the 15 articles concerning 14 studies describing a series of at least 5 patients treated with the same surgical protocol. Table 5 lists the 11 papers describing the 6 studies presenting a comparison of groups of patients, where one surgical method is applied per group.

### Characteristics of the Interventions

Tables 2 and 3 list the characteristics of studies describing nonsurgical therapies of peri-implantitis. Methods to decontaminate the implant surface included debridement using manual or ultrasonic instruments with carbon fiber or plastic tips, air-powder abrasive devices, laser treatment, and the systemic or local application of antimicrobial agents.

**Case Series of Nonsurgical Interventions.** Three case series evaluating manual debridement (using a plastic scaler or carbon fiber curette) with adjunctive antimicrobials were identified. One study included systemic ornidazole prescribed for 10 days,<sup>16</sup> while the others incorporated adjunctive local antibiotic delivery via fibers containing tetracycline hydrochloride (HCl) (Actisite)<sup>17</sup> and minocycline HCl microspheres (Arestin).<sup>18,19</sup> All patients received adjunctive chlorhexidine application as part of the treatment and were followed for 12 months.

**Comparative Studies (RCTs) of Nonsurgical Interventions.** Three studies compared manual debridement versus manual debridement with local antimicrobials. Büchter et al<sup>20</sup> compared manual debridement (plastic scaler and submucosal irrigation of chlorhexidine) to the same debridement technique with adjunctive local delivery of 8.5% doxycycline hyclate gel (Atridox). In both treatment groups, the implant-supported prostheses were removed prior to treatment, and full-mouth debridement with subgingival irrigation with chlorhexidine was performed. Renvert et al<sup>21,22</sup> compared manual debridement using a plastic scaler and chlorhexidine gel application to debridement using a plastic scaler and local delivery of minocycline HCl (Arestin). In another trial by the same authors,<sup>23</sup> manual debridement in conjunction with repeated submucosal application of 1% chlorhexidine gel was compared to manual debridement with repeated application of minocycline HCl microspheres (Arestin). Treatment in both groups was repeated at day 30 and day 90.

Two studies compared manual debridement with ultrasonic debridement. Karring et al,<sup>24</sup> in a split-mouth

**Table 4 Case Series of Surgical Therapies in Peri-implantitis Patients**

Study	Patients	Implants	Implant type	Disease definition	Pretreatment
Aughthun et al <sup>33</sup>	12	15	IMZ	PD ≥ 5 mm, BL ≥ 5 mm	NR
Behneke et al <sup>34</sup>	17	25	Straumann	PD > 5 mm, crater-like BL not observed at > 90% of implant length	Iodine irrigation for 4 wk
Rocuzzo et al <sup>35</sup>	26	26	Straumann: TPS/SLA, S	PD ≥ 6 mm, crater-like BL	Oral hygiene instruction, FMPS, FMBS < 20%
Wiltfang et al <sup>36</sup>	22	36	No data	BL > 4 mm	Nonsurgical debridement, rinsing CHX
Froum et al <sup>37</sup>	38	51	10 brands	PD ≥ 6 mm, BoP, BL ≥ 4 mm	FMD 1 mo prior
Romanos and Nentwig <sup>38</sup>	15	19	Ankylos, Straumann, IMZ	BL > two-thirds implant length	NR
Haas et al <sup>39</sup>	17	24	IMZ	PD > 6 mm, progressive BL during 1 y, narrow vertical BD	NR
Roos-Jansåker et al <sup>40</sup>	12	16	Brånemark	BL ≥ 3 threads (1.8 mm), BOP and/or SUP	NR
Schwarz et al <sup>41</sup>	27	27	4 brands: S	PD > 6 mm, BL > 3 mm	Er:YAG laser
Leonhardt et al <sup>42</sup>	9	26	Brånemark	BL ≥ 3 threads, BOP/SUP	Removal of prosthesis + abutment
Heitz-Mayfield et al <sup>43</sup>	24	36	6 brands	PD ≥ 5 mm, BL ≥ 2 mm, BoP	Nonsurgical debridement
de Mendonça et al <sup>44</sup>	10	10	S	PD ≥ 5 mm, BoP and/or SUP, BL at ≥ 3 threads	Oral hygiene instruction
Maximo et al <sup>45</sup> Duarte et al <sup>46</sup>	13	20	Brånemark	PD ≥ 5 mm, BoP/SUP, BL ≥ 3 threads until half implant length	Supragingival cleaning
Serino and Turri <sup>47</sup>	31	86	Brånemark, Straumann, Astra Tech: S	PD ≥ 6 mm, BoP/SUP, BL ≥ 2 mm	Supra/subgingival debridement, adjustment prosthesis if required

TPS: titanium plasma sprayed; SLA: sandblasted large-grit acid-etched; S: Screw-shaped implant; PD: probing depth; BL: bone loss; BoP: bleeding on probing; SUP: suppuration; NR: not reported; FMPS: full-mouth plaque score; FMBS: full-mouth bleeding score; CHX: chlorhexidine; AUG: Augmentin; FMD: full-mouth debridement; APB: air-powder abrasive with sodium bicarbonate powder; PC: plastic curette; EDTA: ethylene diamine tetra-acetate gel; IPP: Implantoplasty with bur; CFC: carbon fiber curette; TC: titanium curette; PDT: photodynamic therapy; TET: tetracycline; MTR: metronidazole; AMX: amoxicillin; CLI: clindamycin; ePTE: expanded polytetrafluorethylene membrane; ABG: autogenous bone graft; XBM: xenogenic bone mineral (Bio-Oss); EMD: enamel matrix derivative; PDGF: platelet-derived growth factor; CT: connective tissue; PCC: phytogenic calcium carbonate (Algipore); RSM: resorbable synthetic membrane; CM: collagen membrane.

study design, compared manual debridement with carbon fiber curettes to an ultrasonic device (Vector system) with a carbon fiber tip combined with aerosol spray of hydroxyapatite particles. The treatment procedures were repeated after 3 months. A second trial with parallel design compared manual debridement (with a titanium instrument) with the same ultrasonic device (Vector system).<sup>25,26</sup>

Sahm et al<sup>27</sup> compared manual debridement (carbon fiber curettes), with adjunctive submucosal chlorhexidine application with debridement using an air-powder abrasive device and glycine powder. Oral hygiene instruction and supramucosal polishing was provided 4 weeks prior to treatment procedures in both groups.

Two trials conducted by the same authors, using a similar protocol, compared manual debridement (plastic scaler) with adjunctive chlorhexidine (submucosal irrigation and gel application followed by chlorhexidine rinsing for 2 weeks) with debridement using an erbium-doped yttrium aluminium garnet (Er:YAG)

laser.<sup>28,29</sup> Oral hygiene instruction and supramucosal polishing was provided in both studies in a pretreatment phase.

Renvert et al<sup>30</sup> and Persson et al<sup>31</sup> compared treatment with an Er:YAG laser to debridement using an air-powder abrasive device and amino acid glycine powder. The implant-supported prostheses were removed prior to treatment.

Schär et al<sup>32</sup> compared debridement and photodynamic therapy (application of phenothiazine chloride and laser irradiation at a wavelength of 660 nm) (HELBO), which was repeated at 1 week with debridement and adjunctive minocycline HCl microspheres (Arestin). The debridement protocol in both treatment groups involved the use of titanium curettes, glycine-based air-powder abrasion, and submucosal pocket irrigation using 3% hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Oral hygiene instruction was provided in both groups prior to treatment.

Tables 4 and 5 list the studies reporting information from surgical therapies of peri-implantitis. All protocols included the elevation of a mucoperiosteal flap and the

Surface treatment	Antimicrobial	Materials	Maintenance	Follow-up
APB	TET	ePTFE	NR	6–12 mo
APB	MTR	ABG	Oral hygiene instruction every 3 mos for the first year	6–36 mo
PC, EDTA, CHX, saline	AMX+clavulanic acid, CHX	XBM	Tailored maintenance care	12 mo
IPP, phosphoric acid	Ampicillin or CLI	Xenograft (Coloss) + ABG	3 monthly	12 mo
APB, CFC, TC	AMX or CLI, CHX	EMD, PDGF, XBM, CM, CT graft	6–8 weekly rubber cup polishing	90 mo
TC, CO <sub>2</sub> laser	None	ABG or XBM, CM	NR	18 mo
PDT	AUG	ePTFE, ABG	NR	Mean 9.5 mo
H <sub>2</sub> O <sub>2</sub>	AMX+MTR, CHX	PCC, RSM submerged healing	3 monthly rubber cup polishing	12 mo
CFC + saline	CHX	XBM + CM	Once a month for 6 mo, then every 3 mo	12 mo
H <sub>2</sub> O <sub>2</sub>	5 different antibiotics	None	3–6 monthly	5 y
CFC, TC	AMX + MET, CHX	None	3 monthly or as required	12 mo
CFC, APB	CHX	None	3 monthly supramucosal prophylaxis	12 mo
APB, CFC	CHX	None	None	3 mo
US, rubber cup + CHX	CLI, CHX	ABG + bone recontouring, apically positioned flap	3 to 6 monthly	24 mo

removal of the peri-implant inflammatory granulation tissue. Methods to decontaminate and condition the implant surface adjacent to the diseased peri-implant soft tissues included cleaning with carbon or plastic curettes, ultrasonic scalers, air-powder abrasive devices using sodium bicarbonate or glycine powder, irradiation with hard or soft laser light, implantoplasty, and/or the application of acids or various antimicrobial agents. A majority of the protocols included the systemic administration of an antibiotic in addition to chlorhexidine rinsing. In many studies, peri-implant bony defects were filled with graft materials including autogenous bone, allogenic decalcified freeze-dried bone, xenogenic bone mineral, phytogetic calcium carbonate, hydroxyapatite or tricalcium phosphate. Nonresorbable membranes of expanded polytetrafluoroethylene (ePTFE) or resorbable collagen or synthetic membranes were used to cover the graft material.

