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1 **Surgical therapy for peri-implantitis management: a systematic review and meta-analysis**

2 *Abbreviated running title: Surgical peri-implantitis management*

3

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11

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13

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16 by M.F.P, N.C, R.A, and D.W.T. Approval of article was obtained by all authors. Statistics was carried  
17 out by D.F and K.A.K. Data collection was by K.A.K.

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19 Keyword: dental implants, osseointegration, meta-analysis, systematic review

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27 **Abstract**

28 Aim: Peri-implantitis is a common cause of late implant failure. Studies have investigated different  
29 treatment strategies. The effectiveness of these modalities, however, remains unclear. This study  
30 aimed to evaluate the success of surgical peri-implantitis treatment using clinical and radiographic  
31 parameters.

32 Material and methods: A systematic review of published literature was employed. Key words were  
33 selected to conduct an electronic search using four databases for literature on human clinical  
34 studies. Meta-analyses were carried out for clinical probing, pocket depth and radiographic bone  
35 level.

36 Results: A total of 16 papers met the inclusion criteria. Four treatment modalities to supplement  
37 mechanical debridement were identified: 1) apically-repositioned flap, 2) chemical surface  
38 decontamination, 3) implantoplasty and, 4) bone augmentation. Inconsistent results were evident  
39 which were dependent on several treatment-independent factors. No clinical benefits were  
40 identified for the additional use of surface decontamination, while limited evidence demonstrated  
41 improvement of clinical and radiographic outcomes after implantoplasty. The effect of bone  
42 augmentation appeared limited to 'filling' radiographic defects.

43 Conclusions: The outcomes of the currently available surgical interventions for peri-implantitis  
44 remain unpredictable. There is no reliable evidence to suggest which methods are the most  
45 effective. Further randomised-controlled studies are needed to identify the best treatment methods.

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53 **Clinical Relevance**

54 Scientific rationale for study: In the management of patients with peri-implantitis, the treatment  
55 of established bony defects around fixtures remains a significant clinical challenge. Principal  
56 findings: Whilst a range of surgical treatment modalities have been described, from simple  
57 debridement to implantoplasty and attempted guided-tissue regeneration, the individual techniques  
58 employed often appear based on operator-preference. Practical implications: This systematic review  
59 sought to evaluate the existing evidence to compare the existing surgical treatment modalities,  
60 determine their effectiveness and inform the management of these patients, however, the  
61 outcomes remain unpredictable. Further studies are required to discover the optimal surgical  
62 treatment approach for peri-implantitis.

63

64 **Introduction**

65 Implants provide a long-term, generally predictable treatment to restore function <sup>1</sup>, aesthetics <sup>2</sup>,  
66 self-esteem <sup>3</sup>, and quality of life <sup>4</sup> following tooth-loss. The application and use of dental implants  
67 has increased and now represents an indispensable therapeutic option for the replacement of  
68 missing teeth.

69 Peri-implantitis is considered to be the main biological cause of 5-year implant failure <sup>5,6</sup>.

70 Review studies have estimated that peri-implantitis will affect 28%-56% of patients and 12%–43% of  
71 individual implant sites <sup>7,8</sup>. This variation in prevalence may reflect differences in study design,  
72 population size and risk profiles, and the clinical 'definition' of peri-implantitis <sup>7,9</sup>. There remains a  
73 lack of evidence regarding treatment and prognosis of peri-implantitis <sup>8</sup>.

74 The inflammatory destruction of peri-implant tissue is multi-factorial. However, biofilm and  
75 bacterial infection are considered to be the major aetiological features in the development of peri-  
76 implant disease <sup>8</sup>. Smoking is also a strong predictor of implant failure <sup>10</sup>, leading to an increase in  
77 prevalence that is 4.7 times greater than is observed in non-smokers <sup>11</sup>. Implant failure is 6 times  
78 greater in patients with a history of periodontitis than those who did not have a history of

79 periodontitis<sup>11</sup>. Systemic risk factors such as diabetes, cardiovascular diseases, age, gender, and  
80 genetics have been suggested as potential risk factors, although studies are limited<sup>12,13</sup>. Local risk  
81 factors, e.g. excess cement, was associated with signs of peri-implantitis in 100% of patient with a  
82 history of periodontal disease and 65% of healthy controls<sup>14</sup>.

