Title page

Title
Impact of surface decontamination and systemic antimicrobials for surgical treatment of peri-implantitis: A systematic review and meta-analysis of randomized clinical trials

Running title
Infection control in peri-implantitis.

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Conflict of Interest Statement

The authors declare no conflict of interest.

Author contribution statement

GB, FC, NB and MA made substantial contributions to conception of the study. GB, FC, NB, FR and MA contributed to the study design. GB, FC and NB searched and collected the data. GB, FC, FP and FR performed data analysis and interpretation. GB, FC, GMM and FR prepared the first draft of the manuscript. All authors have read, revised critically, and approved the final manuscript.

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Availability of data and material

All data generated or analyzed during this study are included in this published article [and its supplementary information files].
SUMMARY BOX

What is known

- Peri-implantitis is a common biological complication occurring at dental implants, and surgery is usually required to obtain thorough peri-implant infection control.

- No systematic reviews with meta-analysis have assessed surface decontamination protocols for surgical treatment of peri-implantitis, as well as the adjunctive benefit of peri-operative systemic antimicrobials.

What this study adds

- This study offered the first evidence-based synthesis of randomized clinical trials regarding this relevant topic.

- Although protocol heterogeneity was high, a combination of mechanical and chemical implant surface decontamination is recommendable.

- Titanium brushes and local delivery of minocycline showed encouraging results; while the additional benefit of systemic antimicrobials needs to be further determined.
Abstract

Background: Efficient control of infection is essential to achieve desired outcomes in the surgical treatment of peri-implantitis lesions, although methods employed are largely heterogeneous.

Purpose: To compare the impact of different decontamination protocols and adjunctive systemic antimicrobials on the outcomes of surgical treatment of peri-implantitis.

Materials and methods: Randomized clinical trials (RCTs) on surgical treatment of peri-implantitis were selected through an electronic search on Medline, Embase, Scopus, and Central databases. Only studies comparing two or more anti-infective strategies were included. Following data extraction, two different sets of meta-analyses were performed. Firstly, overall impact of different implant surface decontamination methods was assessed by comparing baseline values with outcomes at 6-12 months. Secondly, pairwise comparisons evaluated the potential benefit of adjunctive systemic antimicrobials over placebo. Results were expressed as weighted mean effect (WME), weighed mean difference (WMD) or risk ratio (RR).

Results: Sixteen RCTs were included. No pairwise comparisons were available for different surface decontamination methods. Use of curettes resulted in improved probing depth (PD) (WME = 2.13 mm), but the results in terms of marginal bone levels (MBL) and percentage of disease resolution were unsatisfactory. Moreover, the adjunctive benefit of systemic antimicrobials over placebo was evaluated in two studies, representing a total of 178 implants. Despite not being statistically significant, the meta-analyses identified a higher probability of disease resolution (RR = 1.50) for test procedures. In terms of overall outcome, systemic antimicrobials with open flap debridement resulted in improved MBL (WME = 0.44 mm), reduced PD (WME = 2.46 mm) and 51.4% of disease resolution.

Conclusions: There is not enough evidence to support adjunctive usage of systemic antimicrobials together with the surgical treatment of peri-implantitis. Moreover, higher consistency is required to prove the superiority of a surface decontamination protocol over another (PROSPERO CRD42020182303).
Keywords: implant, antibiotics, peri-implantitis, systematic review, randomized controlled trial
1. Introduction

Peri-implantitis is a rather frequent biological complication negatively affecting the success and survival of dental implants that is characterized by inflammation in the adjacent connective tissue and progressive resorption of supporting bone.\(^1\) Its estimated prevalence is around 22%, although there is a wide variation in case definitions and diagnostic criteria used across the studies.\(^2,3\) Peri-implantitis has a bacterial etiology, and the success of treatment mostly depends on arresting the inflammatory process through efficient control of infection and removal of dysbiotic biofilm from the implant surface.\(^4\)

Treatment of peri-implantitis traditionally involves a first phase of supramucosal plaque control and a subsequent deep debridement of the implant surface.\(^5\) Nonetheless, clinical success of non-surgical methods is limited in resolving peri-implantitis, and surgical intervention is usually recommended for better mechanical access to contaminated implant surfaces and efficient decontamination.\(^6,7\) Although surgical procedures demonstrated favorable treatment outcomes in terms of reductions in probing depth (PD) and inflammation,\(^8\) complete disease resolution (DR) still remains unattainable for most cases.\(^9,10\)

Insufficient implant decontamination may be regarded as a major explanation for these limited outcomes.\(^11\) Due to poor mechanical access to the bottom of bony defects and differences in micro and macro topography of titanium interfaces, appropriate surface decontamination continues to be a challenge.\(^12\) Therefore, there is an increasing interest on adjunctive agents that could possibly restore titanium biocompatibility and promote re-osseointegration.\(^13,14\) Various chemical and mechanical methods including irrigation with saline, air powder abrasion, titanium brushes, citric acid application, ultrasonic and manual debridement, laser therapy, and topical medications have been proposed, but no single method was found to be superior in terms of clinical outcomes.\(^5,15\) Furthermore, controversies still exist regarding the efficacy of adjunctive systemic antimicrobials in infection control and improvement of treatment outcomes.\(^9,16,17\)
There are systematic reviews investigating the efficacy of surgical techniques and biomaterials in improving the clinical parameters of peri-implantitis lesions.\textsuperscript{18,19} However, the clinical impact of available implant surface decontamination procedures has not been systematically evaluated so far. Proving the superiority of a specific method would be of uttermost relevance in enhancing the consistency of outcomes in peri-implantitis treatment and research. Accordingly, the evidence supporting usage of peri-surgical systemic antimicrobials is limited, and further data is required to justify their prescription. Therefore, the aims of the present systematic review were: 1) to evaluate and compare the efficacy of different implant surface decontamination protocols for the surgical treatment of peri-implantitis; 2) to investigate whether adjunctive systemic antimicrobials provide additional clinical benefits.

2. Materials and Methods

2.1 Report and protocol

This systematic review was reported according to the PRISMA statement\textsuperscript{20} and the protocol was registered on PROSPERO (CRD42020182303).

2.2 Focused questions

This systematic review was designed to answer the following focused questions:

\textit{FQ1: In patients receiving surgical treatment of peri-implantitis, is any specific protocol of implant surface decontamination superior to others at improving the outcomes of therapy?}

\textit{FQ2: In patients receiving surgical treatment of peri-implantitis, can adjunctive systemic antimicrobials provide any significant additional benefit in terms of clinical and radiographic outcomes?}

2.3 Eligibility criteria

Inclusion criteria were determined a priori and organized according to the PICOST acronym.

2.3.1 PICO 1

(P) Population. Patients in good general health requiring surgical treatment of peri-implantitis.
(I) **Intervention.** Any type of chemical/physical or mechanical implant surface decontaminating agent, including possible combinations, used during surgical treatment of peri-implantitis.

(C) **Comparison.** Any possible comparisons between different protocols for intra-surgical decontamination.

(O) **Outcome measures.**

   Primary outcome: changes in probing depth (PD) in mm.

   Secondary outcomes: changes in radiographic marginal bone level (MBL), clinical attachment level (CAL), and bleeding/suppuration on probing (BoP/SUP). In addition, implant survival, disease resolution (DR) (possibly adhering to the definition to Carcuac et al.\textsuperscript{21} - residual PD $\leq$ 5 mm, no BoP, no suppuration, no progressive marginal bone loss after treatment), need of retreatment and patient-reported outcome measures (PROMs) were evaluated where available.

### 2.3.2 PICO 2

(P) **Population.** Patients in good general health with a clinical diagnosis of peri-implantitis.

(I) **Intervention.** Surgical treatment of peri-implantitis together with adjunctive systemic antimicrobials.

(C) **Comparison.** Surgical treatment of peri-implantitis without adjunctive systemic antimicrobials.

(O) **Outcome measures.** See above.

### 2.3.3 Studies and timing

(S) **Types of studies.** Randomized clinical trials (RCTs) on surgical treatment of peri-implantitis, with at least 6-month follow-up and a minimum of 10 patients (5 per group) were included. RCTs not directly comparing two anti-infective or surface decontamination agents or protocols were excluded.

(T) **Timing.** Data at 6-12 months after treatment were considered. If a study reported multiple evaluations between 6 and 12 months, data obtained at the latest time point were included. Data from longer follow-up periods were not used for the analysis, unless they were the only available.
2.4 Search methods for the identification of studies

The reviewing authors were calibrated before each phase of the study. Electronic search (Supplementary Table 1) was conducted on Medline (via PubMed), Embase, Scopus, and Cochrane Library electronic databases independently by two authors (GB and FC) with no restrictions on language, date of publication or publication status up to December 2020. In addition, hand searching (GB and NB) was performed on periodontics/implantology-related journals.

2.5 Study selection

Titles and abstracts (when available) of all identified studies were screened by two independent reviewers (NB and GB). Any disagreement was resolved by discussion with a third reviewer (FC). Full text of studies of possible relevance or for which there was insufficient data in the title and abstract were assessed independently by two reviewers (NB and FC). Differences between them were settled by a third reviewing author (GB). The reasons for exclusion after the full text analysis were recorded.

2.6 Data extraction and management

Data from included studies were extracted by two reviewers (GB and FC) independently using predefined data extraction forms (Table 1). If necessary, corresponding authors of the included studies were contacted for clarification of any missing information. If no reply was received within three months, the study was excluded.

Data on general information (first author, year of publication and setting); methods (study design, diagnostic criteria for peri-implantitis, sample size, follow-up period, population); interventions and controls (pre-treatment phase, type of surgery, type/combination of decontaminating agents, biomaterials, post-surgical care) and outcomes (changes in radiographic MBL, CAL, PD, REC percentage of implants with BoP and/or suppuration, implant survival, DR, PROMs) were tabled.
2.7 **Assessment of risk of bias in the included studies**

The risk of bias in the included studies was assessed independently and in duplicate by the two reviewing authors (GB and FC) according to RoB.2 tool.²²

2.8 **Data analyses**

For continuous outcomes at 6-12 months (changes of MBL and PD reduction), mean values and standard deviations were combined and analyzed with weighted mean effect (WME) and 95% confidence intervals (CIs). Dichotomous data were pooled as weighted mean percentage and 95% CIs. In pairwise comparison, the estimates of the effect were expressed as weighted mean differences (WMD) and 95% CIs for continuous outcomes and as risk ratio (RR) and 95% CIs for dichotomous outcomes. In order to account for within-patient correlation in studies which failed to adjust for it, an intracluster correlation coefficient of 0.07 was assumed for the calculation of the effective sample size and CIs. Study-specific estimates were pooled with and random-effects models to account for between studies heterogeneity.²³ The Mantel–Haenszel method was performed to combine the dichotomous outcomes, and the inverse of variance method to combine the continuous outcomes.