**Case Series of Surgical Interventions.** Augthun et al<sup>33</sup> elevated a flap, cleaned the implant surfaces with an air-polishing device, and covered the peri-implant

defects with an ePTFE membrane. Systemic tetracycline was administered.

Three studies reported on regenerative treatments using grafts without membranes. Behneke et al<sup>34</sup> treated peri-implantitis lesions with autogenous bone grafts. Treatment included flap elevation, removal of granulation tissue, air-powder abrasion of implant surfaces with sodium carbonate powder, placement of grafts, and systemic metronidazole. Rocuzzo et al<sup>35</sup> treated peri-implantitis lesions with bovine-derived xenograft (BioOss). After flap elevation and granulation tissue removal, the implant surfaces were cleaned with a plastic curette and a 24% ethylenediaminetetraacetic acid (EDTA) gel was applied for 2 minutes followed by 1% chlorhexidine gel for an additional 2 minutes. The bone defect was then filled with the xenograft, and the flap was closed around the nonsubmerged implants. Amoxicillin with clavulanic acid was prescribed for 6 days and 0.2% chlorhexidine rinse for 3 weeks. Wiltfang et al<sup>36</sup> treated peri-implantitis defects with a mix of autologous bone and a demineralized xenogenic

**Table 5 Comparative Studies of Surgical Therapies in Peri-implantitis Patients**

Study	Pa-tients	Im-plants	Implant type	Disease definition	Pretreatment
Deppe et al <sup>48</sup>	32	17	IMZ, Frialit, Brånemark, Straumann	PD ≥ 5 mm, progressive BL, or BoP	Nonsurgical debridement + CHX rinsing
		22			
		15			
Schwarz et al <sup>49,50</sup>	19	19	10 brands: no HC	PD > 6 mm, intrabony BL > 3 mm	Nonsurgical debridement PS, irrigation CHX + CHX gel
		16			
Khoury and Buchmann <sup>51</sup>	25	12	IMZ, Friadent	BL > 50%	Removal prostheses + PS + CHX irrigation + AB 6 mo prior to surgery
		20			
Roos-Jansåker et al <sup>52,53</sup>	15	27	Astra Tech, Brånemark	BL ≥ 1.8 mm, BoP/SUP	Nonsurgical debridement
		17			
Schwarz et al <sup>54–56</sup>	11	11	7 brands: S	PD > 6 mm, intrabony BL > 3 mm	Nonsurgical debridement PS, irrigation CHX + CHX gel
		11			
Romeo et al <sup>57,58</sup>	10	19	S, HS; all TPS	PD > 4 mm, BoP/SUP, evident BL	Scaling PS, AMX
		9			

S: screw-shaped implant; HC: hollow-cylinder implant; HS: hollow-screw implant; TPS: titanium plasma sprayed; PD: probing depth; BL: bone loss; BoP: bleeding on probing; SUP: suppuration; CHX: chlorhexidine; PS: plastic scaler; AB: systemic antibiotic; AMX: amoxicillin; APB: air-powder abrasive with sodium bicarbonate powder; IPP: implantoplasty with bur; PS: plastic scaler; CA: citric acid; MTR: metronidazole; TET: tetracycline; TCP: beta-tricalcium phosphate; ABG: autogenous bone graft; ePTFE: expanded polytetrafluoroethylene membrane; XBM: xenogenic bone mineral (Bio-Oss); CM, collagen membrane; PCC: phytogetic calcium carbonate (Algipore); RSM: resorbable synthetic membrane; NR: not reported.

bone graft including growth factors (Colloss E). A flap was raised, granulation tissue was removed, the implant surface was decontaminated with a phosphoric acid etching gel, and the defects were filled with the grafting material. Ampicillin (clindamycin in case of allergy) was given perioperatively.

Five studies reported on regenerative treatments with grafts and membranes. Froum et al<sup>37</sup> carried out the following treatment: flap elevation followed by surface decontamination consisting of a six-step protocol including instrumentation with graphite curettes or titanium tips, air-powder abrasion with sodium bicarbonate powder, and application of a tetracycline and a chlorhexidine solution. Following this, enamel matrix derivative and a combination of platelet-derived growth factor (PDGF) with anorganic bovine bone or mineralized freeze-dried bone were applied and covered with a collagen membrane or a subepithelial connective tissue graft. In addition, amoxicillin or clindamycin was prescribed for 10 days. Romanos and Nentwig<sup>38</sup> elevated a flap, mechanically debrided the implant surfaces with titanium curettes, and treated the surfaces using a carbon dioxide (CO<sub>2</sub>) laser. Following this, an autogenous bone graft or a xenogenic bone grafting material (BioOss) was placed and covered with a collagen membrane (Bio-Gide). No systemic antimicrobials were prescribed. Haas et al<sup>39</sup> raised mucoperiosteal flaps and removed the granulation tissue in the bony craters around implants. Implant surfaces were then treated with photo-

dynamic therapy (application of toluidine blue and laser irradiation at a wavelength of 906 nm). The bone defects were filled with autogenous bone and covered with an ePTFE membrane. Systemic penicillin was administered for 5 days. Roos-Jansåker et al<sup>40</sup> raised a mucoperiosteal flap, removed granulomatous tissue, and cleaned the implant surface with H<sub>2</sub>O<sub>2</sub>. The defects were filled with a bone substitute (Algipore), covered with a resorbable synthetic membrane (Osseoquest), and submerged healing was allowed for 6 months. Systemic amoxicillin plus metronidazole was prescribed for 10 days.

Schwarz et al<sup>41</sup> raised mucoperiosteal flaps, removed the granulation tissue, and cleaned the implant surfaces with plastic curettes and swabbing with cotton pellets soaked in saline. The bone defects were then filled with a bovine-derived xenograft (BioOss) and covered with a collagen membrane (Bio-Gide). No systemic antimicrobials were prescribed.

Two studies reported on access surgery and decontamination with systemic antibiotics. Leonhardt et al<sup>42</sup> treated peri-implantitis lesions with a combined surgical and antimicrobial protocol. Implants were surgically exposed and cleaned using H<sub>2</sub>O<sub>2</sub>. Two patients were given systemic amoxicillin and metronidazole, two patients received tetracycline, two ciprofloxacin, one sulfonamide plus trimethoprim, and one metronidazole alone. Heitz-Mayfield et al<sup>43</sup> raised a mucoperiosteal flap and removed granulation tissue, and the implant surfaces were cleaned using titanium coated curettes and by rubbing

Surface treatment	Antimicrobial	Materials	Maintenance	Follow-up
APB, CO <sub>2</sub> laser	None	TCP, ABG, ePTFE None: resective surgery	NR	Up to 5 y
APB		TCP, ABG, ePTFE None: resective surgery		
IPP, Er:YAG-laser	CHX	XBM, CM	1, 3, 6 mo supragingival cleaning, OHI	2 y
IPP, PS + saline		XBM, CM		
CA, CHX, H <sub>2</sub> O <sub>2</sub> + saline	Various unspecified antibiotics, CHX	ABG	Every 3 to 6 mo OHI prophylaxis as required	3 y
H <sub>2</sub> O <sub>2</sub>		ABG, ePTFE		
		ABG, CM		
H <sub>2</sub> O <sub>2</sub>	AMX+MTR, CHX	PCC, RSM	3 monthly polishing rubber cup oral hygiene instruction	3 y
H <sub>2</sub> O <sub>2</sub>		PCC		
PS + saline rinse	CHX	Nanocrystalline HA	1–6 monthly	4 y
		XBM + CM		
Resective IPP, MTR gel, TET	AMX, CHX	None	Strict maintenance care	3 y
Resective MTR gel, TET		None		

with gauze soaked in saline, followed by saline irrigation. Systemic amoxicillin and metronidazole was prescribed for 7 days and chlorhexidine rinsing for 4 weeks.

Two studies reported on access surgery and decontamination without systemic antibiotics. de Mendonça et al<sup>44</sup> gained surgical access, removed granulation tissue, and cleaned the implant surfaces with resin currettes and an air-powder abrasive device using sodium bicarbonate powder. Maximo et al<sup>45</sup> and Duarte et al<sup>46</sup> raised a flap and removed granulation tissue, and implant surfaces were decontaminated with teflon currettes and an air-powder abrasive device using sodium bicarbonate powder.

In the one retrieved study on reconstructive surgery, Serino and Turri<sup>47</sup> raised an access flap and recontoured the bone. The implant surfaces were instrumented using an ultrasonic instrument and rotating rubber cup under chlorhexidine irrigation. Patients received clindamycin for 1 week and rinsed for 2 weeks with chlorhexidine after the intervention.

**Comparative Studies (RCTs) of Surgical Interventions.** Deppe et al<sup>48</sup> treated peri-implantitis lesions using both resective and regenerative procedures with or without CO<sub>2</sub> laser (wavelength 10.6 μm). After flap elevation and granulation tissue removal, all implants were cleaned with an air-powder abrasive. The regenerative procedures included bone augmentation using a combination of autologous bone and beta-tricalcium phosphate covered by an ePTFE membrane.

Schwarz et al<sup>49,50</sup> compared two surface decontamination methods in conjunction with regenerative surgical treatment of peri-implantitis. Following access flap, granulation tissue removal, and implantoplasty at buccally and supracrestally exposed implant parts, the intrabony aspects were randomly allocated to surface cleaning with either (1) Er:YAG laser or (2) plastic currettes plus swabbing with cotton pellets soaked in saline and irrigation with saline. In both groups, the intrabony component was augmented with a xenogenic bone mineral (Bio-Oss) and covered with a collagen membrane.