83 The diagnosis of peri-implantitis depends on the presence of inflammatory signs, bleeding  
84 on probing (BOP) or suppuration on probing (SOP) and the degree of bone loss evident  
85 radiographically<sup>15</sup>. However, it is important to distinguish this diagnosis of peri-implantitis from  
86 bone resorption resulting from bone remodelling which occurs early after implant placement<sup>7</sup>.  
87 Some authors do not consider peri-implantitis as a differential diagnosis unless the implants have  
88 been in place for >12 months<sup>16-18</sup>.

89 The consensus report of the *11<sup>th</sup> European Workshop on Periodontology* highlights steps to  
90 reduce the risk of incidence of peri-implantitis<sup>19</sup>. The indications for appropriate management  
91 strategies that appear in clinical studies have resulted in development of the 'cumulative  
92 interceptive supportive therapy'<sup>15,20,21</sup>. The management of peri-implantitis is based on similar  
93 techniques to those of periodontitis<sup>11</sup> which entail the elimination of inflammation and prevention  
94 of further bone loss; including non-surgical (conventional) and surgical treatment<sup>22</sup>. Conventional  
95 non-surgical treatment can be classified into mechanical, chemical and light-mediated therapies.  
96 Reviews and meta-analyses have concluded that there is no reliable non-surgical treatment which  
97 results in elimination of the disease<sup>23-25</sup>.

98 Surgical treatment allows better access to the implant surface and the surrounding bony  
99 defect<sup>26</sup> and is used in conjunction with patient-directed care, and non-surgical therapy to reduce  
100 bacterial colonization and local inflammation<sup>21</sup>. Mechanical debridement of the implant surface can  
101 be achieved using curettes, ultrasonic scalers, or air-abrasion, in the presence or absence of systemic  
102 antibiotics. A 3-month follow-up study has shown that mechanical debridement alone, following  
103 surgical access, is effective in reducing clinical/microbial parameters<sup>27</sup>. Whilst adjunctive surface  
104 decontamination with antimicrobials such as chlorhexidine (CHX) reduced microbial counts, this had

105 no significant effect on clinical or radiographic parameters<sup>28,29</sup>. Leonhardt et al. (2003) reported  
106 that significant reduction in BOP and PPD (periodontal probing depth) following surgical  
107 debridement and decontamination with H<sub>2</sub>O<sub>2</sub><sup>30</sup>. Although many clinicians employ topical antibiotics  
108 e.g. tetracycline and minocycline, their clinical effect remains unclear<sup>31</sup>.

109 Lasers have been shown to have no additional clinical benefit as a potential surface-  
110 decontamination agents during surgical therapy when compared with mechanical debridement<sup>32,33</sup>.  
111 Photo-dynamic therapy (PDT) was shown to significantly decrease BOP and PPD between test and  
112 control subjects in a randomised control trials (RCT), although the bacterial counts showed no  
113 difference between the two groups<sup>34</sup>.

114 Adjunctive resective surgery using osteoplasty, with or without apically re-positioned flap  
115 (ARF) procedures, has been reported to improve clinical sign of peri-implantitis, where PPD ≥ 6 mm  
116 were eliminated in 77% of subjects<sup>35</sup>. However, the use of ARF in the aesthetic zone is limited<sup>11</sup>.  
117 Implantoplasty is directed to reduce surface-roughness of the implant surface to decrease bacterial  
118 and biofilm accumulation<sup>36</sup>. However, concerns have been raised regarding the reduction of implant  
119 strength<sup>37</sup>, deposits of titanium particles in the soft- and hard-tissues<sup>38</sup> and increased marginal  
120 tissue recession and exposure of the implant surface<sup>31</sup>. Re-osseointegration using bone  
121 augmentation (autogenous bone<sup>39,40</sup> and/or synthetic bone graft materials<sup>41,42</sup> may provide a  
122 significant improvement in clinical and radiographic parameters compared to the baseline. Bone  
123 graft (autogenous or synthetic), however, cannot be integrated on to a metal surface<sup>43</sup>.  
124 Furthermore, it has been shown that the use of membrane/s with autogenous or synthetic materials  
125 has no additional benefit<sup>40,44</sup>.