Two different sets of analyses were conducted. First, the outcome of different protocols for the decontamination of the implant surface was assessed by comparing baseline values with outcomes obtained with follow-up longer than 6 months. Only protocols reported exactly the same procedures, including the type of surgery [i.e. open flap debridement (OFD), resective or regenerative], in two or more studies were included. For studies with multiple arms, each decontaminating intervention was considered separately. Secondly, RCTs were used to evaluate the potential benefit of adjunctive systemic antimicrobials in OFD. For this analysis, no discrimination was made between the different methods of surface decontamination. OFD without systemic antimicrobials was considered as control.
Statistical heterogeneity among studies was explored using the $I^2$ index\textsuperscript{24,25} and the Cochrane's Q statistic ($p < 0.1$). For each meta-analysis forest plots were generated. Statistical significance was set to $p < 0.05$. Statistical analyses were performed using statistical software package OpenMeta [Analyst].\textsuperscript{26}

3. Results

3.1 Search

As outlined in Supplementary Figure 1, the electronic search yielded 1,835 publications and hand searching identified 5 additional studies. After removal of duplicates, the total number of articles screened was 1,497. Twenty-five records were identified as potentially relevant during screening (Kappa = 0.63, substantial agreement). Of these, four records were excluded after full text reading (Kappa = 0.911, almost perfect agreement), while six records were excluded as double-data, with the most relevant data retained for analysis.\textsuperscript{9,27–31} Finally, 16 RCTs were included in the qualitative analysis and 9 were used for meta-analyses. Reasons for article exclusion were reported in Supplementary Table 2.

3.2 Description of selected studies

3.2.1 Design

As shown in Table 1, all RCTs had a parallel arm design, 14 studies included one experimental group and one control group and two studies adopted multiple interventional arms.\textsuperscript{21,32} Six studies included multiple dental implants patient and did not account for clustering. Of these, five were included in the meta-analyses after correcting for the within-patient correlation.\textsuperscript{21,32–35} Six studies reported results at 6 months, and 6 studies at 12 months.

3.2.2 Study sample

Sample size varied from 17 to 100. All trials were carried out in European Universities, except from one that was performed at the Yonsei Dental Hospital of Seoul,\textsuperscript{36} one at the University of
Michigan,\(^{37}\) and one in a private practice in Saudi Arabia.\(^{38}\) Diagnosis of peri-implantitis followed the last update of the World Workshop on the Classification of Periodontal and Peri-Implant Diseases\(^{39}\) only in two studies;\(^{36,40}\) but was consistent across all studies except for minor differences (either MBL ≥ 2 or 3 mm together with PD ≥5 or 6 mm and BoP/SUP). Only three studies considered the intrasurgical morphology of the bony defect among inclusion criteria.\(^{41–43}\) Mean age of patients ranged from 54.3 to 71.7 years, while the proportion of females varied from 25% to 80.9%. In three studies smokers were excluded;\(^{33,36,37}\) two studies did not report any information on smoking habits;\(^{32,44}\) while the remaining trials included a variable number of smokers, ranging from 14.2% to 50%. Five studies presented implants with machined surface, with proportions ranging from 1.3 to 35%; four studies did not treat turned implant surfaces,\(^{32,33,36,37}\) without this being a specific exclusion criteria; while for seven studies this information was not available.

### 3.2.3 Interventions

In total, 849 implants were treated in 604 patients. Eight studies performed a non-surgical deep implant debridement prior to the intended treatment; while the other eight only performed supragingival scaling or did not report this information.\(^{17,21,32,33,36–38,44}\) Systemic antibiotics were administered prior to the surgical treatment in two RCTs;\(^{21,45}\) in six studies they were prescribed on the day of the surgery;\(^{17,36–38,42,43}\) while in the other eight studies no systemic antimicrobials were used. Eight studies reported decontaminating protocols applied to OFD;\(^{17,21,32,33,36,38,44,46}\) five studies to reconstructive or combined procedures;\(^{37,40–43}\) and three studies to apically positioned flap and osseous resective surgery (ORS).\(^{34,35,45}\) Five RCTs used mechanical decontamination,\(^{17,32,33,41,44}\) two studies chemical decontamination,\(^{34,35}\) while nine studies a combination of both. Curettes were the most preferred method for mechanical debridement, used in 25 arms of 12 RCTs, either alone or in combination with other devices; together with gauzes soaked in saline in 16 arms of 7 studies. Ultrasonic scalers were adopted in 10 arms of five studies; powder spray in five arms of four studies; titanium brushes in four arms of three studies, while implantoplasty was carried out in six arms of four studies. Among chemical and physical decontaminations, chlorhexidine (CHX) at 0.12
or 0.2 formulations was applied in four arms of three studies; lasers were used in three test groups of three different studies; a gel of metronidazole followed by a solution of tetracycline hydrochloride was rubbed on implant surfaces in both arms of the study by Romeo et al.; while enamel matrix derivatives (EMD); ozone therapy; photodynamic therapy; electrolytic current; and minocycline ointments were part of only one study arm. The main outcomes of the included studies are presented in Table 2.

3.3 Risk of bias in individual studies

The risk of bias assessment for the included RCTs is summarized in Figure 1. Ten papers had a low risk of bias. Three studies exhibited selection bias, one attrition bias, and one missing outcome data. One study was considered to have a high risk of bias due to the selection of reported results.

3.4 Outcomes of different decontamination protocols in OFD

A total of 452 implants in 339 patients were treated by OFD procedures. The MBL change ranged from a reduction of -0.96 mm in a control arm in which only titanium curettes plus gauze soaked in saline were employed, to a gain of 1.12 mm with the use of titanium brushes. The single use of curettes for surface decontamination resulted in a negligible MBL reduction (WME = -0.05 mm, 95% CI: -0.90/0.81) in three studies (three arms), with high heterogeneity ($I^2 = 94.82$ p < 0.001). In terms of PD reduction, the analysis included four studies (4 arms) yielding a WME of 2.14 mm (95% CI: 1.07/3.20); while the weighed mean percentage of DR amounted to 25% (95% CI: 16/33) with no heterogeneity (Figure 2A,B,C).

None of the studies gave information on defect fill or PROMs, and implant survival was described in only two with results ranging from 90.9% to 100% on the implant level.

3.5 Outcomes of different decontamination protocols in reconstructive surgery
A total of 192 implants in 156 patients were treated using reconstructive or combined procedures. None of the study arms provided comparable decontamination protocols, thus data meta-analysis was not possible.

### 3.6 Outcomes of different decontamination protocols in resective surgery

A total of 222 implants in 156 patients were treated by resective procedures. The use of CHX and cetylpyridinium chloride (CPC) together with ORS was investigated in two arms of two different studies by the same research group and no systemic antibiotics were used.\(^{34,35}\) WME in terms of post-treatment MBL was -0.49 mm (95% CI: -1.02/0.04) with significant heterogeneity \(I^2 = 85.73; p = 0.008\), WME for PD reduction was 2.05 mm (95% CI: 1.72/2.38) with no heterogeneity \(I^2 = 0; p = 0.633\). Eighteen out of 85 implants were successfully treated, and this accounted for a weighted mean percentage of DR of 17% with significant heterogeneity \(I^2 = 92.72; p < 0.001\) (Figure 2D,E,F).

### 3.7 Potential advantages of adjunctive systemic antimicrobials

Only two studies directly compared OFD with and without adjunctive systemic antibiotics.\(^ {17,21}\), while no data were available for the other surgical treatment approaches. The analysis evaluated 178 implants for PD reduction as outcome and a total of implants ranging from 178 to 209 for the secondary outcomes. Implant survival rate was comprised between 93.3% and 100%.

Figure 3 depicts the results of the pairwise meta-analysis for MBL changes. Only one study with four arms reported on radiographic changes. A statistically significant benefit (WMD = 1.17 mm; 95% CI: 0.58/1.76, \(p<0.001\)) in terms of MBL changes was observed in favor of the adjunctive systemic antimicrobials at 12 months, with a heterogeneity of 60.72%.

PD reduction was reported in two studies accounting for a total of six arms, failing to identify a statistically significant benefit at the test sites (WMD = 0.83 mm; 95% CI: −0.08/1.74). Disease resolution according to the criteria of Carcuac et al.\(^ {21}\) was reported in the same two studies, with a
RR of 1.50 (95% CI: 0.94/2.38; p = 0.086) favoring the antibiotics administration with low heterogeneity. None of the studies reported on defect fill or PROMs, while implant survival over one year or more was described in two.

Figure 4 illustrates changes in clinical parameters from baseline to 6-12 months postsurgery around implants treated using OFD with or without systemic antimicrobials. When adjunctive systemic antimicrobials were prescribed together with OFD (Figure 4A,B,C), MBL changes amounted to 0.44 mm (95% CI: 0.22/0.67) based on four arms in two studies. Regarding the secondary outcomes, PD reduction was assessed in five arms of three studies and amounted to 2.46 mm (95% CI: 1.74/3.18); while mean percentage of DR was 51% (95% CI: 33/69), and was based on three arms of two studies.

Considering OFD without adjunctive systemic antimicrobials (Figures 4D,E,F) the WME of MBL amounted to 0.33 mm (95% CI: 0.01/0.65), based on nine arms of four studies with high heterogeneity. PD reduction was assessed in five studies (10 arms) and amounted to 2.33 mm (95% CI: 1.66/2.80). Finally, DR was calculated in three studies (five arms) with a percentage of 29% (95% CI: 23/35) and no heterogeneity.

ORS was performed with or without systemic antibiotics but no study provided a direct comparison, thus, it was not possible to perform a pair-wise meta-analysis. As depicted in Figure 5, only two arms of the same study reported data on MBL changes 12 months after ORS combined with systemic antibiotics. The WME was −0.27 mm (95% CI: −0.82/0.29) with significant heterogeneity. Four arms in two different studies from the same research group used ORS without systemic antibiotics. WME for MBL accounted for -0.40 mm (95% CI: -0.67/0.13) with significant heterogeneity ($I^2 = 81.76; p < 0.001$), WME for PD reduction was 1.81 mm (95% CI: 1.59/2.03) with non-significant heterogeneity ($I^2 = 23.05, p = 0.273$). The same studies reported DR in a total of 26 successfully treated implants out of 171. This accounted for a weighted DR percentage of 11% (95% CI: 1/22) with significant heterogeneity ($I^2 = 83; p < 0.001$).
4. Discussion

Peri-implantitis has become a rather prevalent complication with the increasing placement of dental implants for the rehabilitation of missing teeth.\textsuperscript{47,48} Infection control has a pivotal role in the treatment of peri-implantitis, and there is a need for reliable and replicable methods. The present systematic review aimed at evaluating the efficacy of different anti-infective protocols for the surgical treatment of dental implants with clinical diagnosis of peri-implantitis. Overall, 16 RCTs were included in the qualitative and 9 in the quantitative analysis. Cohort studies or case series were excluded to obtain a higher quality of data and decrease the risk of bias.