Two studies reported on regenerative treatments using grafts with or without barrier membranes. Khoury and Buchmann<sup>51</sup> evaluated three regenerative protocols. The implants were treated with flap surgery plus autogenous bone grafts alone, graft plus ePTFE barrier membranes, or graft plus bioabsorbable barrier membranes (Bio-Gide). After flap elevation and granulation tissue removal, the surgical sites were rinsed with chlorhexidine and the implant surfaces were treated with citric acid, irrigated with H<sub>2</sub>O<sub>2</sub>, and rinsed with saline. Augmentation procedures were then completed and systemic antimicrobials were administered with the choice of drug based on a microbiological examination. Roos-Jansäker et al<sup>52,53</sup> evaluated regenerative treatment of peri-implantitis comparing a bone substitute with or without a barrier membrane. Following flap elevation, the implant surfaces were mechanically

cleaned, treated with 3% H<sub>2</sub>O<sub>2</sub>, and rinsed with saline. Peri-implant defects were treated with a phyto-genic calcium carbonate bone substitute (Algipore) or with the bone substitute and a resorbable synthetic membrane (Osseoquest). Systemic amoxicillin and metronidazole was prescribed for 10 days, and patients rinsed with chlorhexidine.

Schwarz et al<sup>54-56</sup> elevated a flap, removed granulation tissue, and cleaned the implant surfaces with plastic curettes and rinsed with saline solution. The defects were filled with either a synthetic nanocrystalline hydroxyapatite (Ostim) or a bovine-derived xenogenic bone mineral (BioOss), and covered with a collagen membrane (Bio-Gide). No systemic antimicrobials were prescribed.

Romeo et al<sup>57,58</sup> compared two different surgical approaches. Patients were treated either with resective surgery and implantoplasty (modification of the implant surface topography using a sequence of different burs and polishers) or with resective surgery alone. A pretreatment phase included nonsurgical debridement and systemic antibiotics for 8 days. Following flap elevation and granulation tissue removal, alveolar bone peaks were removed. Metronidazole gel was applied and a tetracycline HCl solution was rubbed on the implant surface for 3 minutes and then rinsed off with saline. The flaps were apically positioned.

**Nonsurgical versus Surgical Interventions.** No trials were found reporting on nonsurgical versus surgical interventions.

### Case Definitions

The inclusion criteria for each study are presented in Tables 2 and 3 for nonsurgical interventions and Tables 4 and 5 for surgical interventions. The criteria used varied widely between studies. As outlined in the Materials and Methods section, the authors of this review rated the case definition of each study as clear, unclear, or inadequate.

**Case Series of Nonsurgical Interventions (3 Studies).** One study was assigned as having a clear case definition<sup>18</sup> and two studies with an unclear case definition.<sup>16,17</sup>

**Comparative Studies of Nonsurgical Interventions (10 Studies).** Two studies were assigned as having a clear case definition,<sup>24,30</sup> seven studies with an unclear case definition,<sup>12,21,23,25,27,28,32</sup> and one study with an inadequate case definition.<sup>20</sup>

**Case Series of Surgical Interventions (14 Studies).** Seven studies were assigned as having a clear case definition,<sup>37,40,42-45,47</sup> five with an unclear case definition,<sup>33-35,39,41</sup> and two studies with an inadequate case definition.<sup>36,38</sup>

**Comparative Studies of Surgical Interventions (6 Studies).** One study was assigned as having a clear

case definition,<sup>52</sup> four with an unclear case definition,<sup>48-50,54-58</sup> and one study with an inadequate case definition.<sup>51</sup>

### Quality Assessment and Risk of Bias Assessment

**Case Series of Nonsurgical Interventions.** Examiner blinding and calibration were not reported in any of the case series.

A standardized probing force and the use of a parallel radiographic technique for standardizing radiographs were reported in one case series.<sup>18</sup>

**Case Series of Surgical Interventions.** Examiner blinding was reported in five studies.<sup>35-37,40,41</sup> Examiner calibration was reported in five studies.<sup>35,37,41,44,45</sup> A standardized probing force was reported in two studies.<sup>40,43</sup> A paralleling technique for standardizing radiographs was reported in seven studies.<sup>34,35,39,40,42-44</sup> One study reported use of a bite block for standardization of radiographs.<sup>40</sup>

**Comparative Studies.** Tables 6 and 7 outline the risk of bias assessment, as judged by the authors of this review, for non-surgical and surgical comparative studies (RCTs) respectively.

The majority of comparative studies were judged to be at unclear risk of bias. Two studies were judged to have a high risk of bias.<sup>28,29</sup>

### Outcome Measures Reported in the Included Studies

The following treatment outcomes were reported in the included studies.

#### Case Series of Nonsurgical Interventions

- Implant failure leading to loss or removal of the implant was evaluated in all studies.<sup>16-18</sup>
- Persistence or recurrence of peri-implantitis, ie, suppuration from the peri-implant sulcus, was evaluated in two studies.<sup>17,18</sup>
- Change in peri-implant PD was evaluated in all studies.<sup>16-18</sup>
- Change in BoP was evaluated in all studies.<sup>16-18</sup>
- Change in mucosal recession was evaluated in all studies.<sup>16-18</sup>
- Radiographic marginal bone levels were evaluated in two studies.<sup>17,18</sup>
- Complications and side effects were not reported in any of the studies.

#### Comparative Studies of Nonsurgical Interventions

- Implant failure leading to loss or removal of the implant was evaluated in all studies.<sup>20,21,23-25,27-30,32</sup>
- Persistence or recurrence of peri-implantitis, ie, suppuration from the peri-implant sulcus, was evaluated in five studies.<sup>24,28-30,32</sup>
- Change in peri-implant PD was evaluated in all studies.<sup>20,21,23-25,27-30,32</sup>

**Table 6 Risk of Bias Assessment for Nonsurgical Comparative (RCT) Studies**

	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Summary assessment
Büchter et al <sup>20</sup>	+	?	+	+	+	+	Unclear
Karring et al <sup>24</sup>	?	?	+	+	?	+	Unclear
Renvert et al <sup>30</sup> Persson et al <sup>31</sup>	+	?	+	+	?	+	Unclear
Renvert et al <sup>25</sup> Persson et al <sup>26</sup>	+	?	+	–	?	+	Unclear
Renvert et al <sup>21</sup>	+	+	+	–	?	+	Unclear
Renvert et al <sup>23</sup>	+	?	+	+	?	+	Unclear
Sahm et al <sup>27</sup>	+	?	?	+	?	+	Unclear
Schär et al <sup>32</sup>	+	?	+	+	?	+	Unclear
Schwarz et al <sup>28</sup>	+	?	–	–	–	+	High
Schwarz et al <sup>29</sup>	+	?	?	–	–	+	High

+ low risk; ? unclear risk; – high risk.

**Table 7 Risk of Bias Assessment for Surgical Comparative (RCT) Studies**

	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Summary assessment
Deppe et al <sup>48</sup>	?	?	?	?	+	+	Unclear
Khoury and Buchmann <sup>51</sup>	?	?	?	+	?	+	Unclear
Romeo et al <sup>57,58</sup>	?	?	?	+	?	+	Unclear
Roos-Jansåker et al <sup>52,53</sup>	?	?	?	–	?	+	Unclear
Schwarz et al <sup>54–56</sup>	+	?	+	–	?	+	Unclear
Schwarz et al <sup>49,50</sup>	–	?	?	?	?	+	Unclear

+ low risk; ? unclear risk; – high risk.

- Change in BoP was evaluated in all studies.<sup>20,21,23–25,27–30,32</sup>
- Change in mucosal recession was evaluated in four studies.<sup>27–29,32</sup>
- Radiographic marginal bone levels were evaluated in four studies.<sup>23,24,29,30</sup>
- Complications and side effects were evaluated in four studies.<sup>25,27–29</sup>

#### **Case Series of Surgical Interventions**

- Implant failure leading to loss or removal of the implant was evaluated in all studies.<sup>33–45,47</sup>
- Persistence or recurrence of peri-implantitis, ie, suppuration from the peri-implant sulcus, was evaluated in seven studies.<sup>36,37,41,44,45,47</sup>
- Change in peri-implant PD was evaluated in all studies except two.<sup>38,42</sup>
- Change in BoP was evaluated in 10 studies.<sup>33,35–37,40–45</sup>
- Change in mucosal recession was evaluated in five studies.<sup>36,40,41,43,44</sup>
- Radiographic marginal bone levels/change were evaluated in 10 studies.<sup>33–40,42,43</sup>
- Complications and side effects were evaluated in 11 studies.<sup>33–41,43,44</sup>

#### **Comparative Studies of Surgical Interventions**

- Implant failure leading to loss or removal of the implant was evaluated in all studies.<sup>48,49,51,52,54,57</sup>
- Persistence or recurrence of peri-implantitis, ie, suppuration from the peri-implant sulcus, was reported in two studies.<sup>49,50,54</sup>
- Change in peri-implant PD was evaluated in all studies.<sup>48,49,51,52,54,57</sup>
- Change in BoP was evaluated in four studies.<sup>49,50,52,54,57,58</sup>
- Change in mucosal recession was evaluated in five studies.<sup>48–50,52,57</sup>
- Radiographic marginal bone levels were evaluated in three studies.<sup>51–53,57</sup>
- Complications and side effects were evaluated in four studies.<sup>49–52,54</sup>

#### **Treatment Outcomes**

**Case Series of Nonsurgical Interventions.** Mombelli and Lang<sup>16</sup> evaluated manual debridement with systemic ornidazole in 9 patients with 9 implants. There were no withdrawals, no implant losses and no complications reported. At 12 months there was a reduction

in mean PD from 5.9 mm to 3.4 mm. The mean BoP reduced from 89% to 43%, and the mean recession increased from 1.1 mm to 2.1 mm. There were no radiographic data presented.