126 The aim of this systematic review was to critically evaluate the current literature on the  
127 surgical treatment of peri-implantitis and assess the effectiveness of treatment modalities (and  
128 adjunctive therapies) on peri-implant and periodontal radiographic outcomes. The objective was to  
129 identify the most predictable and reliable treatment modalities by a quantitative comparison of  
130 outcomes using meta-analysis.

131 **Materials and methods**

132 **Search Strategy**

133 In order to achieve the aims of this study, an electronic literature search was conducted using Ovid  
134 MEDLINE, EMBASE and EBM Review – Cochrane Central Register of Control Trials and Cochrane  
135 Database of Systematic Reviews. The following keywords were combined: *'Tooth Implantation'* OR  
136 *'Dental Implants'* OR *'Tooth implants'* OR *'Oral Implants'* OR *'Endosseous implants'* OR  
137 *'Osseointegrated implants'* AND *'Periimplantitis'* OR *'Peri-implantitis'* OR *'Peri-implant disease'* OR  
138 *'Peri-implant defect'* OR *'Peri-implant infection'* OR *'Peri-implant inflammation'* OR *'Peri-implant*  
139 *bone loss'* AND *'Management'* OR *'Treatment'* OR *'Therapy'* AND *'Surgery'* OR *'Surgical'* OR *'Surgical*  
140 *approach'* OR *'Open flap'* OR *'Access flap'* OR *'Resective'* OR *'Regenerative'* OR *'Bone regeneration'*  
141 OR *'Bone augmentation'* (Table 1).

142

143 **Study Selection Criteria**

144 The criteria for inclusion of specific studies in this review were human studies published in the  
145 English language. Studies were selected for randomized controlled trials or prospective cohort  
146 studies only with  $\geq 10$  patients and  $\geq 6$  months follow-up (the longest follow up period was chosen in  
147 longitudinal studies which were published more than once). Experimental animal or studies *in vitro*  
148 were excluded.

149

150 **Primary and secondary outcomes**

151 The primary outcome for this review study was the reduction of BOP in implants treated surgically  
152 for peri-implantitis. The secondary outcomes were the assessment of PPD and RBL (radiographic  
153 bone loss).

154

155 **Qualitative assessment methods (Risk of bias)**

156 The modified 'Critical Appraisal Skills Program' (CASP) checklists was used to assess the quality of the  
157 studies <sup>45</sup>. The risks of bias were categorized into; low risk (all the criteria were met), moderate risk  
158 (1-2 criteria were missed) or high risk (>2 criteria were missed).

159

## 160 **Statistical Analysis**

161 Meta-analyses were conducted separately for the parameters PPD and RBL using computer software  
162 (Stata<sup>®</sup> V13). All data used in meta-analysis were those measurements made at the end of the  
163 observation period for both control and intervention arms. Forest plots were produced to represent  
164 the standardized mean difference (SMD) between control and test groups. Pooled estimates and  
165 associated 95% confidence interval (CI) from meta-analysis for each type of intervention were  
166 indicated by 'diamond' symbols in Fig. 5; the center of the diamond (with respect to the x-axis)  
167 indicates the pooled point estimate and the edges indicate the pooled 95% CI. I-squared values and a  
168 chi-squared test were used to assess the heterogeneity of the studies.<sup>46</sup> Where heterogeneity was not  
169 problematic fixed-effects meta-analysis was employed and random-effects meta-analysis was  
170 otherwise employed. Although some evidence of an outlier was observed for RBL for some studies  
171 <sup>49,50</sup>, results for this study were included in Forest plots because it was not used to form any 'pooled'  
172 estimates (it was the only study in the 'implantoplasty' group).

173

## 174 **Results**

### 175 **Literature on peri-implant disease**

176 Initial results highlighted the increase in published research on peri-implant disease over the last 15  
177 years (Fig. 1a). There were significantly more publications on peri-implantitis and its surgical  
178 treatment compared to the numbers of publications regarding peri-implant mucositis and non-  
179 surgical treatment (Fig. 1b).