4.1 Surface decontamination

Implant surface decontamination represents a fundamental step to achieve resolution of peri-implantitis lesions. However, the available clinical protocols show great variation and there is no evidence for the most effective procedure.\textsuperscript{5} Generally, there is a distinction between mechanical and chemical/physical decontamination methods, although a combination is usually recommended.\textsuperscript{12} Unfortunately, due to a significant heterogeneity within and among RCTs in terms of study design (definition of peri-implantitis, outcome, decontamination protocols, supportive care) and characteristics of the population (patient, implant and prosthetic features), a pairwise comparison between decontamination strategies was not possible and it remains unclear whether one protocol would provide greater benefits than others. However, the performances of different methods have still been assessed pooling data across studies.

OFD represents the best model for studies investigating clinical impact of different surface decontamination protocols at dental implants as it enables evaluation of the individual effect of the particular decontamination method on the final outcomes. Curettes are the most commonly used instruments for mechanical decontamination. Four study arms employed curettes alone to clean the implant surface during OFD. Improved PD values were reported (WME = 2.14 mm), while no significant differences were found in MBL changes (WME = -0.05 mm), and the effect in disease
resolution was very modest (25%). It has to be kept in mind that the type of curettes (titanium or plastic) may account for a small variability in the findings. The RCT by Toma et al. offers a direct comparison between three different methods of mechanical decontamination. The titanium brush and glycine air-polishing devices were more effective than the plastic curettes, but treatment success remained low for all three treatment modalities (33%, 29% and 22%, respectively).

The two RCTs by de Waal et al. indicated no additional significant benefit for the adjunctive employment of 0.12% CHX + 0.05% CPC with ORS. It is likely that implant surface decontamination may have less prominent effect when ORS is combined with apically positioned flap as a submucosal part becomes usually exposed by the surgical procedure. Moreover, there is controversial evidence on the role of implantoplasty. Romeo et al. reported superior 3-year clinical and radiographic results with this intervention. On the contrary, no clinical benefit of implantoplasty on implant survival rate was observed in a long-term retrospective study, with other factors such as the initial defect depth and the frequency of recalls accounting for a larger influence on the outcomes. However, maintenance may be easier for smooth surfaces than surfaces with micro- and macro-plaque-retentive elements.

Ideally, implant surface decontamination should remove biofilm without causing surface damage not to render surfaces more conducive to bacterial colonization. In vitro studies indicated that non-metal curettes and rubber cups were minimally traumatic but ineffective to clean contaminated titanium surfaces; while ultrasonic scalers, metal curettes and rotating titanium brushes were effective particularly on modified titanium surfaces. The air abrasive system was effective in all types of implant surfaces, with glycine powder causing less alterations than sodium bicarbonate. Nevertheless, in vitro studies do not properly simulate accessibility to the implant surface during surgical intervention. Anatomical factors and thread geometry can limit access of the decontamination devices, and implants with lower thread pitch and thread depth values may cause insufficient cleaning especially for instruments such as plastic curettes and air powder inserts with less flexibility.
Removal of bacterial biofilm from contaminated implant surfaces with air-powder abrasion has been reported to provide significantly superior microbiological outcomes than chemical decontamination with hydrogen peroxide and chlorhexidine gluconate. Coupling mechanic instruments with chemical/physical agents may improve the overall cleaning ability as the chemical agent may reach niches inaccessible for the instruments. Numerous chemical decontaminants have been tested, although their efficacy has been difficult to demonstrate. Different concentrations of CHX showed limited efficacy both in in vitro models and in clinical trials, as it exerts cytotoxic activity. Carcuac et al. failed to find an influence of chemical decontamination on 1- and 3-year success using 0.2% CHX regardless of the implant surface and even in terms of microbiological modifications. The present finding of lack of efficacy with 0.12% CHX + 0.05% CPC in ORS partially confirms the report of Carcuac et al.

Review articles and controlled clinical studies indicated that local delivery of antibiotics combined with non-surgical treatment of peri-implantitis lesions improved clinical parameters. Particularly, repeated application of locally delivered minocycline during post-surgical follow-up enhanced the clinical and microbiological effect of OFD, achieving 0.72 mm of vertical bone gain and 66.7% of disease resolution.

On the other hand, current evidence shows that laser or photodynamic therapy in combination with surgical/non-surgical treatment of peri-implant diseases provided minimal benefit in PD reduction, CAL gain, and MBL improvements. However, properly controlled clinical trials with low risk of bias are warranted to better clarify the issue.

Within the context of surgical regenerative treatment of peri-implantitis, several decontamination techniques have been described, but the large heterogeneity in flap design, biomaterials, bone defect anatomy and post-operative care restricts the conclusion on their efficacy. Encouraging outcomes were obtained by Isehed et al., with EMD applied on fixture surfaces switching subgingival microbiota to Gram+ aerobic populations. This ecological shift was linked with an increase in bone levels as compared with non-EMD controls. Decontamination of the supra-
and the intra-osseous part of the defect-adjacent implant surface has a particular importance. To achieve this, Schwarz et al., proposed a combined approach with regenerative treatment attempted apically and a resective approach with implantoplasty carried out in the supra-osseous part of the fixture, where re-osseointegration cannot be achieved. The adoption of the combined approach yielded a 66.7% of disease resolution in a RCT which used titanium brushes to decontaminate the intra-osseous part of the implant.43

4.2 Adjunctive systemic antimicrobials

Systemic antimicrobials are likely to have a place in the anti-infective strategies for implant surface decontamination and they have been traditionally prescribed in spite of the debate on global concerns of bacterial resistance development.61 Meta-analyses identified significantly larger MBL gain (WMD = 1.17 mm) with peri-surgical systemic antimicrobials, whereas probability of disease resolution (RR = 1.50) and differences in PD reduction approached statistical significance. Moderate to substantial heterogeneity was found and none of the included studies addressed PROMs. Carcuac et al.21 employed four parallel study arms to evaluate the single and combined effect of local decontaminant and systemic antimicrobials in OFD. While no added benefit was observed for CHX, a significant adjunctive effect in terms of MBL, PD reduction and DR was reported for the two groups with systemic antimicrobial prescriptions. Conversely, Hallström et al.17 did not find significant differences with systemic antibiotics. This discrepancy could be partially explained by different sample sizes or type and regimen of antibiotics used in these two different RCTs.62 The systemic antibiotic was started three days before the surgery and continued for 10 days in the RCT by Carcuac et al.,21, emphasizing the importance of pre-operative infection control. Overall, the findings of the present systematic review support the use of systemic antibiotics in the surgical treatment of peri-implantitis, even though a careful risk/benefit analysis is mandatory considering PROMs and the growing issue of antibiotic resistances. The available RCTs included in this review fail to adequately address these aspects.
4.3 Limitations and suggested future research

The present study has some limitations mainly related with the nature of the available literature. Several factors such as implant surface characteristics, configuration of peri-implant defect, frequency and quality of supportive therapy can affect the results of surgical treatment of peri-implantitis, but none of these factors could be considered in the present meta-analyses. Furthermore, 6-month follow-up in some of the included RCTs may be too short for detection of significant effect on MBL changes and may not account for the relatively high incidence of disease recurrence following surgical therapy of peri-implantitis. This threshold was chosen for two reasons: firstly to increase the number of eligible studies; and secondly to focus on the short-term clinical outcomes that are more likely to be explained by the decontamination procedures.

To the best of our knowledge, this systematic review is the first attempting to provide a qualitative and quantitative evaluation of the clinical outcomes of anti-infective protocols across different surgical procedures reported in published RCTs. This systematic review had a rather wide scope including RCTs using regenerative, resective, and combined surgery. This approach and the information outlined in Table 2 may provide valuable insight for the clinicians in treatment planning. The 8th European Workshop on Periodontology stated that “a proven method of decontaminating the implant surface” is a critical component of surgical treatment, yet available clinical, radiographic, and microbiological data do not favor any decontamination approach in surgical therapy so far. However, this finding does not mean that no treatment option is effective, but there is just no consensus on the best treatment procedure. Reasons may be imputable to different advantages and disadvantages associated with each method, and the tendency to adopt multiple combinations of decontaminants to increase the likelihood of success. Well-designed in vitro and in vivo studies with adequate sample size allowing comparisons with low risk
of bias are warranted in order to establish an evidence-based protocol for decontamination during the surgical treatment of peri-implantitis.

5. Conclusion

There is lack of evidence to support one intra-surgical protocol of implant surface decontamination over others. The use of curettes during OFD is able to produce PD reduction but has limited effect on MBL and DR; while different CHX formulations do not offer any benefits. Lack of replication was observed for all other chemical and mechanical decontamination methods and future research should aim for higher consistency. In parallel, the use of adjunctive systemic antimicrobials with the surgical treatment of peri-implantitis seems to be supported by a tendency for a clinical improvement at short-term, even though the risk/benefit ratio should be cautiously assessed by the clinicians.
References

1. Schwarz F, Derks J, Monje A, Wang H-L. Peri-implantitis. *J Clin Periodontol*. 2018;45 Suppl 20:S246-S266. doi:10.1111/jcpe.12954

2. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. *J Clin Periodontol*. 2015;42 Suppl 16:S158-171. doi:10.1111/jcpe.12334

3. Romandini M, Berglundh J, Derks J, Sanz M, Berglundh T. Diagnosis of peri-implantitis in the absence of baseline data: a diagnostic accuracy study. *Clin Oral Implants Res*. Published online December 19, 2020. doi:10.1111/clr.13700

4. Lindhe J, Meyle J, on behalf of Group D of the European Workshop on Periodontology. Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. *J Clin Periodontol*. 2008;35:282-285. doi:10.1111/j.1600-051X.2008.01283.x

5. Figuero E, Graziani F, Sanz I, Herrera D, Sanz M. Management of peri-implant mucositis and peri-implantitis. *Periodontol 2000*. 2014;66(1):255-273. doi:10.1111/prd.12049

6. Heitz-Mayfield LJA, Mombelli A. The therapy of peri-implantitis: a systematic review. *Int J Oral Maxillofac Implants*. 2014;29 Suppl:325-345. doi:10.11607/jomi.2014suppl.g5.3

7. Suárez-López del Amo F, Yu S-H, Wang H-L. Non-Surgical Therapy for Peri-Implant Diseases: a Systematic Review. *J Oral Maxillofac Res*. 2016;7(3). doi:10.5037/jomr.2016.7313

8. Roccuzzo M, Layton DM, Roccuzzo A, Heitz-Mayfield LJ. Clinical outcomes of peri-implantitis treatment and supportive care: A systematic review. *Clin Oral Implants Res*. 2018;29(S16):331-350. doi:10.1111/clr.13287
9. Carcuac O, Derks J, Abrahamsson I, Wennström JL, Petzold M, Berglundh T. Surgical treatment of peri-implantitis: 3-year results from a randomized controlled clinical trial. *J Clin Periodontol.* 2017;44(12):1294-1303. doi:10.1111/jcpe.12813

10. Khoury F, Keeve PL, Ramanauskaite A, et al. Surgical treatment of peri-implantitis – Consensus report of working group 4. *Int Dent J.* 2019;69(S2):18-22. doi:10.1111/idj.12505

11. Meyle J. Mechanical, chemical and laser treatments of the implant surface in the presence of marginal bone loss around implants. *Eur J Oral Implantol.* 2012;5 Suppl:S71-81.