Mombelli et al<sup>17</sup> evaluated manual debridement with local delivery of tetracycline fibers in 25 patients with 30 implants. At 6 months, 2 patients (3 implants) were discontinued from the study due to persistent peri-implantitis and suppuration on probing. There were no implant losses and no complications reported. The mean PD was 4.7 mm at baseline and 3.5 mm at 12 months, and the mean BoP reduced from 90% to 40% at the deepest implant site. Mean radiographic bone levels were 5.2 mm at baseline and 4.9 mm at 12 months.

Salvi et al<sup>18</sup> evaluated manual debridement with local delivery of minocycline in 25 patients with 31 implants. Six implants in 6 patients were withdrawn from the study due to persistent peri-implantitis and suppuration on probing. The mean PD was 4.5 mm at baseline and 3.5 mm at 12 months, and the mean % of sites with BoP reduced from 69% to 19% at 12 months. Radiographic analysis, while not possible at all implants, showed no significant change in the marginal bone levels.

**Comparative Studies (RCTs) of Nonsurgical Interventions.** Three studies compared manual debridement with manual debridement using local antimicrobials. Büchter et al<sup>20</sup> evaluated a local antimicrobial (doxycycline) as an adjunct to manual debridement as well as manual debridement alone. The 28 patients (14 in each group) were followed for 4.5 months with no loss to follow-up. No implant loss and no complications were reported. Both treatment groups showed a reduction in mean probing depths and mean BoP from baseline to 4.5 months, with a greater reduction in the doxycycline group. However, at the completion of the study there was incomplete resolution of disease in both groups, with a mean PD of 5.4 mm and mean BoP of 50% in the manual debridement group compared with a mean PD of 4.5 mm and mean BoP of 27% in the doxycycline group. There were no radiographic data presented and no reporting on presence/absence of suppuration on probing.

Renvert et al<sup>21,22</sup> evaluated a local delivery of minocycline as an adjunct to manual debridement in comparison with manual debridement with submucosal chlorhexidine application. Thirty-two patients were treated (16 in each group) and 2 were lost to follow-up, leaving 30 patients for reevaluation at 12 months. No implant loss was reported. In the manual debridement group, the mean PD was 3.9 mm at baseline with no change at 12 months, while there was a reduction in the mean BoP from 86% at baseline to 78% at 12 months. In the minocycline group, the mean PD was 3.9 mm at baseline and 3.6 mm at 12 months, and the mean BoP was reduced from 88% at baseline to 71% at

12 months. There were no radiographic data reported and no reporting on presence/absence of suppuration on probing.

In a second trial, Renvert et al<sup>23</sup> evaluated a similar protocol in which the treatments in each group were repeated after day 30 and 90. Fifteen patients were included in the manual debridement group and 17 patients in the minocycline group. There were no withdrawals and no implant losses. In the manual debridement group, the mean PD was 3.9 mm at baseline and 3.7 mm at 12 months, and there was a reduction in mean BoP from 89% at baseline to 64% at 12 months. In the minocycline group, the mean PD was 3.9 mm at baseline and 3.6 mm at 12 months, and the BoP was reduced from 87% at baseline to 48% at 12 months. Radiographic bone levels were reported with minor changes at 12 months. There was no reporting on the presence/absence of suppuration on probing or complications or side effects.

Two studies compared manual debridement with ultrasonic debridement. Karring et al<sup>24</sup> compared manual debridement with the Vector method in a split-mouth design in 11 patients. Both interventions were repeated after 3 months. Six months after treatment, no implants were lost and there were no changes in the marginal bone levels reported in either treatment group. There was also no reduction in the mean PD in either treatment group. In the group treated by the Vector method, 4 patients showed resolution of disease (no BoP), while in the group treated with manual debridement, 1 patient showed resolution of disease (no BoP). In both treatment groups, 2 patients had recurrence of disease according to the authors' criteria of PD > 4 mm with BoP. Despite one of the inclusion criteria in this study being positive BoP, not all patients had implants with positive BoP at baseline.

Renvert et al<sup>25</sup> and Persson et al<sup>26</sup> in a parallel design study, compared manual debridement with the Vector method. Two of the 19 patients were lost to follow-up in the manual debridement group, while 4 of the 18 patients were lost to follow-up in the Vector group. Six months after treatment, no implants were lost; however, there was no reduction in mean probing depth or mean number of BoP sites in either treatment group. The authors of the study concluded that there were no clinically relevant changes within the groups over a 6-month period. No radiographic data were reported and there were no adverse events reported by the patients participating in the study.

Sahm et al<sup>27</sup> evaluated manual debridement with submucosal chlorhexidine compared to debridement using an air-powder abrasive device. Thirty-two patients were included (16 in each group) and 1 patient in each group was lost to follow-up. At 6 months, there was no implant loss and no complications were reported. In the air-powder abrasive group, the mean PD was

4.0 mm at baseline and 3.5 mm at 6 months, with a reduction in mean BoP from 95% to 51%. In the manual debridement group, the mean PD was 3.8 mm at baseline and 3.2 mm at 6 months, with a reduction in mean BoP from 95% to 84%. No radiographic evaluation or data on suppuration on probing were reported.

Two studies with a similar protocol evaluated the 12-month outcomes of manual debridement and sub-mucosal chlorhexidine compared with Er:YAG laser treatment.<sup>28,29</sup> Schwarz et al<sup>29</sup> evaluated 20 patients (10 patients with 20 implants in each group) 12 months following treatment. Two patients with 4 implants were excluded from the manual debridement group prior to the 12-month follow-up due to persistent peri-implantitis with pus formation. One patient in the Er:YAG laser group had a healing complication that resulted in marked mucosal recession. There were no implant losses reported. At 12 months in the manual debridement group, the initial deep peri-implant pockets (mean PD 6.0 mm) had reduced to a mean PD of 5.6 mm. In the Er:YAG laser group, the initial deep peri-implant pockets (mean PD 5.9 mm) had reduced to a mean PD of 5.5 mm. The authors reported a greater reduction in BoP in the laser group; however, no numerical data were presented. The authors reported that there were no changes in radiolucency; however, no radiographic measurements were reported. In this study, all patients were discontinued at 12 months and received further treatment (surgical procedures), indicating that none of the patients had resolution of disease.

Schwarz et al<sup>28</sup> reported 6-month treatment outcomes in 20 patients (10 patients with 16 implants in each treatment group). One patient (with 2 implants) in the manual debridement group was excluded from the 6-month evaluation due to persistent peri-implantitis and suppuration. There were no implant losses reported and no adverse effects of treatment. The mean PD was reduced from 5.5 mm to 4.8 mm in the manual debridement group, with a reduction in mean BoP from 80% to 58%. In the Er:YAG laser group, the mean PD was reduced from 5.4 mm to 4.6 mm and there was a reduction in mean BoP from 83% to 31% at 6 months. No radiographic data were reported.

Renvert et al<sup>30</sup> evaluated the 6-month outcomes following treatment with an Er:YAG laser (21 patients with 55 implants) compared with an air-abrasive device (21 patients with 45 implants). There were no patient withdrawals, no implant losses, and no adverse effects of treatment reported. At baseline, 31% of the implants in the laser group and 38% of the implants in the air-powder abrasive group had suppuration on probing. After 6 months, both treatment groups reported 11% of implants with suppuration on probing. At the patient level, 25% of the patients in the laser group had a mean PD reduction  $\geq 1$  mm, whereas 38%

of the patients in the air-abrasive group had an average PD reduction  $\geq 1$  mm. The mean BoP was reduced from 100% to 75% in the air-powder abrasive treatment group and from 100% to 70% in the Er:YAG laser treatment group. Radiographic evaluation showed a mean bone loss of 0.1 mm in the air-powder abrasive group and a mean bone loss of 0.3 mm in the Er:YAG laser treatment group. The authors reported that none of the implants in either group had a positive outcome (defined as having PD  $\geq 5$  mm with BoP and suppuration at baseline, but no PD  $\geq 5$  mm and no BoP or suppuration at 6 months).

Schär et al<sup>32</sup> evaluated the 6-month treatment outcome of photodynamic therapy compared to local delivery of minocycline (20 patients with 20 implants in each group). There were no withdrawals and no implant losses. At 6 months, the minocycline group had a mean PD reduction from 4.4 mm to 3.9 mm, with a reduction in mean number of sites with BoP from 4.4 to 2.1 sites. The photodynamic group had a mean PD reduction from 4.2 mm to 3.8 mm, with a reduction in mean number of sites with BoP from 4.0 to 2.3 sites. At 6 months, 15% of the implants in the minocycline group had complete resolution of mucosal inflammation compared to 30% in the photodynamic treatment group. There were no data on radiographic bone levels, suppuration on probing, or complications reported.

**Case Series of Surgical Interventions.** Augthun et al<sup>33</sup> (treated 15 implants in 12 patients by implant surface decontamination with an air-powder abrasive device, placement of an ePTFE membrane, and administration of systemic tetracycline. In 13 of 15 treated implants, premature membrane removal was required due to wound-healing complications. No implant losses were reported. At 12 months there was no change in BoP and a mean bone loss of 0.8 mm. Peri-implant probing depths were reduced by a mean of 1 mm.