180

### 181 **Manuscript selection**



182 The literature search identified 320 studies, and 25 were selected for full-text evaluation following  
183 title and abstract screening. A further 9 papers were excluded following careful review (Fig. 2), and  
184 the remaining 16 studies included and reviewed for detailed qualitative and quantitative assessment  
185 (see Supplementary Information for a summary of the included studies). Selection was based on the  
186 'Preferred Reporting Items for Systematic review and Meta-Analysis' flow chart PRISMA <sup>48</sup>. Of the 16  
187 studies included, 9 were RCTs, 4 were comparative prospective studies, and 3 were single group  
188 prospective studies. The CASP checklist revealed that 53% of the included studies have a high risk of  
189 bias, 35% have a moderate risk, and the remaining studies (12%) have a low risk of bias. The follow-  
190 up periods of the studies that were included in the review ranged from 6 to 60 months. However,  
191 the participants were observed for 12 months in most of the studies.

192

193

194

### 195 **Surgical interventions**

196 The main type of surgical intervention was bone augmentation following mechanical debridement,  
197 which was examined in 44% of the studies (Fig. 3a). The effect of mechanical debridement combined  
198 with surface decontamination was examined in 38% of the studies. Relatively few studies (12%)  
199 considered the effects of mechanical debridement only; 6% of the studies examined mechanical  
200 debridement with implantoplasty. Xenograft materials were used for 64% of the bone augmentation  
201 cases, whilst autogenous bone was used for 20% of the augmentation studies. CHX was the most  
202 common surface decontamination method (57%) and was used in all of the cases (which included  
203 debridement plus surface decontamination; Fig. 3b).

204

### 205 **Study outcomes**

206 The parameters used in clinical measurement of peri-implantitis were BOP, PPD, and RBL. The  
207 majority of studies used both clinical and radiographic outcomes (69%), and the remaining studies

208 employed clinical parameters only (31%). Three studies<sup>28, 29, 49</sup> measured change in outcome  
209 measurements with time (3, 6, and 12 months follow-up) and they showed that the mean BOP was  
210 significantly decreased ( $P < 0.05$ ) after 3 and 6 months followed by a gradual increase from 6 to 12  
211 months (Fig. 4a). The mean PPD was also decreased significantly ( $P < 0.05$ ) at 3-month follow-up  
212 then remained relatively constant during the remaining periods (Fig. 4b). By contrast, RBL had not  
213 increased significantly ( $P > 0.05$ ) after 3 months.

214

### 215 **Meta-analysis**

216 The meta-analysis was conducted using 8 RCTs<sup>28, 29, 32, 34, 50-53</sup> and 2 controlled prospective cohort  
217 studies<sup>40, 44</sup> as they reported mean reductions (and standard deviations) for PPD and RBL. The forest  
218 plots for PPD and RBL are represented by the four methods for surgical peri-implantitis treatment  
219 identified: 1) surface decontamination, 2) implantoplasty, 3) bone augmentation, and 4) additional  
220 use of membranes in bone regeneration. Few studies have published data relating to BOP, and so no  
221 meta-analysis could be conducted for this parameter.

222 Meta-analysis demonstrated that implants treated with surface decontamination had SMD of -0.21  
223 (95% CI: -1.70 to 1.27) for PPD reduction. Only one study<sup>50, 51</sup> reported the effect of implantoplasty  
224 on PPD reduction which shows a significant SMD of -3.33 (95% CI: -4.37 mm to -2.28 mm). Bone  
225 augmentation with grafting materials and the additional use of membrane resulted in SMD of 0.15  
226 mm (95% CI: -0.55 to 0.84 mm) and 0.30 mm (95% CI: -0.31 to 0.91 mm) respectively (Fig. 5a). In  
227 terms of RBL changes, the use of surface decontamination methods resulted in SMD of 0.54 mm  
228 (95% CI: -0.20 to 1.28 mm). Whereas implant treated with implantoplasty, had SMD of -3.38 (95% CI:  
229 -4.43 to -2.33 mm). The SMD for RBL changes after the use of bone augmentation was -1.50 (95% CI:  
230 -0.80 to -0.31 mm). However, the additional use of membrane has SMD of -0.16 (95% CI: -0.56 to  
231 0.24 mm) (Fig. 5b). Whilst implantoplasty and bone augmentation resulted in significant  
232 improvement in RBL, the use of surface decontamination or additional membrane application failed  
233 to significantly affect observed treatment outcomes.