12. Koo K-T, Khoury F, Keeve PL, et al. Implant Surface Decontamination by Surgical Treatment of Periimplantitis: A Literature Review. *Implant Dent.* 2019;28(2):173-176. doi:10.1097/ID.0000000000000840

13. Schou S, Holmstrup P, Jørgensen T, et al. Implant surface preparation in the surgical treatment of experimental peri-implantitis with autogenous bone graft and ePTFE membrane in cynomolgus monkeys: Implant surface preparation in the treatment of peri-implantitis. *Clin Oral Implants Res.* 2003;14(4):412-422. doi:10.1034/j.1600-0501.2003.00912.x

14. Louropoulou A, Slot DE, Weijden F. The effects of mechanical instruments on contaminated titanium dental implant surfaces: a systematic review. *Clin Oral Implants Res.* 2014;25(10):1149-1160. doi:10.1111/cnr.12224

15. Claffey N, Clarke E, Polyzois I, Renvert S. Surgical treatment of peri-implantitis. *J Clin Periodontol.* 2008;35:316-332. doi:10.1111/j.1600-051X.2008.01277.x

16. 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 232-233. doi:10.1034/j.1600-051x.29.s3.13.x
17. Hallström H, Persson GR, Lindgren S, Renvert S. Open flap debridement of peri-implantitis with or without adjunctive systemic antibiotics: A randomized clinical trial. *J Clin Periodontol.* 2017;44(12):1285-1293. doi:10.1111/jcpe.12805

18. Ramanauskaite A, Daugela P, Juodzbalys G. Treatment of peri-implantitis: Meta-analysis of findings in a systematic literature review and novel protocol proposal. *Quintessence Int Berl Ger 1985.* 2016;47(5):379-393. doi:10.3290/j.qi.a35131

19. Tomasi C, Regidor E, Ortiz-Vigón A, Derks J. Efficacy of reconstructive surgical therapy at peri-implantitis-related bone defects. A systematic review and meta-analysis. *J Clin Periodontol.* 2019;46:340-356. doi:10.1111/jcpe.13070

20. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-1012. doi:10.1016/j.jclinepi.2009.06.005

21. Carcuac O, Derks J, Charalampakis G, Abrahamsson I, Wennström J, Berglundh T. Adjunctive Systemic and Local Antimicrobial Therapy in the Surgical Treatment of Peri-implantitis: A Randomized Controlled Clinical Trial. *J Dent Res.* 2016;95(1):50-57. doi:10.1177/0022034515601961

22. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898. doi:10.1136/bmj.l4898

23. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2

24. Higgins JPT. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-560. doi:10.1136/bmj.327.7414.557
25. Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. Basics of meta-analysis: $I^2$ is not an absolute measure of heterogeneity: $I^2$ is not an absolute measure of heterogeneity. *Res Synth Methods*. 2017;8(1):5-18. doi:10.1002/jrsm.1230

26. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the Gap between Methodologists and End-Users: R as a Computational Back-End. *J Stat Softw*. 2012;49(1):1-15. doi:10.18637/jss.v049.i05

27. 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(2):179-187. doi:10.1111/j.1600-0501.2006.01318.x

28. Schwarz F, John G, Mainusch S, Sahm 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(8):789-797. doi:10.1111/j.1600-051X.2012.01867.x

29. Schwarz F, Hegewald A, John G, Sahm N, Becker J. Four-year follow-up of combined surgical therapy of advanced peri-implantitis evaluating two methods of surface decontamination. *J Clin Periodontol*. 2013;40(10):962-967. doi:10.1111/jcpe.12143

30. Schwarz F, John G, Schmucker A, Sahm N, Becker J. Combined surgical therapy of advanced peri-implantitis evaluating two methods of surface decontamination: a 7-year follow-up observation. *J Clin Periodontol*. 2017;44(3):337-342. doi:10.1111/jcpe.12648

31. Isehed C, Svenson B, Lundberg P, Holmlund A. Surgical treatment of peri-implantitis using enamel matrix derivative, an RCT: 3- and 5-year follow-up. *J Clin Periodontol*. 2018;45(6):744-753. doi:10.1111/jcpe.12894
32. Toma S, Brecx MC, Lasserre JF. Clinical Evaluation of Three Surgical Modalities in the Treatment of Peri-Implantitis: A Randomized Controlled Clinical Trial. *J Clin Med*. 2019;8(7):966. doi:10.3390/jcm8070966

33. Lasserre J, Brecx M, Toma S. Implantoplasty Versus Glycine Air Abrasion for the Surgical Treatment of Peri-implantitis: A Randomized Clinical Trial. *Int J Oral Maxillofac Implants*. 2020;35(1):197-206. doi:10.11607/jomi.6677

34. de Waal YCM, Raghoebar GM, Meijer HJA, Winkel EG, van Winkelhoff AJ. Implant decontamination with 2% chlorhexidine during surgical peri-implantitis treatment: a randomized, double-blind, controlled trial. *Clin Oral Implants Res*. 2015;26(9):1015-1023. doi:10.1111/clr.12419

35. de Waal YCM, Raghoebar GM, Huddleston Slater JJR, Meijer HJA, Winkel EG, van Winkelhoff AJ. Implant decontamination during surgical peri-implantitis treatment: a randomized, double-blind, placebo-controlled trial. *J Clin Periodontol*. 2013;40(2):186-195. doi:10.1111/jcpe.12034

36. Cha JK, Lee JS, Kim CS. Surgical Therapy of Peri-Implantitis with Local Minocycline: A 6-Month Randomized Controlled Clinical Trial. *J Dent Res*. 2019;98(3):288-295. doi:10.1177/0022034518818479

37. Wang C, Ashnagar S, Gianflippo RD, Arnett M, Kinney J, Wang H. Laser-assisted regenerative surgical therapy for peri-implantitis: A randomized controlled clinical trial. *J Periodontol*. Published online August 25, 2020:JPER.20-0040. doi:10.1002/JPER.20-0040

38. Albaker AM, ArRejaie AS, Alrabiah M, et al. Effect of antimicrobial photodynamic therapy in open flap debridement in the treatment of peri-implantitis: A randomized controlled trial. *Photodiagnosis Photodyn Ther*. 2018;23:71-74. doi:10.1016/j.pdpdt.2018.05.003
39. Berglundh T, Armitage G, Araujo MG, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol*. 2018;45(S20):S286-S291. doi:https://doi.org/10.1111/jcpe.12957

40. Schlee, Rathe, Brodbeck, Ratka, Weigl, Zipprich. Treatment of Peri-implantitis—Electrolytic Cleaning Versus Mechanical and Electrolytic Cleaning—A Randomized Controlled Clinical Trial—Six-Month Results. *J Clin Med*. 2019;8(11):1909. doi:10.3390/jcm8111909

41. Schwarz F, Sahm 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: Surgical therapy of peri-implantitis. *J Clin Periodontol*. 2011;38(3):276-284. doi:10.1111/j.1600-051X.2010.01690.x

42. Isler SC, Unsal B, Soysal F, Ozcan G, Peker E, Karaca IR. The effects of ozone therapy as an adjunct to the surgical treatment of peri-implantitis. *J Periodontal Implant Sci*. 2018;48(3):136. doi:10.5051/jpis.2018.48.3.136

43. Tapia B, Valles C, Ribeiro-Amaral T, et al. The adjunctive effect of a titanium brush in implant surface decontamination at peri-implantitis surgical regenerative interventions: A randomized controlled clinical trial. *J Clin Periodontol*. 2019;46(5):586-596. doi:10.1111/jcpe.13095

44. Papadopoulos CA, Vouros I, Menexes G, Konstantinidis A. The utilization of a diode laser in the surgical treatment of peri-implantitis. A randomized clinical trial. *Clin Oral Investig*. 2015;19(8):1851-1860. doi:10.1007/s00784-014-1397-9

45. 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. 2004;16(1):9-18. doi:10.1111/j.1600-0501.2004.01084.x

46. Isehed C, Holmlund A, Renvert S, Svenson B, Johansson I, Lundberg P. Effectiveness of enamel matrix derivative on the clinical and microbiological outcomes following surgical regenerative treatment of peri-implantitis. A randomized controlled trial. J Clin Periodontol. 2016;43(10):863-873. doi:10.1111/jcpe.12583

47. Romandini M, Lima C, Pedrinaci I, Araoz A, Soldini MC, Sanz M. Prevalence and risk/protective indicators of peri-implant diseases: A university-representative cross-sectional study. Clin Oral Implants Res. 2021;32(1):112-122. doi:10.1111/clr.13684

48. Romandini M, Lima C, Pedrinaci I, Araoz A, Costanza Soldini M, Sanz M. Clinical signs, symptoms, perceptions, and impact on quality of life in patients suffering from peri-implant diseases: a university-representative cross-sectional study. Clin Oral Implants Res. 2021;32(1):100-111. doi:10.1111/clr.13683

49. Schmage P, Thielemann J, Nergiz I, Scorziello TM, Pfeiffer P. Effects of 10 cleaning instruments on four different implant surfaces. Int J Oral Maxillofac Implants. 2012;27(2):308-317.