Three studies reported on regenerative treatment using grafts without membranes. Behneke et al<sup>34</sup> treated 25 implants in 17 patients with an air-powder abrasive, autogenous bone grafts, and systemic metronidazole. Healing complications were reported in 6 patients. One graft was removed after 40 days because of flap dehiscence and graft mobility. In another patient, healing was uneventful but the graft was resorbed entirely. There were no implant losses reported. At 12 months there was a mean PD reduction from 5.3 mm at baseline to 2.2 mm. A radiographic median marginal bone gain of 4 mm was reported at 12 months. There were no data presented for BoP. Positive outcomes were documented up to 3 years; however, not all implants were followed. Rocuzzo et al<sup>35</sup> reported on 26 patients with 26 implants with two different surfaces (TPS and SLA). Regenerative treatment, using bovine-derived xenograft following implant cleaning with a

plastic curette, application of EDTA, and chlorhexidine and antibiotic therapy, resulted in 12-month mean PD reductions of 2.1 mm at implants with a TPS surface and 3.4 mm at implants with a SLA surface. Complete defect fill was not found around TPS implants, while it occurred in 3 out of 12 SLA-surface implants. At 12 months, 4 of the 26 patients had implants with suppuration. Two of these implants were removed after 12 months. Mean BoP decreased from 91% to 57% (TPS) and from 75% to 15% (SLA). Overall, the mean PD reduced from 7.0 mm to 4.2 mm, and the mean BoP reduced from 83% to 36% at 12 months. There was a mean radiographic bone gain of 1.7 mm, with incomplete defect fill in 75% of the implants.

Wiltfang et al<sup>36</sup> evaluated 22 patients with 36 implants. Regenerative treatment was performed following implant-surface decontamination and implantoplasty using a mix of autologous bone and a demineralized xenogenic bone graft including growth factors in combination with systemic antimicrobials. One implant had a local infection 1 week after treatment, resulting in loss of the graft. At 1 year, 1 implant was lost due to mobility. Probing depths were reduced by 4 mm on average and were > 4 mm at 7 of the 36 treated implants. Before surgical intervention, BoP was observed in 61% of the implants and in 25% after 1 year. The corresponding values for suppuration were 80% and 8%. After 12 months, a mean gain in bone height of 3.5 mm was reported (evaluated using panoramic radiographs). Recessions increased from 0.7 mm before surgery to 2 mm 1 year after surgery.

Five studies reported on regenerative treatment using grafts and membranes. Froum et al<sup>37</sup> evaluated a regenerative approach including surface decontamination, use of enamel matrix derivative, a combination of PDGF with anorganic bovine bone or mineralized freeze-dried bone, and coverage with a collagen membrane or a subepithelial connective tissue graft. None of the 51 implants in 38 patients were lost after 3 to 7.5 years of follow-up. At the final evaluation, the mean PD reduction was 5.3 mm (from 8.4 mm pretreatment to 3.1 mm). There was a reduction in BoP from 100% to 18% of implants and mean radiographic bone gain of 3.4 mm. No implant recorded an increase in buccal mucosal recession. Twelve-month results were not provided, and the authors reported that 6 patients required two or three surgical procedures to achieve the desired outcome.

Romanos and Nentwig<sup>38</sup> evaluated regenerative treatment; following mechanical debridement and CO<sub>2</sub> laser irradiation, they placed either an autogenous bone graft (10 implants) or a xenogenic bone graft covered by a collagen membrane (9 implants). In the 15 patients who were treated and followed for 27 ± 18 months, no implants were lost. A mean PD reduction from 6.0 mm

to 2.5 mm postoperatively was reported. Implants treated with xenogenic bone grafting material had complete radiographic bone fill, while partial fill was reported for defects treated with autogenous bone. There were no data on complications or BoP reported.

Haas et al<sup>39</sup> evaluated regenerative treatment in 17 patients (24 implants) using autogenous bone and an ePTFE membrane in conjunction with photodynamic therapy and systemic penicillin. Premature membrane exposure occurred in all patients; however, the membranes were left in situ for 6 weeks in all patients except one. Two implants with severe initial bone loss were removed, one after 10 months and another after 35 months. The mean radiographic peri-implant bone gain amounted to 2 mm at 9.5 months. There were no data on BoP or PD changes reported.

Roos-Jansåker et al<sup>40</sup> evaluated regenerative treatment in 12 patients (16 implants) using a phytogetic bone substitute combined with a resorbable synthetic membrane, systemic antimicrobials, and submerged healing. Two weeks postoperatively, 63% of the implants had inadequate primary healing. One patient reported an allergic reaction to the systemic antimicrobials. There were no implants lost at the 12-month follow-up. At the deepest implant site there was a mean PD reduction from 6.4 mm to 2.2 mm, and a reduction in BoP from 75% to 13% at 12 months. All implants had a defect fill of at least one thread (0.6 mm) with a mean radiographic defect fill of 2.3 mm. Suppuration on probing was recorded at 94% of the implants prior to treatment. The presence/absence of suppuration was not reported at 12 months.

Schwarz et al<sup>41</sup> evaluated regenerative treatment in 27 patients (27 implants) using bovine-derived xenograft covered with a collagen membrane and nonsubmerged healing. The results at 6 and 12 months were presented for three different defect types separately. Circumferential intrabony defects showed higher changes in mean probing depth and clinical attachment level than circumferential or semicircumferential lesions with a buccal dehiscence. All patients were followed, no implants were lost, and there were no postoperative complications reported. Overall, there was a reduction in mean PD from 6.9 mm to 2.0 mm and a reduction in mean BoP from 83% to 41%. There were no radiographic data presented.

Leonhardt et al<sup>42</sup> reported the outcome of access surgery and implant-surface decontamination with H<sub>2</sub>O<sub>2</sub> and administration of five different systemic antibiotics in 9 patients (26 implants). Seven implants in 4 patients were lost during a 5-year follow-up period. Despite a significant reduction in the presence of plaque and sulcus bleeding, 4 implants continued to lose bone, 9 had an unchanged bone level, and 6 gained bone. The benefit of administering systemic

antibiotics according to a susceptibility test of presumed target bacteria remained unclear. The authors concluded 58% treatment success after 5 years based on implant and radiographic bone loss. There was no peri-implant probing performed.

Heitz-Mayfield et al<sup>43</sup> evaluated access surgery and implant surface cleaning with titanium-coated curettes and by rubbing with gauze soaked in saline, plus prescription of amoxicillin and metronidazole in 24 patients (36 implants). At 12 months, all patients were followed and there were no implant losses. Six patients reported side effects related to mild gastrointestinal disturbance. The mean PD was reduced from 5.3 mm at baseline to 2.9 mm at 12 months. At 12 months, all treated implants had a mean PD < 5 mm and 47% of implants had no BoP. The mean recession of the buccal peri-implant mucosa at 12 months was 1 mm. At 12 months follow-up, 3 implants in 3 patients had radiographic bone loss, 3 implants in 3 patients showed bone gain, while the remaining implants had stable crestal bone levels.

Maximo et al<sup>45</sup> and Duarte et al<sup>46</sup> reported on access surgery and decontamination without systemic antibiotics in the same group of 13 patients (20 implants) with peri-implantitis. Access surgery and mechanical implant cleaning with teflon curettes and an air-powder device was evaluated at 3 months. There were no postoperative complications, no patient withdrawals and no implant losses reported. At 3 months there was a reduction in mean PD from 7.5 mm to 4.4 mm and a reduction in mean BoP from 100% to 53%. The frequency of implants that presented with a mean PD  $\geq$  5 mm and concomitant BoP or suppuration was 100% at baseline and 25% at 3 months. The frequency of implants with suppuration on probing at baseline was 65% at baseline and 5% at 3 months. There were no radiographic data presented.

de Mendonca et al<sup>44</sup> evaluated access surgery and mechanical implant cleaning with resin curettes and air-powder abrasion in 10 patients (10 implants). There were no implant losses, no patient withdrawals, and no postoperative complications reported. Prior to treatment, 7 patients had suppuration on probing, while none had suppuration at 12 months. At 12 months, the mean PD reduced from 6.7 mm to 4.3 mm, and the mean BoP from 100% to 27%. There was a mean increase in recession of 2.0 mm. At 12 months, 40% of the patients had implants with a mean PD  $\geq$  5 mm with concomitant BoP. No radiographic data were reported.

Serino and Turri<sup>47</sup> reported the outcome of a resective surgical procedure that included pocket elimination and bone recontouring at 86 peri-implantitis lesions in 31 patients. At 3 months, 7 of the 18 implants with advanced bone loss ( $\geq$  7 mm) were removed due to persistent peri-implantitis. Two years after therapy,

15 patients displayed no signs of peri-implant disease (no BoP and/or suppuration). At 2 years, 24 patients had no implants with a PD  $\geq$  6 mm with concomitant bleeding and/or suppuration upon probing. Between the 6-month and 2-year evaluation, the number of implants with PD  $\geq$  6 mm and BoP or suppuration increased. Out of 86 implants with an initial diagnosis of peri-implantitis, 36 (42%) still presented peri-implant disease despite treatment. No radiographic data were provided following treatment.

**Comparative Studies (RCTs) of Surgical Interventions.** Deppe et al<sup>48</sup> evaluated resective and regenerative treatment with and without CO<sub>2</sub> laser for the treatment of peri-implantitis in 32 patients with 73 implants. Four months after therapy, 4 implants were lost in a patient treated with laser and 4 implants in a patient treated without laser. Four months after treatment, the mean PD in the laser group was 3 mm for implants in residual bone and 2.7 mm for implants in augmented bone. In the non-laser group, the mean PD was 3.6 mm for implants in residual bone and 4.7 mm for implants in augmented bone. At 4 months there were no significant differences in the distance from implant shoulder to the first bone contact between implants treated with or without the laser. The follow-up period varied between 20 and 236 weeks post-treatment. There were no data presented for BoP or radiographic bone levels, and no reporting on the presence or absence of complications.