234 Heterogeneity was found to be small or moderate for the additional membrane subgroup  
235 (i.e.: RBL, I-squared = 0.0%, P = 0.64; PPD, I-squared = 52.1%, P = 0.152) and so random-effects meta-  
236 analysis should provide a reasonable pooled estimates in this case. Heterogeneity was found to be  
237 high for the surface decontamination subgroup (i.e.: RBL, I-squared = 88.6%, P < 0.001; PPD, I-  
238 squared = 97.1%, P < 0.001). A sensitivity analysis for RBL and for the additional membrane subgroup  
239 could not be carried out for due to the small number of studies in this case. A sensitivity analysis  
240 could be carried out for PPD for this subgroup, where removal of the study with the smallest sample  
241 size of seventeen subjects in total (namely, Schwartz et al., 2013) did not affect pooled results very  
242 greatly (i.e., SMD = -0.253 and 95% CI = -2.001 to 1.494), whereas removal of the only “outlying”  
243 study that indicated a positive mean difference (namely, de Waal et al., 2015) did affect pooled  
244 results (i.e., SMD = -0.866 and 95% CI = -1.663 to -0.069). This result indicates a significant reduction  
245 in PPD for surface decontamination subgroup in this circumstance, although caution should still be  
246 exercised due to the small number of studies and heterogeneity. Again, funnel plots are likely to  
247 yield limited information only due to the small number of the studies included in the analysis.

248

249 **Discussion**

250 This systematic review and meta-analysis was conducted to explore the literature relating to the  
251 surgical management of peri-implantitis. It was evident that the patient selection criteria for entry  
252 into the studies (and the definition of ‘peri-implantitis’) varied considerably between the included  
253 studies. For example, one study defined peri-implantitis by implants with RBL indicating >50% of  
254 bone loss <sup>40</sup>, whereas other studies defined peri-implantitis as affecting implants that exhibited PPD  
255 >6mm with radiographically visible bony defects <sup>32, 54, 55</sup>.

256 Radiographic interpretation of results was found to be inconsistent. Defect configuration  
257 needs to be taken into account, and this is particularly evident where bone regeneration is to be  
258 attempted using guided bone regeneration <sup>55</sup>. Rocuzzo et al. (2016) went on to show that the  
259 circumferential defects showed better bone regeneration compared with the other types of defect.

260 However, another four-year study which included combined surgical therapy, surface  
261 decontamination, and implantoplasty revealed that the outcomes were not directly affected by the  
262 defect configuration <sup>32</sup>.

263 Plaque control is pivotally important in peri-implant disease and response to treatment <sup>15</sup>.  
264 Adequate oral hygiene maintaining plaque scores at lower levels ( $PI \leq 1$ ) was important for reducing  
265 the incidence of BOP <sup>56</sup>. The severity of peri-implantitis at the commencement of treatment (as  
266 measured by the PPD and RBL) may clearly influence treatment outcomes <sup>35, 57</sup>. Other important  
267 plaque-retentive factors, e.g. surface roughness are an important consideration when conducting  
268 comparative studies <sup>49, 53, 54</sup>. A history of both smoking and periodontitis has been shown to have an  
269 adverse effect on the treatment of peri-implantitis <sup>44, 52, 58</sup>. Due to the small numbers of patients,  
270 variation in tobacco usage, and incomplete assessment of the severity of the previous periodontal  
271 disease in the papers included within this study, this correlation could not be linked to the outcomes  
272 of surgical peri-implantitis treatment.

273 The definition of a successful treatment also varied between studies. In marked contrast,  
274 some studies <sup>49</sup> simply considered the survival of the affected implants following treatment to  
275 represent success. Other studies <sup>28, 29, 53, 57</sup> have considered no further bone loss and presence of PPD  
276  $\leq 5$ mm, with no BOP, to be a successful treatment. Inter- and intra-examiner bias may also lead to  
277 variable in outcome measures, for example, force of probing <sup>59</sup>. Furthermore, PPD alone is  
278 considered as an invalid marker for the progression of the disease as the reduction in PPD post-  
279 treatment may simply reflect gingival recession and/or the surgical technique e.g. apically-  
280 repositioned flap procedures <sup>52, 60</sup>. Although radiographic assessment is the only truly non-invasive  
281 method for measuring marginal bone levels <sup>52</sup> it can only indicate 'defect-fill' but not the actual re-  
282 osseointegration <sup>44</sup> and represents the mesial and distal bone levels only <sup>61</sup>. More recently, cone-  
283 beam CT has been used to detect the levels of buccal and lingual bones, although concerns have  
284 been raised regarding both radiation exposure and their validity due to a radiolucent halo that may  
285 occur around the implant <sup>51</sup>.