50. Ravidà A, Siqueira R, Saleh I, Saleh MHA, Giannobile A, Wang HL. Lack of Clinical Benefit of Implantoplasty to Improve Implant Survival Rate. J Dent Res. 2020;99(12):1348-1355. doi:10.1177/0022034520944158

51. John G, Becker J, Schwarz F. Rotating titanium brush for plaque removal from rough titanium surfaces - an in vitro study. Clin Oral Implants Res. 2014;25(7):838-842. doi:10.1111/clr.12147
52. Cochis A, Fini M, Carrassi A, Migliario M, Visai L, Rimondini L. Effect of air polishing with glycine powder on titanium abutment surfaces. *Clin Oral Implants Res*. 2013;24(8):904-909. doi:10.1111/j.1600-0501.2012.02490.x

53. Sanz-Martín I, Paeng K, Park H, Cha J-K, Jung U-W, Sanz M. Significance of implant design on the efficacy of different peri-implantitis decontamination protocols. *Clin Oral Investig*. Published online November 10, 2020. doi:10.1007/s00784-020-03681-y

54. Pranno N, Cristalli MP, Mengoni F, et al. Comparison of the effects of air-powder abrasion, chemical decontamination, or their combination in open-flap surface decontamination of implants failed for peri-implantitis: an ex vivo study. *Clin Oral Investig*. Published online September 25, 2020. doi:10.1007/s00784-020-03578-w

55. Schwarz F, Sculean A, Romanos G, et al. Influence of different treatment approaches on the removal of early plaque biofilms and the viability of SAOS2 osteoblasts grown on titanium implants. *Clin Oral Investig*. 2005;9(2):111-117. doi:10.1007/s00784-005-0305-8

56. 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. doi:10.1111/j.1600-0501.2012.02542.x

57. Bassetti M, Schär D, Wicki B, et al. Anti-infective therapy of peri-implantitis with adjunctive local drug delivery or photodynamic therapy: 12-month outcomes of a randomized controlled clinical trial. *Clin Oral Implants Res*. 2014;25(3):279-287. doi:10.1111/clr.12155

58. 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(1):104-110. doi:10.1111/j.1600-0501.2012.02494.x
59. Lin G-H, Suárez López Del Amo F, Wang H-L. Laser therapy for treatment of peri-implant mucositis and peri-implantitis: An American Academy of Periodontology best evidence review. *J Periodontol*. 2018;89(7):766-782. doi:10.1902/jop.2017.160483

60. Chambrone L, Wang H-L, Romanos GE. Antimicrobial photodynamic therapy for the treatment of periodontitis and peri-implantitis: An American Academy of Periodontology best evidence review. :21.

61. Romandini M, De Tullio I, Congedi F, et al. Antibiotic prophylaxis at dental implant placement: Which is the best protocol? A systematic review and network meta-analysis. *J Clin Periodontol*. 2019;46(3):382-395. doi:10.1111/jcpe.13080

62. Charalampakis G, Leonhardt Å, Rabe P, Dahlén G. Clinical and microbiological characteristics of peri-implantitis cases: a retrospective multicentre study. *Clin Oral Implants Res*. 2012;23(9):1045-1054. doi:10.1111/j.1600-0501.2011.02258.x

63. Berglundh T, Wennström JL, Lindhe J. Long-term outcome of surgical treatment of peri-implantitis. A 2-11-year retrospective study. *Clin Oral Implants Res*. 2018;29(4):404-410. doi:10.1111/clr.13138

64. Schwarz F, Sahm 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(5):449-455. doi:10.1111/j.1600-051X.2010.01540.x

65. Berglundh J, Romandini M, Derks J, Sanz M, Berglundh T. Clinical findings and history of bone loss at implant sites. *Clin Oral Implants Res*. Published online December 19, 2020. doi:10.1111/clr.13701

66. Romandini M, Cordaro M, Donno S, Cordaro L. Discrepancy between patient satisfaction and biologic complication rate in patients rehabilitated with overdentures and not participating in a
structured maintenance program after 7 to 12 years of loading. *Int J Oral Maxillofac Implants*. 2019;34(5):1143-1151. doi:10.11607/jomi.7465

67. Carcuac O, Derks J, Abrahamsson I, Wennström JL, Berglundh T. Risk for recurrence of disease following surgical therapy of peri-implantitis—A prospective longitudinal study. *Clin Oral Implants Res*. 2020;31(11):1072-1077. doi:10.1111/clr.13653

68. Sanz M, Chapple IL, Working Group 4 of the VIII European Workshop on Periodontology. Clinical research on peri-implant diseases: consensus report of Working Group 4. *J Clin Periodontol*. 2012;39 Suppl 12:202-206. doi:10.1111/j.1600-051X.2011.01837.x

69. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: treatment of peri-implantitis. *Cochrane Database Syst Rev*. 2012;1:CD004970. doi:10.1002/14651858.CD004970.pub5
Table 1. Included studies: anti-infective protocols employed

| Study            | Type of study | Type of surgery | Groups                            | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination | Chemical/physical decontamination | Biomaterials | Post-op | Frequency of SPT |
|------------------|---------------|-----------------|-----------------------------------|---------------------|--------------------|----------------|-------------------------------|-------------------------------------------|-------------|---------------------|--------------------------------|--------------|---------|------------------|
| Lasserre et al (2020) | RCT parallel (test/control) | OFD | Implantoplasty | 16                  | 22                 | 6               | MBL ≥2 mm, PPD ≥5 mm, BOP and/or SUP | OHI and supragingival cleaning with scalers, polishing paste, and rubber cups 4 w before surgery | No          | Plastic curettes, diamond burs | Sterile saline | NA          | 0.2% CHX x 10 d; ibuprofen 3 x 600 mg for 2 d, paracetamol 1 g | 1w, 3m, 6m  |
| Cha et al (2019)  | RCT parallel (test/control) | OFD | Minocycline ointments | 25                  | 25                 | 12              | MBL ≥3 mm, PPD ≥6 mm, and BOP | Supragingival cleaning, and standardized OHI | Amoxicillin 3 x 500 mg for 3 d | Titanium curettes, ultrasonic scaler, titanium brush, air-powder device | Placebo ointment | NA          | 1w, 1m, 3m, 6m (Minocycline or placebo administered at 1 and 3 mo) |       |
| Toma et al (2019) | RCT parallel (2 test/1 control) | OFD | Perio Flow | 16                  | 22                 | 6               | MBL ≥2 mm, PPD ≥5 mm, BOP and/or SUP | 2 w before surgery, OHI and professional supragingival cleaning, using a rubber cup with polishing paste | No          | Air powder device | Titanium brushes | NA          | 0.2% CHX and paracetamol 3 g for 10 d | 1w, 3m, 6m  |
|                  |               |                 | Plastic curettes | 15                  | 25                 |                 |                               |                                            |                                        |                       | Plastic curettes |                       |             |         |                   |
| Study                          | Type of study | Type of surgery | Groups                      | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis                               | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination                  | Chemical/physical decontamination | Bio-materials | Post-op | Frequency of SPT |
|-------------------------------|---------------|-----------------|-----------------------------|---------------------|--------------------|-----------------|----------------------------------------------------------|------------------------------------------|----------------|--------------------------------------------|-----------------------------------|----------------|---------|------------------|
| Albaker et al (2018)          | RCT parallel  | OFD             | Photodynamic Therapy + OFD  | 11                  | 11                 | 12              | MBL ≥ 2 mm, PPD ≥ 5 mm, BOP and/or SUP                    | Full mouth SRP using ultrasonic scaler and hand instruments | Augmentin 3 × 625 mg for 7 d | Curettes plus saline soaked cotton gauzes | Photodynamic therapy (methylene blue + diode laser) | NA             | NA      | 1w, 3m, 6m, 9m, 12m |
|                               | (test/control)|                 | OFD alone                   | 13                  | 13                 |                 |                                                          |                                          |                             | Curettes plus saline soaked cotton gauzes | Sterile saline                              |                             |           |         |                  |
| Hallström et al (2017)        | RCT parallel  | OFD             | ODF + Systemic antimicrobials | 20                  | 20                 | 12              | MBL ≥ 3 mm, PPD ≥ 5 mm and BOP/SUP                       | NR                                        |                              | Titanium curettes plus gauze soaked in saline | NA                        | NA             | 2w, 6w, 3m, 6m, 12m |
|                               | (test/control)|                 | ODF + placebo               | 19                  | 19                 |                 |                                                          | No                                        |                              | Titanium curettes plus gauze soaked in saline | NA                        |               |         |                  |
| Carcuac et al (2016)          | RCT parallel  | OFD             | Antibiotic + Antiseptic +   | 27                  | 47                 | 12              | MBL ≥ 2 mm, PPD ≥ 6 mm, BOP and/or SUP                   | Supragingival cleaning using rubber cups, polishing paste, and OHI | Amoxicillin 2 × 750 mg for 10 d commenced 3 d prior to surgery | Titanium curettes               | Gauze soaked in 0.2% CHX | NA       | 2w, 3m, 6m, 9m, 12m |
|                               | (2 test/2     |                 | Antibiotic + Antiseptic -   | 25                  | 46                 |                 |                                                          |                                           |                              |                                             |                       |               |         |                  | control) |
|                               | control)      |                 |                             |                     |                    |                 |                                                          |                                           |                              |                                             |                       |               |         |                  |
| Study | Type of study | Type of surgery | Groups | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination | Chemical/physical decontamination | Bio-materials | Post-op | Frequency of SPT |
|-------|---------------|-----------------|--------|-------------------|--------------------|---------------|-----------------------------|--------------------------------|-------------|----------------------|-------------------|--------------|---------|------------------|
| Isheh et al (2016) | RCT parallel (test/control) | EMD | 15 | 15 | 12 | MBL ≥3 mm, PPD ≥5 mm BOP and/or SUP | Periodontal disease was treated with mechanical debridement and OHI | No | Ultrasonic scaler, titanium curettes | Sterile saline plus EMD | NA | 2 x 10 ml CHX for 6 w and not chew or brush on the treated side for 2 weeks |
| |
| Papadopoulos et al (2015) | RCT parallel (test/control) | Diode laser | 9 | 9 | 6 | MBL ≥2 mm, PPD ≥5 mm BOP and/or SUP | Mechanical debridement using ultrasonics and hand instruments to the whole dentition | No | Plastic curettes, plus gauzes soaked in saline | Diode laser | NA | 2 x 0.12 % CHX for 2 w and a careful tooth brushing with a soft toothbrush |
| |
| Wang et al (2020) | RCT parallel | Combined Er:Yag Laser | 12 | 12 | 6 | MBL ≥2 mm, PPD ≥5 | Full mouth prophylaxis | Amoxicillin 3 x 500 mg | Ultrasonic scaler, stainless-steel | Er:Yag Laser | Alloplastic bone graft | 2 x CHX for 1 w and | 2w, 1m, 3m, 6m |
| Study                  | Type of study | Type of surgery | Groups | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination | Chemical/physical decontamination | Bio-materials | Post-op               | Frequency of SPT |
|-----------------------|---------------|-----------------|--------|--------------------|--------------------|---------------|-------------------------------|-----------------------------------|-------------|----------------------|----------------------------------|---------------|----------------------|-----------------|
| deTapia et al (2019)  | RCT parallel  | Titanium brushes | 15     | 15                 | 12                 | 12            | MBL >30%, PPD ≥6 mm and BOP ≥6 mm and/or SUP | Subgingival scaling with plastic curettes and irrigation with 0.12% CHX | Amoxicillin 3 x 500 mg and Metronidazole 3 x 500 mg for 7 d | Plastic ultrasonic scaler, titanium brushes (infraosseous) | 3% H2O2 | Placebo laser application | 2 x 0.12% CHX for 2 w |
|                       | (test/control) | Ultrasonic scalers | 15     | 15                 |                    |               |                               |                                    |                                        | Plastic ultrasonic scaler (infraosseous) |                   |                      | 2w, 2w, 6w, 6m   |
| Schwarz et al 2011    | RCT parallel, single blind (test/control) | Er:Yag Laser | 16     | 16                 | 6                 | 6             | PPD of ≥5 mm and an intrabony component of >3 mm as estimated clinically | Non-surgical instrumentation using plastic curettes, combined with 0.2% CHX solution and CHX gel 0.2%. | No | Plastic curettes + cotton pellets soaked in saline (infraosseous part) | Er:Yag Laser (infraosseous part) | NA |                      | 2 x 0.12% CHX for 2 w |
|                       |               | Plastic curettes | 16     | 16                 |                    |               |                               |                                    |                                        |                                        |                   |                      | 2w, 4w, 6w, 8w, 4m, 6m |
| Schlee et al (2019)   | RCT parallel  | Electrolytic method (EC) | 12     | 12                 | 6                 | 6             | MBL ≥3 mm, PPD ≥6 mm, and Suprastructures removed 14 days before | No | Curettes and/or ultrasonic devices | Pilot electrolytic approach for 120 s, then sterile | Autogenous bone graft and | NR | 2w, 6w, 6m    |
|                       | (test/control) |                        |        |                    |                    |               |                               |                                    |                                        |                                        |                   |                      |                  |
| Study            | Type of study | Type of surgery | Groups                  | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination | Chemical/physic al decontamination | Bio-materials | Post-op | Frequency of SPT |
|------------------|---------------|-----------------|-------------------------|---------------------|---------------------|----------------|-------------------------------|-------------------------------------------|---------------|--------------------------|-------------------------------------|---------------|----------|------------------|
| Isler et al      | RCT parallel  | Reg             | Powder spray plus EC    | 12                  | 12                  |                | BOP and/or SUP surgery, implants cleaned by powder spray and CHX. Cover screw was placed | Curettes and/or ultrasonic devices plus powder spray | saline.      | Sterile saline + ozone delivery | Sterile saline + growth factors | xenograft 50:50 + collagen membrane |          |                    |
| (2018)           |  (test/control) |                 |                         |                      |                     |                |                               |                                           |                           |                         |                                      |                        |          |                    |
|                  |               |                 | Saline irrigation       | 23                  | 42                  |                | MBL ≥2 mm, deepening PPD, and BOP and/or SUP | Non-surgical treatment provided. In test group, ozone therapy was initiated | Amoxicillin 3 x 500 mg and Metronidazole 3 x 500 mg for 1 week | Titanium curettes | Sterile saline | 2 x 0.12% CHX for 2 weeks, anti-inflammatory and analgesic drugs for the first 3 d |
| de Waal et al    | RCT parallel, double blind (test/control) | ORS | 2% CHX                  | 22                  | 49                  |                | MBL ≥2 mm, PPD ≥5 mm and BOP and/or SUP | Mechanical debridement of implants, superstructures, and remaining dentition | No | Gauze soaked in saline | Placebo solution | NA | 0.12% CHX + 0.05% CPC without alcohol (two times daily x 2 weeks) | 2w, 3m, 6m, 9m, 12m |
| (2015)           |               |                 | 0.12% CHX + 0.05% CPC   | 22                  | 59                  |                |                               |                                           |                           |                         |                                      |                        |          |                    |
| Study                                      | Type of study | Type of surgery | Groups                             | N patients baseline | N implants baseline | Follow-up (mo) | Diagnosis of peri-implantitis                                                                 | Pre-treatment phase at affected implants | Systemic ABX | Mechanical decontamination | Chemical/physical decontamination | Bio-materials | Post-op | Frequency of SPT |
|-------------------------------------------|---------------|----------------|------------------------------------|---------------------|---------------------|-----------------|---------------------------------------------------------------------------------------------|------------------------------------------|---------------|--------------------------|-----------------------------------|----------------|----------|-------------------|
| de Waal et al (2013)                      | RCT           | ORS            | Gauze soaked in saline             | 15                  | 31                  | 12              | MBL ≥ 2 mm, PPD ≥ 5 mm and BOP and/or SUP                                               | Mechanical debridement of implants, suprastructures, and remaining dentition | No           | Gauze soaked in saline | 2% CHX x 1 min                    | NA            |          | 2w, 3m, 6m, 9m, 12m |
|                                         | parallel, single blind (test/control) |                |                                    |                     |                     |                 |                                                                                           |                                          |               |                          | 0.12% CHX + 0.05% CPC without alcohol (two times daily x 2 weeks) |              |          |                   |
| Romeo et al (2005)                        | RCT           | ORS            | Implantoplasty                     | NR                  | 19                  | 12              | PPD ≥ 5 mm, radiographic evidence of horizontal peri-implant radiolucency and BOP and/or SUP | Implantoplasty (burs)                    | Amoxicillin 50 mg/kg/die for 8 d per os | None | Gel of metronidazole plus a solution of tetracycline hydrochloride | 0.2% CHX (10ml for 1 min at interval of 8 h for 2 w) | NA            |          | NR                 |
| also reported in: Romeo et al (2007)      | RCT           | ORS            | No implantoplasty                  | NR                  | 16                  | 12              |                                                                                           |                                          |                           |                          |                                    |              |          |                   |