Two studies reported on regenerative treatments using grafts with or without barrier membranes. Khoury and Buchmann<sup>51</sup> evaluated the outcomes of three regenerative treatment protocols for peri-implantitis. In 25 patients, 41 peri-implant defects were treated with either flap surgery plus autogenous bone graft alone (n = 12); autogenous bone graft plus nonresorbable membrane (n = 20); or autogenous bone graft plus bioabsorbable barrier (n = 9) and various systemic antimicrobials. At 12 months, no implants were lost. The treatment groups in which a barrier membrane was used had healing complications: in 60% of cases using ePTFE membrane and in 56% of cases in which a collagen membrane was used. At 12 months, the mean PD at implants treated with autogenous bone graft alone was 5.4 mm, ePTFE membrane 4.8 mm, collagen membrane 3.3 mm. After 3 years, significant changes in mean probing depth from baseline were noted in all three groups. Three-year radiographic evaluation showed a mean bone gain in all treatment groups. The differences between the three surgical treatment protocols were not significant. There were no data presented for BoP.

Roos-Jansåker et al<sup>52,53</sup> evaluated the extent of radiographic bone fill 12 months and 3 years following regenerative surgical treatment of peri-implantitis us-

ing a graft with or without a membrane. Prior to augmentation, the implants were mechanically cleaned, treated with H<sub>2</sub>O<sub>2</sub>, and rinsed with saline. Thirty-eight patients were treated; however, 2 died before the 12-month follow-up, leaving 17 patients with 29 implants in the group treated with bone substitute and resorbable membrane and 19 patients with 36 implants in the group treated with bone substitute alone. Systemic amoxicillin and metronidazole were administered for 10 days, and patients rinsed with chlorhexidine. One patient reported an allergic reaction to the antibiotics and 5 patients reported postoperative healing complications (pain, swelling). When membranes were used, membrane exposure occurred in 44% of the treated implants. In the bone substitute plus membrane group the mean PD was 5.4 mm at baseline and 2.5 mm at 12 months. The mean percentage of sites with BoP was 79% at baseline and 22% at 12 months. In the bone substitute group, the mean PD was 5.6 mm at baseline and 2.2 mm at 12 months. The mean BoP was 96% at baseline and 25% at 12 months. At 12 months, the mean radiographic defect fill was 1.5 mm in the bone substitute plus membrane group compared to 1.4 mm in the bone substitute group. At 12 months, there were no implant losses; however, 6 implants continued to lose bone (1 implant lost two threads, and 5 implants lost one thread). Information on the number of patients with further bone loss was not provided.

Four patients in the group treated with bone substitute alone were lost to follow-up during the 1- to 3-year period, leaving 15 patients with 27 implants in this group after 3 years. Statistical analysis failed to demonstrate changes in bone fill between 1 and 3 years both between and within procedure groups. There were no PD or BoP data presented at the 3-year follow-up.

Romeo et al<sup>57,58</sup> compared the clinical outcome of resective surgery and modification of surface topography (implantoplasty) with resective surgery alone for the treatment of peri-implantitis in 17 patients. All patients received systemic amoxicillin for 8 days. At 12 months there were no implant losses and no complications reported. The mean PD in the implantoplasty group had reduced from 5.8 mm at baseline to 3.4 mm at 12 months, and the mean number of sites with positive BoP from 2.8 mm at baseline to 0.4 mm at 12 months. The mean recession in the implantoplasty group was increased from 0.5 mm to 2.3 mm. In the group treated with resective surgery alone, the mean PD had reduced from 6.5 mm to 5.9 mm and the mean number of sites with BoP had reduced from 2.9 at baseline to 2.7 at 12 months. The mean recession had increased from 0.2 mm to 1.4 mm.

After 24 months, Romeo et al<sup>58</sup> reported the loss of 2 hollow-screw implants from the resective surgery group due to mobility. After 3 years, 1 patient

was lost to follow-up in the implantoplasty group and 2 patients in the resective surgery group. The mean marginal bone level was unchanged 3 years after implantoplasty, while in the resective surgery group there was a mean bone loss of 1.4 mm at the mesial and 1.5 mm at the distal surfaces.

Schwarz et al<sup>55,56</sup> evaluated the 6-month and 1-, 2-, and 4-year results of regenerative treatment of 22 peri-implantitis lesions in 22 patients. The defects were filled with a graft material in combination with a collagen membrane. The graft was either a nanocrystalline hydroxyapatite or a xenogenic bone mineral (11 patients with 11 implants in each group). Two patients treated with nanocrystalline hydroxyapatite experienced severe pus formation at 12 months and were withdrawn from the study. One patient receiving xenogenic bone mineral was withdrawn due to severe pus formation at 3 years. At 12 months, the mean PD was reduced from 6.9 mm to 4.9 mm, with a reduction of BoP from 80% to 36% in the hydroxyapatite group. In the xenogenic bone mineral group, the mean PD was reduced from 7.1 mm to 4.4 mm, with a reduction in the mean BoP from 78% to 29%. There were no radiographic data reported. Higher mean probing depth reductions and clinical attachment level gains were reported at 4 years in the group treated with xenogenic bone mineral and covered with a collagen membrane. No implant loss or complications were reported.

Schwarz et al<sup>49,50</sup> investigated the impact of two surface debridement/decontamination methods on the clinical outcomes of a combined surgical treatment of peri-implantitis. Thirty-two patients suffering from advanced peri-implantitis were treated with flap surgery, implantoplasty, and xenogenic bone mineral covered with a collagen membrane. The intrabony aspects were randomly allocated to surface cleaning with either (1) Er:YAG laser or (2) plastic curettes, followed by cotton swabbing with pellets soaked in saline. Clinical parameters were recorded at baseline and after 6 and 24 months of nonsubmerged healing. One patient was lost to follow-up at 3 months in the laser group and a further 5 patients between 6 and 24 months. One patient was lost to follow-up at 6 months in the plastic curette debridement group and a further patient between 6 and 24 months. There were no implant losses reported. All barrier membranes became exposed; however, there were no infections reported. At 12 months, the mean PD had reduced from 4.9 mm to 3.2 mm and the mean BoP from 97% to 42% in the laser group. In the plastic curette group, the 12-month mean PD reduced from 5.2 mm to 3.2 mm and the mean BoP reduced from 100% to 40%. The mean recession increased from 1.5 mm to 1.9 mm in the laser group and from 1.3 mm to 1.8 mm in the plastic curette group. The authors reported both groups showed comparable radiographic bone fill at the in-

trabony defect component at 6 months; however, no radiographic bone level data were reported at 12 months. At 24 months there were 5 implants in both groups with recurrent peri-implantitis, which were retreated. No radiographic data were reported.

### Successful Treatment Outcome Criterion

Table 8 includes 11 studies in which data were presented such that the number of patients (or implants) with successful treatment outcomes at 12 months could be determined according to the proposed success criterion (implant survival with mean PD < 5 mm and no further bone loss).

Six studies evaluating regenerative protocols,<sup>33,35–37,40,52</sup> one study evaluating access surgery,<sup>43</sup> one study evaluating resective surgery,<sup>57,58</sup> and three studies evaluating nonsurgical treatment<sup>17,18,29</sup> were included in Table 8. Successful treatment outcomes at 12 months were reported from between 76% to 100% of the patients treated in seven of the studies. Two studies reported successful treatment outcomes from 75% to 93% of implants treated. The two remaining studies in Table 8 reported none of the patients with a successful outcome according to the success criterion. One evaluated nonsurgical treatment in deep peri-implantitis lesions where all patients required surgery after 12 months follow-up,<sup>29</sup> while the other used a regenerative protocol using a nonresorbable membrane, where frequent barrier membrane exposure occurred, with no clinical improvement after 12 months.<sup>33</sup>

This does not mean that the other studies included in this review did not achieve successful outcomes; however, the data were not available to evaluate the proposed success criterion.

## DISCUSSION

Given that the field of research into peri-implantitis is relatively new, it is not surprising that there are many different treatment approaches reported in the literature. Until now, no particular treatment protocol has been shown to be definitively effective (ie, a gold standard) so no one specific treatment protocol could be validly considered as a control in an RCT. Therefore, the RCTs included in the present review were analyzed for treatment outcomes for each treatment arm and not comparatively.

The effectiveness of a treatment protocol for the resolution of the disease could be measured in a number of ways. Ideally, resolution of disease would mean absence of clinical inflammation (bleeding on probing). Few studies reported on the number of patients with implants with absence of BoP. While most studies showed a reduction in mean BoP, 19% to 84% of implant

sites still bled on probing following nonsurgical treatment, while 13% to 53% of sites bled on probing following surgical treatment. Few studies provided individual data on the probing depth associated with bleeding sites or the frequency of patients with implants with deep sites (PD > 5 mm) with concomitant BoP.

The authors have proposed a composite criterion designed to provide a threshold or delimitation separating the need for further treatment of disease versus the need for maintenance of health. This would be meaningful for both the patient and clinician. The criterion includes a PD threshold of 5 mm with no concomitant BoP and absence of further bone loss. The difficulty in any attempt to review the diverse treatments described in this review in the context of such a criterion is that the presentation of the outcome data is also quite diverse. Many studies did not provide data in a form that could be used to assess this composite criterion. Therefore, Table 8 includes studies where successful treatment referred to implant survival with a mean PD < 5 mm and with no further bone loss. While it is recognized that there is an inherent high risk of bias in case series studies, the data in the case series were often presented in a form easier to analyze regarding the composite criterion than the comparative trials. This does not decrease the value of any one trial; rather, it varies the confidence with which we can make conclusions about the treatments trialed.