*Note.* BOP: bleeding on probing; CHX: chlorhexidine; CPC: cetylpyridinium chloride; EMD, enamel matrix derivatives; MBL: mean bone level; NR: not reported; OFD: open flap debridement; ORS: osseous resective surgery; PPD: peri-implant pocket depth; Reg: regenerative surgery; SUP: suppuration on probing.
Table 2. Included studies: summary of outcomes

| Study                  | Type of surgery | Methods of decontamination                                      | Systemic AB | N patients final | N implants final | Outcomes of different treatments                                                                 | Benefit of test procedure                                                                 | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments                                                                 |
|------------------------|-----------------|-----------------------------------------------------------------|--------------|-----------------|------------------|-------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|-----------------------|--------------------------|--------------------------|--------------------------------------------------------------------------|
| Lasserre et al (2020)  | OFD             | Test: Plastic curettes, diamond burs                             | No           | 15              | 20               | ΔMBL: -0.26 ± 1.08 mm  
ΔPD: -4.0 ± 1.83 mm  
ΔRAL: -3.5 ± 1.75 mm  
ΔBOP% (implants): -62.5  
ΔSUP% (implants): -70 | Mean changes kindly provided by the authors. Comlications and PROMs not reported. No turned implants included. | 20 (90.9)   | 3 (15.0)       | ≥0.5 mm from baseline                                                                 |                                                                                           |
|                        |                 | Control: Plastic curettes, glycine air polishing                 | No           | 14              | 18               | ΔMBL: -0.53 ± 0.94 mm  
ΔPD: -3.29 ± 1.73 mm  
ΔRAL: -2.7 ± 1.56 mm  
ΔBOP% (implants): -60.5  
ΔSUP% (implants): -71 |                                                                                       | 20 (100)   | 5 (26.0)       | PPD <5 mm, no BoP/SoP, and no further bone loss ≥0.5 mm from baseline | Repeated local delivery of minocycline at follow up visits. Recovered, SUP and PROMs not reported. Only one turned implant included in control group. |
| Cha et al (2019)       | OFD             | Test: Titanium curettes, ultrasonic scaler, titanium brush, air-powder device plus minocycline ointments | Yes          | 24              | 24               | ΔMBL: -0.72 ± 0.56 mm  
ΔmPD: -2.66 ± 1.73 mm  
ΔwPD: -3.58 ± 2.32 mm  
ΔBOP% (implants): -58 |                                                                                       | 24 (100)   | 16 (66.7)      | PPD <5 mm, no BoP, and no further bone loss                                                                 | Repeated local delivery of minocycline at follow up visits. Recovered, SUP and PROMs not reported. Only one turned implant included in control group. |

ΔMBL: ΔMarginal Bone Level
ΔPD: ΔProbing Depth
ΔRAL: ΔRecession Angle Lateral
ΔBOP% (implants): ΔBleeding on Probing of Implants
ΔSUP% (implants): ΔSuppurative Implant
| Study                      | Type of surgery          | Methods of decontamination                                                                 | Systemic AB | N patients final | N implants final | Outcomes of different treatments                                                                 | Benefit of test procedure                                                                 | Implant survival N (%) | Disease resolution N (%) |
|---------------------------|--------------------------|-------------------------------------------------------------------------------------------|--------------|-----------------|-----------------|------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------------|--------------------------|
|                           |                          | Control: Titanium curettes, ultrasonic scaler, titanium brush, air-powder device plus placebo ointments | Yes          | 22              | 22              | ΔMBL: -0.31 ± 0.49 mm  
ΔmPD: -1.55 ± 1.86 mm  
ΔwPD: -2.45 ± 2.13 mm  
ΔBOP% (implants): -31 | 22 (100)                                                                                           | 8 (36.3)                                           |
| Toma et al (2019)         | OFD                      | Test A: Air powder device                                                                  | No           | 16              | 22              | ΔMBL: -0.95 ± 0.24 mm  
ΔPD: -2.39 ± 1.12 mm  
ΔRAL: -2.75 ± 1.56 mm  
ΔBOP% (implants): -36 | 21 (95.5)                                                                                           | 6 (29.0)                                           |
|                           |                          | Test B: Titanium brushes                                                                   | No           | 16              | 23              | ΔMBL: -1.12 ± 0.24 mm  
ΔPD: -2.41 ± 0.48 mm  
ΔRAL: -2.84 ± 1.64 mm  
ΔBOP% (implants): -39 | 23 (100)                                                                                           | 8 (33.0)                                           |
| Control: Plastic curettes |                          |                                                                                            | No           | 15              | 25              | ΔMBL: -0.51 ± 0.17 mm  
ΔPD: -1.37 ± 0.87 mm  
ΔRAL: -1.82 ± 1.65 mm  
ΔBOP% (implants): -25 | 25 (100)                                                                                           | 6 (22.0)                                           |
| Study                        | Type of surgery | Methods of decontamination                  | N patients final | N implants final | Outcomes of different treatments | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments                                                                 |
|-----------------------------|-----------------|---------------------------------------------|------------------|------------------|----------------------------------|--------------------------|------------------------|------------------------|-----------------|--------------------------------------------------------------------------|
| Albaker et al (2018)        | OFD             | Test: Photodynamic Therapy + curettes       | Yes              | 11               | NR                               | NR                       | NR                     | NR                     | NR              | Only baseline and 6 months data available, but no mean changes.          |
|                             |                 | Control: Curettes                           | Yes              | 13               | NR                               | NR                       | NR                     | NR                     | NR              | 50% of smokers included.                                                |
| Hallström et al (2017)      | OFD             | Test: Titanium curettes + systemic ABX      | Yes              | 15               | $\Delta MBL$: NR $\Delta PD$: -1.7 ± 1.1 mm $\Delta BOP\%$ (sites): -88 | $\Delta MBL$: 0.5 mm (in favour of control group) $\Delta PD$: 0.1 mm $\Delta BOP\%$ (sites): 25 | 15 (100)                | 7 (46.6)               | PPD ≤ 5 mm, no BoP/SoP, and no further bone loss ≥ 0.5 mm from baseline to 1y | 16 (100) | Two implants in the test and control group had need of retreatment SUP and PROMs not reported. |
|                             |                 | Control: Titanium curettes + placebo        | No               | 16               | $\Delta MBL$: NR $\Delta PD$: -1.6 ± 1.5 mm $\Delta BOP\%$ (sites): -63 | $\Delta MBL$: 0.5 mm $\Delta PD$: -1.7 mm $\Delta BOP\%$ (sites): -10 | 16 (100)                | 4 (25.0)               | Two implants in the test and control group had need of retreatment SUP and PROMs not reported. |
| Carcuac et al (2016)        | OFD             | Test A: Titanium curettes + gauze soaked in 0.2% CHX + systemic ABX | Yes              | 27               | $\Delta MBL$: -0.18 ± 1.15 mm $\Delta wPD$: -2.80 ± 1.87 mm $\Delta BOP\%$ (implants): -18 $\Delta SUP\%$ (implants): -18 | $\Delta MBL$: 0.87 mm $\Delta wPD$: 0.64 mm $\Delta BOP\%$ (implants): -2 $\Delta SUP\%$ (implants): -2 | 46 (97.8)               | 19 (40.4)              | PPD ≤ 5 mm, no BoP/SoP, and no further bone loss ≥ 0.5 mm from baseline | 84% of patients had a history of periodontitis. REC and PROMs not reported. |
| also reported in: Carcuac et al (2017) |                 |                                              |                  |                  |                                  |                          |                        |                        | 84% of patients had a history of periodontitis. REC and PROMs not reported. |                        | Microbiological outcomes assessed.                                      |
| Study          | Type of surgery | Methods of decontamination | Systemic AB | N patients final | N implants final | Outcomes of different treatments | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments |
|---------------|-----------------|----------------------------|-------------|-----------------|-----------------|-------------------------------|--------------------------|-----------------------|-----------------------|--------------------------|----------|
| Test B: Titanium curettes + gauze soaked in saline + systemic ABX | Yes          | 25             | 46                   | ΔMBL: -0.51 ± 0.84 mm | ΔwPD: -3.44 ± 1.66 mm | ΔBOP% (implants): -16 | ΔSUP% (implants): -16 | Test B vs Control B | ΔMBL: 1.47 mm | ΔwPD: 1.75 mm | ΔBOP% (implants): -2 | ΔSUP% (implants): -2 | 46 (100) | 30 (65.2) |
| Control A: Titanium curettes + gauze soaked in 0.2% CHX | No           | 23             | 48                   | ΔMBL: +0.69 ± 1.32 mm | ΔwPD: -2.16 ± 1.79 mm | ΔBOP% (implants): -20 | ΔSUP% (implants): -20 | Test A vs Test B | ΔMBL: 0.33 mm* | ΔwPD: 0.64 mm* | ΔBOP% (implants): 2 | ΔSUP% (implants): 2 | 45 (93.3) | 18 (37.5) |
| Control B: Titanium curettes + gauze soaked in saline | No           | 24             | 37                   | ΔMBL: +0.96 ± 1.42 mm | ΔwPD: -1.69 ± 2.22 mm | ΔBOP% (implants): -18 | ΔSUP% (implants): -18 | Control A vs Control B | ΔMBL: 0.3 mm | ΔwPD: 0.47 mm | ΔBOP% (implants): 2 | ΔSUP% (implants): 2 | 35 (94.6) | 13 (35.1) |

Isehed et al (2016) also reported in: Isehed et al (2018)

OFD Test: Ultrasonic scaler, titanium curettes, + EMD

| Study          | Type of surgery | Methods of decontamination | Systemic AB | N patients final | N implants final | Outcomes of different treatments | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments |
|---------------|-----------------|----------------------------|-------------|-----------------|-----------------|-------------------------------|--------------------------|-----------------------|-----------------------|--------------------------|----------|
| Test: Ultrasonic scaler, titanium curettes, + EMD | No           | 12             | 12                   | ΔMBL: -0.7 ± 1.1 mm | ΔPD: -2.5 ± 2.0 mm | ΔBOP% (implants): -20 | ΔSUP% (implants): -53 | Test A vs Test B | ΔMBL: 0.5 mm | ΔPD: 1.5 mm (in favour of control group) | ΔBOP% (implants): 0 | ΔSUP% (implants): 17 | 12 (85.7) | NR | NR | Disease resolution, SUP and PROMs not reported. Microbiological outcomes assessed. |

Isehed et al (2016) also reported in: Isehed et al (2018)
| Study                  | Type of surgery | Methods of decontamination          | Systemic AB | N patients final | N implants final | Outcomes of different treatments                                                                 | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments                                                                 |
|-----------------------|-----------------|-------------------------------------|-------------|-----------------|-----------------|-------------------------------------------------------------------------------------------------|--------------------------|------------------------|------------------------|------------------|--------------------------------------------------------------------------|
| Papadopoulos et al (2015) | OFD            | Control: Ultrasonic scaler, titanium curettes | No          | 13              | 13              | $\Delta$MBL: -0.2 ± 1.1 mm  
$\Delta$PD: -4.0 ± 2.9 mm  
$\Delta$BOP% (implants): -20  
$\Delta$SUP% (implants): -36                                                                 | 13 (92.9)                | NR                     | NR                     | NR               | Only baseline and 6 months data available, but no mean changes. REC, SUP and PROMs not reported. |
|                       |                 | Test: Plastic curettes plus diode Laser | No          | 8               | 8               | NR                                                                                               | NR                       | NR                     | NR                     | NR               |                                                                          |
|                       |                 | Control: Plastic curettes             | No          | 8               | 8               | NR                                                                                               | NR                       | NR                     | NR                     | NR               |                                                                          |
| Wang et al (2020)     | Combined        | Test: Er:Yag Laser                   | Yes         | 12              | 12              | $\Delta$MBL: -1.27 ± 1.14 mm  
$\Delta$PD: -2.65 ± 2.14 mm  
$\Delta$CAL: -1.90 ± 2.28 mm  
$\Delta$BOP% (sites): -31                                                                 | 12 (100)                 | NR                     | NR                     | NR               | SUP and PROMs not reported. Only rough surfaces included. |
|                       |                 | Control: Placebo                     | Yes         | 12              | 12              | $\Delta$MBL: -1.08 ± 1.04 mm  
$\Delta$PD: -1.85 ± 1.71 mm  
$\Delta$CAL: -1.47 ± 1.76 mm  
$\Delta$BOP% (sites): -39                                                                 | 12 (100)                 | NR                     | NR                     | NR               |                                                                          |
| deTapia et al (2019)  | Combined        | Test: Titanium brushes               | Yes         | 15              | 15              | $\Delta$MBL: -2.51 ± 1.21 mm  
$\Delta$mPD: -2.84 ± 0.93 mm  
$\Delta$wPD: -4.87 ± 1.55 mm  
$\Delta$Rec: 0.60 ± 0.62 mm  
$\Delta$BOP% (implants): -80  
$\Delta$SUP% (implants): -40                                                                 | 15 (100)                 | 10 (66.7)              | History of periodontitis and type of implant surface not reported. PROMs not reported.         |
| Study           | Type of surgery | Methods of decontamination | Systemic AB | N patients final | N implants final | Outcomes of different treatments                                                                 | Benefit of test procedure           | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments |
|----------------|----------------|---------------------------|--------------|------------------|------------------|-----------------------------------------------------------------------------------------------|-------------------------------------|------------------------|------------------------|-----------------|----------|
| Schwarz et al 2011 | Control: Ultrasonic scalers | Yes | 12 | 12 | ΔMBL: -0.73 ± 1.26 mm | ΔmPD: -1.55 ± 1.86 mm | ΔwPD: -2.85 ± 1.91 mm | ΔRec: -0.21 ± 0.50 mm | ΔBOP% (implants): -54 | ΔSUP% (implants): -23 | 11 (91.7) | 3 (23.0) |
| also reported in: Schwarz et al (2012, 2013, 2017) | Test: Er:Yag Laser | No | 15 | 15 | ΔPD: -1.7 ± 1.4 mm | ΔRec: -0.2 ± 0.2 | ΔBOP% (implants): -47.8 | ΔPD: 0.7 mm (in favour of control group) | ΔRec: 0 | ΔBOP% (implants): 7 (in favour of control group) | NR | NR |
| Schlee et al (2019) | Control: Plastic curettes | No | 15 | 15 | ΔPD: -2.4 ± 1.5 mm | ΔRec: -0.2 ± 0.3 | ΔBOP% (implants): -55 | | | | |
| Reg | Test: Electrolytic method (EC) | No | 12 | 12 | ΔMBL: -2.71 ± 1.70 mm | ΔMBL: 0.10 mm (in favour of control group) | | | | | |
| Control: Powder spray plus EC | No | 11 | 11 | ΔMBL: -2.81 ± 2.15 mm | ΔMBL: 1.15 mm | | | | | |
| Isler et al (2018) | Reg | Test: Ozone therapy | Yes | 20 | 30 | ΔMBL: -2.32 ± 1.28 mm | ΔPD: -3.5 ± 1.31 mm | ΔBOP% (implants): -80.3 | ΔMBL: 1.15 mm | ΔPD: 1.1 mm | ΔBOP% (implants): 7 | 29 (96.7) | 15 (50.0) |
| | | | | | | | | | PD <5 mm without BOP and/or SoP, no | Mean Δ kindly provided by the authors. |