On the basis of the analysis of the studies, commonalities in treatment approaches between studies included (1) a pretreatment phase, (2) cause-related therapy, and (3) a maintenance care phase. A surgical approach with elevation of a mucoperiosteal flap was performed where access to the implant surface was judged as inadequate due to a deep peri-implant pocket. The majority of the surgical protocols included administration of perioperative or postoperative systemic antibiotics and postoperative chlorhexidine rinsing. However, there were no randomized controlled trials found comparing treatment with or without systemic antimicrobials.

An important observation was that the peri-implantitis case definition for inclusion varied considerably between studies. In some studies it was not clear from the information provided relating to bone loss whether the patients had peri-implantitis or peri-implant mucositis. Furthermore, some studies did not provide information regarding presence of clinical inflammation (bleeding or suppuration on probing) in the inclusion criteria. The severity of disease (initial PD and amount of bone loss) also varied between studies and among patients within studies.

It is also important to realize that most studies had specific exclusion criteria, including exclusion of: patients who smoked<sup>27–29,32</sup> or smoked  $\geq 10$  cigarettes

**Table 8 Successful Treatment Outcomes At 12 Months**

Study	Study type and treatment	Patients	Successful treatment outcome (% patients)	12 mo mean % of sites with BoP (*deepest site)
Mombelli et al <sup>17</sup>	Case series, nonsurgical LDD: Actisite	25	84%	NR 41%*
Salvi et al <sup>18</sup>	Case series, nonsurgical LDD: Arestin	25	76%	19% 44%*
Schwarz et al <sup>29</sup>	RCT, nonsurgical manual debridement Laser	8 10	0% 0%	58% (estimated from figure in paper) 65% (estimated from figure in paper)
Augthun et al <sup>33</sup>	Case series, regenerative surgery	12	0%	47% implants
Heitz-Mayfield et al <sup>43</sup>	Case series, access surgery	24	88%	25%
Roccuzzo et al <sup>35</sup>	Case series, regenerative surgery	26	85%	36%
Wiltfang et al <sup>36</sup>	Case series, regenerative surgery	22	75% of implants	25% of implants
Roos-Jansåker et al <sup>40</sup>	Case series, regenerative surgery	12	100%	13%*
Froum et al <sup>37</sup>	Case series, regenerative surgery	38	84% (36–90 mo results)	18%*
Romeo et al <sup>57,58</sup>	Comparative trial, Resective surgery + IPP	10	100%	NR Modified bleeding index 2.7
	Resective surgery	9	0%	NR Modified bleeding index 0.4
Roos-Jansåker et al <sup>52</sup>	Comparative trial, Bone substitute + membrane	17	93% of implants	22%
	Bone substitute	19	89% of implants	25%

Includes studies that reported on implant loss, mean PD, % of sites or implants with bleeding and/or suppuration on probing, and radiographic bone levels at 12 mo (or longer) following treatment. Successful treatment outcome defined as: implant survival with no mean PD  $\geq$  5 mm and no further bone loss 12 mo after treatment.  
LDD: local delivery device; IPP: implantoplasty with bur; NR: not reported.

per day<sup>41</sup>; patients with FMPS > 20% or FMBS > 20%<sup>43</sup> or a Plaque Index > 1<sup>27,29,41,54–56</sup>; patients with periodontal pockets > 5 mm<sup>24</sup>; pregnant or lactating women<sup>18,21,23,32,43</sup>; patients with poorly controlled diabetes<sup>25–27,30,31,41,43</sup>; patients taking bisphosphonate medication<sup>27,41,47,49,50,54–56</sup>; patients who had taken systemic antibiotics in recent months prior to treatment<sup>3,18,21,22,24–26,29–32,42–46</sup>; patients with implants with < 2 mm keratinized mucosa,<sup>27</sup> or no keratinized mucosa.<sup>28,54–56</sup> Therefore, the results reported in individual studies should be interpreted with this in mind and may not apply to all patients.

The length of follow-up in the included studies also varied from 3 months to 7.5 years. Whilst clinical healing could be expected to be complete by 3 months following cause-related therapy (ie, removal of the biofilm),<sup>43,45</sup> detectable changes in radiographic marginal bone levels may not be apparent at this time. Therefore, a 12-month reevaluation period for assessment of successful treatment outcome was chosen for this review. However, it should be recognized that successful outcomes at 12 months might be influenced by the quality of maintenance care.

It is also likely that risk factors for peri-implantitis, including smoking, poor oral hygiene, untreated periodontal disease, and diabetes,<sup>1,9,59,60</sup> may modify both the initial outcome of treatment as well as the long-term outcome. There were 11 studies included in this review with follow-up greater than 12 months. While longer-term studies are desirable, the question remains as to whether recurrence of disease after 12 months constitutes failure of initial treatment or rather the institution of a new disease process. Continuous collection of data over 5 years or longer could provide valuable insights into answering this question.

Further questions, which remain unanswered, include the influence of implant surface and topography on treatment outcomes. Most of the studies include a number of implant brands and designs. One study<sup>35</sup> reported differences in outcomes for implants with TPS or SLA surfaces. It is conceivable that protocols for surface decontamination may have different effects depending on macro- and microstructure of the surface and that not all methods may work equally well in all instances. To what extent bacterial and nonbacterial residues have to be removed from an implant surface

12-mo mean PD	Baseline mean PD	12-mo radiographic bone change	Comments
3.5 mm 3.9 mm*	4.7 mm 6 mm*	No significant change	Case definition unclear: BoP and BL threshold not included individual implant data available
3.5 mm 4.2 mm*	4.5 mm 5.9 mm*	No significant change	6 patients (6 implants) with persistent suppuration
5.6 mm 5.5 mm	6.0 mm 5.9 mm	No significant change	Advanced lesions included in this table All patients re-treated after 12 mo
4.1 mm	5.2 mm	0.8 mm mean bone loss	Case definition unclear: BoP not included
2.9 mm	5.3 mm	No change or bone gain	3 patients with further bone loss + suppuration 47% of implants had absence of BoP at 12 mo
4.3 mm	7.0 mm	1.7 mm mean bone gain	4 patients with TPS-surface implants with suppuration
3.5 mm	7.5 mm	3.5 mm mean bone gain	8% of implants had suppuration, 1 patient lost 1 implant
2.2 mm*	6.4 mm*	2.3 mm mean bone gain	6 mo submerged healing
3.0 mm*	8.3 mm*	3.4 mm mean bone gain	6 patients required 2 or 3 surgical procedures, no implants lost bone
3.4 mm	5.8 mm	No change	No BoP data
5.9 mm	6.5 mm	0.5 mm mean bone loss	No BoP data, 2 implants removed at 2 y, 2 implants removed at 3 y
2.5 mm	5.4 mm	2 implants lost, 1 thread bone	
2.2 mm	5.6 mm	1 implant lost 2 threads, 3 implants lost 1 thread	

to obtain a predictable and stable clinical result after treatment remains to be elucidated. The requirements for a clean implant surface may differ depending on the goal of therapy. While a reduction in the bacterial load and suppression of pathogens in the peri-implant pocket may be enough to establish a balance between the peri-implant microbiota and the host defense, the implant surface may not be biocompatible for direct reapposition of bone.

The influence of defect morphology and the initial severity of disease may also influence the treatment outcome for certain interventions. There is evidence that nonsurgical therapy is ineffective in advanced peri-implantitis cases where access to the contaminated implant surface is limited.<sup>29</sup> Intraosseous defect configuration may also impact on treatment outcome following a regenerative protocol.<sup>41</sup> Other factors that may play a role in the success of peri-implantitis treatment and warrant further investigation include the proximity of adjacent implants, the position of implants within the arch, and the absence of keratinized peri-implant mucosa.

In a recent Cochrane systematic review of randomized controlled trials, no clinically relevant advantage of one treatment over another was identified.<sup>6</sup> In the included trials in the Cochrane systematic review, and the present review, many different treatments were frequently combined, making it difficult to evaluate the effectiveness of a single procedure. Future RCTs might include single procedures believed to be the most effective as controls, such as some protocols identified in Table 8, rather than combining numerous techniques and materials all at once. In this review, no studies were considered at low risk of bias. In future studies, power calculations should be performed to ensure an adequate sample size and efforts should be made to reduce the risk of bias (adequate randomization and blinding). Reporting should account for patient dropouts, withdrawals and failures. Treatment outcomes, including esthetic parameters, patient preference, and relative cost of treatments, should be considered. It would be useful for studies to document the number of patients with resolution of peri-implantitis or successful treatment outcome (defined as implant survival with no PD  $\geq$  5 mm with concomitant BoP or suppuration or further bone loss).

## CONCLUSIONS

This review showed that successful treatment outcomes 12 months following therapy of peri-implantitis could be achieved in a majority of patients in seven studies. While favorable short-term outcomes were reported in many studies, lack of disease resolution as well as progression or recurrence of disease and implant loss despite treatment were also reported. All studies included in this review had either an unclear or high risk of bias, which should be considered when interpreting the results. Furthermore, the reported outcomes must be viewed in the context of the varied peri-implantitis case definitions and severity of disease included, as well as the heterogeneity in study design, length of follow-up, and exclusion/inclusion criteria.