MBL, SUP and PROMs not reported.
| Study | Type of surgery | Methods of decontamination | Systemic AB | N patients final | N implants final | Outcomes of different treatments | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments |
|-------|----------------|---------------------------|-------------|----------------|----------------|-------------------------------|--------------------------|----------------------|----------------------|------------------|----------|
| de Waal et al (2015) | ORS | Control: Saline irrigation | Yes | 21 | 30 | ΔMBL: -1.17 ± 0.77 mm  
ΔPD: -2.42 ± 1.23 mm  
ΔBOP% (implants): -73.3 | 30 (100) | 11 (36.6) | further BL, and DF ≥1 mm |
| | | Test: 2% CHX | No | 21 | 48 | ΔMBL: -0.24 ± 0.72 mm  
ΔPD: -1.68 ± 0.16 mm  
ΔCAL: -1.5 ± 1.4 mm  
ΔBOP% (sites): -40  
ΔSUP% (implants): -19 | 48 (97.9) | 7 (14.3) | PPD ≤ 5 mm, no BoP/SoP, and no further bone loss ≥ 0.5 mm from baseline |
| | | Control: 0.12% CHX + 0.05% CPC | No | 20 | 54 | ΔMBL: -0.14 ± 0.49 mm  
ΔPD: -2.01 ± 1.26 mm  
ΔCAL: -2.2 ± 1.4 mm  
ΔBOP% (sites): -37  
ΔSUP% (implants): -18 | 54 (91.5) | 17 (28.8) | Mean Δ kindly provided by the authors. No differences in the number of analgesic taken between test and control. |
| de Waal et al (2013) | ORS | Control: Gauze soaked in saline | No | 12 | 38 | ΔMBL: -0.78 mm ± 0.93 mm  
ΔPD: -2.21 ± 2.01 mm  
ΔBOP% (implants): -19  
ΔSUP% (implants): -17 | 31 (100) | 1 (3.2) | PPD ≤ 5 mm, no BoP/SoP, and no further bone loss ≥ 0.5 mm from baseline |
| | | Test: 0.12% CHX + 0.05% CPC | No | 15 | 31 | ΔMBL: -0.58 mm ± 0.86 mm  
ΔPD: -1.64 ± 1.03 mm  
ΔBOP% (implants): -21  
ΔSUP% (implants): -8 | 38 (97.1) | 1 (2.1) | Mean Δ kindly provided by the authors. REC and PROMs not reported. |
| Study                        | Type of surgery | Methods of decontamination | Systemic AB | N patients final | N implants final | Outcomes of different treatments | Benefit of test procedure | Implant survival N (%) | Disease resolution N (%) | Success criteria | Comments                                      |
|------------------------------|-----------------|-----------------------------|-------------|-----------------|-----------------|-------------------------------|--------------------------|------------------------|------------------------|-----------------|-----------------------------------------------|
| Romeo et al (2005)           | ORS             | Test: Implantoplasty        | Yes         | 19              | 19              | \(\Delta mMBL: 0 \pm 0.14 \text{ mm} \) \(\Delta dMBL: -0.01 \pm 0.13 \text{ mm}\) | 19 (100) | NR                                  | Mean \(\Delta MBL\) provided in Romeo et al. (2007). For meta-analysis, the worst \(\Delta MBL\) value was chosen for mesial and distal. |
| also reported in: Romeo et al (2007) |                 | Control: No implantoplasty  | Yes         | 16              | 16              | \(\Delta mMBL: +0.51 \pm 0.49 \text{ mm}\) \(\Delta dMBL: +0.56 \pm 0.43 \text{ mm}\) | 15 (87.5) | NR                                  |                                      |

*Note.* ABX: systemic antibiotics; BOP: bleeding on probing; CHX: chlorhexidine; CPC: cetylpyridinium chloride; MBL: mean bone level (mMBL: mesial; dMBL: distal); mPD: mean pocket depth; OFD: open flap debridement; ORS: osseous resective surgery; PROMs: patient-reported outcome measures; REC: recession; Reg: regenerative surgery; SUP: suppuration on probing; wPD: worst pocket depth.
Figure Caption.

**Figure 1.** Risk of bias for studies in the systematic review.

**Figure 2.** Forest plots of weighted mean effect (WME) for different clinical parameters after implant surface decontamination with curettes or chlorhexidine (CHX), and cetylpyridinium chloride (CPC) without systemic antimicrobials. A) Marginal bone levels (MBL) changes with curettes in open flap debridement (OFD), B) Pocket depth (PD) reduction with curettes in OFD, C) Disease resolution with curettes in OFD. D) MBL changes with CHX + CPC in osseous resective surgery (ORS), E) PD reduction with CHX + CPC in ORS, F) Disease resolution with CHX + CPC in ORS.

**Figure 3.** Forest plots of the pairwise meta-analyses of open flap debridement (OFD) with antibiotics vs. OFD without antibiotics for A) Marginal bone levels (MBL) changes (weighted mean difference, WMD), B) Pocket depth (PD) reduction (weighted mean difference, WMD), and C) Disease resolution (risk ratio, RR).

**Figure 4.** Forest plots of weighted mean effect (WME) for different clinical parameters after open flap debridement (OFD) with or without systemic antibiotics A) Marginal bone levels (MBL) changes with systemic antibiotics, B) Pocket depth (PD) reduction with systemic antibiotics, C) Disease resolution with systemic antibiotics. D) MBL changes without systemic antibiotics, E) PD reduction without systemic antibiotics, F) Disease resolution without systemic antibiotics.

**Figure 5.** Forest plots of weighted mean effect (WME) for different clinical parameters after osseous resective surgery (ORS) with or without systemic antibiotic. A) Marginal bone levels (MBL) changes after ORS with systemic antibiotics, B) MBL changes after ORS without systemic
antibiotics, C) Pocket depth (PD) reduction after ORS without systemic antibiotics, D) Disease resolution after ORS without systemic antibiotics.

Supplementary Figure 1. PRISMA flow diagram depicting the selection process.
| Study                      | Randomization | Deviations from intended intervention | Missing outcome data | Measurement of the outcome | Selection of reported results | Overall risk of bias |
|---------------------------|---------------|----------------------------------------|----------------------|---------------------------|-------------------------------|---------------------|
| Romeo et al. 2005         | +             | +                                      | +                    | +                         | +                             | Low risk            |
| Schwartz et al. 2011      | +             | +                                      | +                    | +                         | +                             | Some concerns       |
| De Waal et al. 2013       | +             | +                                      | +                    | +                         | +                             | High risk           |
| Papadopoulos et al. 2015  | +             | +                                      | +                    | +                         | +                             |                     |
| De Waal et al. 2015       | +             | +                                      | +                    | +                         | +                             | +                   |
| Ished et al. 2016         | +             | +                                      | +                    | +                         | +                             | +                   |
| Carcuac et al. 2016       | +             | +                                      | +                    | +                         | +                             | +                   |
| Isler et al. 2018         | ?             | +                                      | +                    | +                         | +                             | ?                   |
| Albaker et al. 2018       | +             | ?                                      | +                    | +                         | +                             | ?                   |
| Thoma et al. 2019         | ?             | +                                      | +                    | +                         | +                             | ?                   |
| Schlee et al. 2019        | +             | +                                      | +                    | +                         | +                             | ?                   |
| De Tapia et al. 2019      | +             | +                                      | +                    | +                         | +                             | +                   |
| Cha et al. 2019           | +             | +                                      | +                    | +                         | +                             | +                   |
| Lassere et al. 2020       | ?             | +                                      | +                    | +                         | +                             | ?                   |
| Wang et al. 2020          | +             | +                                      | +                    | +                         | +                             | +                   |
A) Change of MBL

Studies

| Study                                      | Estimate (95% C.I.) |
|--------------------------------------------|---------------------|
| Carcuac et al. (CHX) 2016                  | 0.870 (0.355, 1.385) |
| Carcuac et al. (saline) 2016               | 1.470 (0.943, 1.997) |
| Overall (I^2=6072 %, P=0.111)             | 1.167 (0.579, 1.755) |

B) PD reduction

Studies

| Study                                      | Estimate (95% C.I.) |
|--------------------------------------------|---------------------|
| Hallstrom et al. 2017                      | 0.100 (-0.822, 1.022) |
| Carcuac et al. (CHX) 2016                  | 0.640 (-0.120, 1.400) |
| Carcuac et al. (saline) 2016               | 1.750 (0.871, 2.629) |
| Overall (I^2=7084 %, P=0.032)             | 0.832 (-0.079, 1.743) |

C) Disease resolution

Studies

| Study                                      | Estimate (95% C.I.) | Ev/Trt | Ev/Ctrl |
|--------------------------------------------|---------------------|--------|---------|
| Hallstrom et al. 2017                      | 1.867 (0.682, 5.107) | 7/15   | 4/16    |
| Carcuac et al. (CHX) 2016                  | 1.035 (0.618, 1.735) | 18/45  | 17/44   |
| Carcuac et al. (saline) 2016               | 1.977 (1.189, 3.288) | 29/44  | 12/36   |
| Overall (I^2=3921 %, P=0.193)             | 1.500 (0.944, 2.381) | 54/104 | 33/96   |
A) Change of MBL

Studies

Romeo et al. (test) 2005 0.010 (-0.048, 0.068)
Romeo et al. (control) 2005 -0.560 (-0.771, -0.349)

Overall (I^2=9617 %, P< 0.001) -0.266 (-0.824, 0.293)

B) Change of MBL

Studies

de Waal et al. (test) 2013 -0.780 (-1.118, -0.442)
de Waal et al. (control) 2013 -0.580 (-0.873, -0.287)
de Waal et al. (test) 2015 -0.240 (-0.453, -0.027)
de Waal et al. (control) 2015 -0.140 (-0.279, -0.001)

Overall (I^2=8176 %, P< 0.001) -0.404 (-0.674, -0.133)

C) PD reduction

Studies

de Waal et al. (test) 2013 2.210 (1.478, 2.942)
de Waal et al. (control) 2013 1.640 (1.289, 1.991)
de Waal et al. (test) 2015 1.680 (1.367, 1.993)
de Waal et al. (control) 2015 2.010 (1.654, 2.366)

Overall (I^2=2305 %, P=0.273) 1.807 (1.585, 2.029)

D) Disease resolution

Studies

de Waal et al. (test) 2013 0.034 (0.000, 0.101) 1/29
de Waal et al. (control) 2013 0.030 (0.000, 0.089) 1/33
de Waal et al. (test) 2015 0.136 (0.035, 0.238) 6/44
de Waal et al. (control) 2015 0.312 (0.181, 0.444) 15/48

Overall (I^2=8300 %, P< 0.001) 0.114 (0.014, 0.215) 23/154