While the currently available evidence does not allow any firm specific recommendations for nonsurgical or surgical therapy of peri-implantitis, the following elements of therapy seem to be beneficial:

### *A pretreatment phase including*

- Oral hygiene instruction and counseling for smoking cessation
- Assessment of the prosthesis for access for plaque control
- Prosthesis removal and adjustment if required
- Nonsurgical debridement with or without antimicrobials

### *Surgical access (when resolution of peri-implantitis is not achieved with nonsurgical treatment)*

- Full-thickness mucoperiosteal flap to allow thorough cleaning of the contaminated implant surfaces (numerous techniques, may involve modification of the implant surface topography).
- The stabilization of the intraosseous peri-implant defect with a bone substitute/bone graft/bioactive substance with or without a resorbable barrier membrane

### *Postoperative anti-infective protocol*

- Peri- or postoperative systemic antibiotics
- Chlorhexidine rinses during the healing period (several weeks)

### *Maintenance care*

- Three- to 6-month maintenance, including oral hygiene instruction and supramucosal biofilm removal

## ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

## REFERENCES

1. Mombelli A, Müller N, Cionca N. The epidemiology of peri-implantitis. *Clin Oral Implants Res* 2012;23(suppl 6):67–76.
2. Klinge B, Gustafsson A, Berglundh T. A systematic review of the effect of anti-infective therapy in the treatment of peri-implantitis. *J Clin Periodontol* 2002;29(suppl 3):213–225; discussion 232–213.
3. Renvert S, Roos-Jansaker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: A literature review. *J Clin Periodontol* 2008;35:305–315.
4. Renvert S, Polyzois I, Claffey N. Surgical therapy for the control of peri-implantitis. *Clin Oral Implants Res* 2012;23(suppl 6):84–94.
5. Muthukuru M, Zainvi A, Esplugues EO, Flemmig TF. Non-surgical therapy for the management of peri-implantitis: A systematic review. *Clin Oral Implants Res* 2012;23(suppl 6):77–83.
6. Esposito M, Grusovin MG, Worthington HV. Treatment of peri-implantitis: What interventions are effective? A Cochrane systematic review. *Eur J Oral Implantol* 2012;5(suppl):s21–s41.
7. Mombelli A, Moene R, Decaillet F. Surgical treatments of peri-implantitis. *Eur J Oral Implantol* 2012;5(suppl):s61–s70.
8. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: Treatment of peri-implantitis. *Cochrane Database Syst Rev* 2012;1:CD004970.
9. Heitz-Mayfield LJ. Peri-implant diseases: Diagnosis and risk indicators. *J Clin Periodontol* 2008;35:292–304.
10. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
11. Bach G, Neckel C, Mall C, Krekeler G. Conventional versus laser-assisted therapy of peri-implantitis: A five-year comparative study. *Implant Dent* 2000;9:247–251.
12. Schwarz F, Bieling K, Nuesry E, Sculean A, Becker J. Clinical and histological healing pattern of peri-implantitis lesions following non-surgical treatment with an Er:YAG laser. *Lasers Surg Med* 2006;38:663–671.
13. Charalampakis G, Rabe P, Leonhardt A, Dahlen G. A follow-up study of peri-implantitis cases after treatment. *J Clin Periodontol* 2011;38:864–871.
14. Zhou L, Lin Y, Qiu L-X, Chen B, Hu X-I, Wang X. [Clinical study of periocline on peri-implantitis treatment.] *Zhonghua Kou Qiang Yi Xue Za Zhi* 2006;41:299–303.
15. Tang Z, Cao C, Sha Y, Lin Y, Wang X. [Effects of non-surgical treatment modalities on peri-implantitis.] *Zhonghua Kou Qiang Yi Xue Za Zhi* 2002;37:173–175.
16. Mombelli A, Lang NP. Antimicrobial treatment of peri-implant infections. *Clin Oral Implants Res* 1992;3:162–168.
17. Mombelli A, Feloutzis A, Bragger U, Lang NP. Treatment of peri-implantitis by local delivery of tetracycline. Clinical, microbiological, and radiological results. *Clin Oral Implants Res* 2001;12:287–294.
18. Salvi GE, Persson GR, Heitz-Mayfield LJA, Frei M, Lang NP. Adjunctive local antibiotic therapy in the treatment of peri-implantitis II: Clinical and radiographic outcomes. *Clin Oral Implants Res* 2007;18:281–285.
19. Persson GR, Salvi GE, Heitz-Mayfield LJA, Lang NP. Antimicrobial therapy using a local drug delivery system (Arestin) in the treatment of peri-implantitis. I: Microbiological outcomes. *Clin Oral Implants Res* 2006;17:386–393.
20. Büchter A, Meyer U, Kruse-Lösler B, Joos U, Kleinheinz J. Sustained release of doxycycline for the treatment of peri-implantitis: Randomized controlled trial. *Br J Oral Maxillofac Surg* 2004;42:439–444.
21. 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;33:362–369.
22. Renvert S, Lessem J, Lindahl C, Svensson M. Treatment of incipient peri-implant infections using topical minocycline microspheres versus topical chlorhexidine gel as an adjunct to mechanical debridement. *J Int Acad Periodontol* 2004;6:154–159.
23. 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;79:836–844.

24. Karring ES, Stavropoulos A, Ellegaard B, Karring T. Treatment of peri-implantitis by the Vector system. A pilot study. *Clin Oral Implants Res* 2005;16:288–293.
25. Renvert S, Samuelsson E, Lindahl C, Persson GR. Mechanical non-surgical treatment of peri-implantitis: a double-blind randomized longitudinal clinical study. I: clinical results. [Erratum appears in *J Clin Periodontol* 2009 Dec;36:1076]. *J Clin Periodontol* 2009;36:604–609.
26. 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;37:563–573.
27. 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;38:872–878.
28. 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.
29. Schwarz F, Bieling K, Bonsmann M, Latz T, Becker J. Nonsurgical treatment of moderate and advanced peri-implantitis lesions: A controlled clinical study. *Clin Oral Investig* 2006;10:279–288.
30. Renvert S, Lindahl C, Roos Jansaker 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.
31. Persson GR, Roos-Jansaker 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;82:1267–1278.
32. 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;24:104–110.
33. Augthun M, Richter E-J, Hauptmann S, Yildirim M. Untersuchungen zur Behandlung von tiefen periimplantären Knochentaschen mit ePTFE-Membranen. *Z Zahnärztl Implantol* 1992;8:246–250.
34. Behneke A, Behneke N, d'Hoedt B. Treatment of peri-implantitis defects with autogenous bone grafts: Six-month to 3-year results of a prospective study in 17 patients. *Int J Oral Maxillofac Implants* 2000;15:125–138.
35. 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. *J Clin Periodontol* 2011;38:738–745.
36. Wiltfang J, Zernial O, Behrens E, Schlegel A, Warnke PH, Becker ST. Regenerative treatment of peri-implantitis bone defects with a combination of autologous bone and a demineralized xenogenic bone graft: A series of 36 defects. *Clin Implant Dent Relat Res* 2012;14:421–427.
37. Froum SJ, Froum SH, Rosen PS. Successful management of peri-implantitis with a regenerative approach: A consecutive series of 51 treated implants with 3- to 7.5-year follow-up. *Int J Periodontics Restorative Dent* 2012;32:11–20.
38. Romanos GE, Nentwig GH. Regenerative therapy of deep peri-implant infrabony defects after CO<sub>2</sub> laser implant surface decontamination. *Int J Periodontics Restorative Dent* 2008;28:245–255.
39. Haas R, Baron M, Dortbudak O, Watzek G. Lethal photosensitization, autogenous bone, and ePTFE membrane for the treatment of peri-implantitis: Preliminary results. *Int J Oral Maxillofac Implants* 2000;15:374–382.
40. Roos-Jansaker A-M, Renvert H, Lindahl C, Renvert S. Submerged healing following surgical treatment of peri-implantitis: A case series. *J Clin Periodontol* 2007;34:723–727.
41. 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;37:449–455.
42. Leonhardt A, Dahlen G, Renvert S. Five-year clinical, microbiological, and radiological outcome following treatment of peri-implantitis in man. *J Periodontol* 2003;74:1415–1422.
43. Heitz-Mayfield LJA, Salvi GE, Mombelli A, Faddy M, Lang NP, Implant Complication Research G. Anti-infective surgical therapy of peri-implantitis. A 12-month prospective clinical study. *Clin Oral Implants Res* 2012;23:205–210.
44. de Mendonça AC, Santos VR, Cesar-Neto JB, Duarte PM. Tumor necrosis factor-alpha levels after surgical anti-infective mechanical therapy for peri-implantitis: A 12-month follow-up. *J Periodontol* 2009;80:693–699.
45. 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.
46. Duarte PM, de Mendonca AC, Maximo MBB, 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;80:234–243.
47. Serino G, Turri A. Outcome of surgical treatment of peri-implantitis: Results from a 2-year prospective clinical study in humans. *Clin Oral Implants Res* 2011;22:1214–1220.
48. Deppe H, Horch HH, Neff A. Conventional versus CO<sub>2</sub> 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.
49. 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 Periodontol* 2011;38:276–284.
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;39:789–797.
51. 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;72:1498–1508.
52. Roos-Jansaker A-M, 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;34:625–632.
53. Roos-Jansaker 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;38:590–597.
54. 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;33:491–499.
55. 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;35:80–87.
56. 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;36:807–814.
57. 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.
58. 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;18:179–187.
59. Pjetursson BE, Helbling C, Weber HP, Matuliene G, Salvi GE, Bragger U, et al. Peri-implantitis susceptibility as it relates to periodontal therapy and supportive care. *Clin Oral Implants Res* 2012;23:888–894.
60. Bornstein MM, Cionca N, Mombelli A. Systemic conditions and treatments as risks for implant therapy. *Int J Oral Maxillofac Implants* 2009;24(suppl):12–27.