286           The rationale behind the use of adjunctive systemic antibiotics in the management of peri-  
287 implantitis was considered in three studies <sup>40, 49, 58</sup>. There is a lack of evidence to support the  
288 prescription of antibiotics in peri-implantitis treatment, which appears operator-dependent. An RCT  
289 investigating the effectiveness on systemic antibiotics failed to demonstrate any effect on local  
290 microbiological parameters within the defect <sup>53</sup>.

291           The most popular surface decontaminant was CHX, which has been tested extensively and  
292 approved to have a broad-spectrum anti-bacterial activity <sup>62</sup>. Variation occurred in the CHX  
293 concentrations used in two studies (0.12% CHX Vs placebo<sup>29</sup> or 2% CHX Vs 0.12% <sup>28</sup>). Although both  
294 studies reported reduced microbial loads when compared to control groups, this did not translate  
295 into demonstrable clinical effects on peri-implantitis. Although other chemical antimicrobial  
296 treatments were employed e.g. H<sub>2</sub>O<sub>2</sub>, H<sub>3</sub>PO<sub>4</sub>, and EDTA, no studies compared their effects to other  
297 adjunctive treatments (or placebo-treated control groups). A 4-year review revealed that curette  
298 and saline mechanical debridement showed better results than those treated with Er:YAG laser <sup>32</sup>,  
299 although one study indicates that the Er:YAG laser gave better outcomes at 2-year follow-up <sup>63</sup>.  
300 Meta-analysis failed to detect any significant difference in the use of surface decontamination (via  
301 CHX or Laser) on PPD and RBL. Previous studies have indicated that treatment results are  
302 independent of decontamination method and that other risk factors such as oral hygiene, defect  
303 configuration are better predictors of treatment success <sup>33, 55</sup>.

304           Implantoplasty reduces the macro-surface texture (threads) of the implants. The authors  
305 feel that the procedure is effective, partly as it is associated with complete elimination of the  
306 primary aetiological factor in peri-implantitis- namely the biofilm. Barbour et al. (2007) reports that  
307 it may increase the micro-surface roughness leading to biofilm retention. Furthermore, it may alter  
308 implant strength <sup>37, 64</sup> and increase the temperature of the implants surface <sup>65</sup>, leading to adverse  
309 effects on bone cellularity <sup>66</sup>. The significant improvement of clinical and radiographic parameters  
310 following implantoplasty was only based on one study <sup>50, 51</sup> and further research regarding this  
311 method is needed.

312 Bone augmentation is limited due to the biological principle of bone regeneration which  
313 needs a blood supply to provide nutrition, inflammatory cells to induce bone formation  
314 (osseointegration), and collagen matrix for osseointegration<sup>43</sup>. The significant effect of bone  
315 augmentation on RBL relates to the bone grafts material occluding the defect; no effect on clinical  
316 outcome (PPD) is evident<sup>52</sup>. Autogenous bone particles ± membranes in multi-walled defects  
317 resulted in significant improvement in PPD and RBL at 36 months<sup>40</sup>. In contrast, Aghazadeh et al.  
318 (2012) demonstrated that bovine-derived xenograft (BDX) was more effective than autogenous  
319 particulate bone<sup>58</sup>. Khoury and Buchmann (2001) and Roos-Jansåker et al. (2014) were unable to  
320 demonstrate any additional benefits in comparison to defects treated with graft material alone<sup>40,44</sup>.

321 There are several limitations of this current study due to the inclusion of English language  
322 papers only, as well as considerable variability between the different studies included in this review  
323 relating to the inclusion/ exclusion criteria. Furthermore, there were only a small number of studies  
324 included for each type of surgical intervention, with most studies consisting of relatively small  
325 sample sizes and high risk of selection bias in patient inclusion. The high degree of heterogeneity  
326 between studies prevents quantitative comparison between the groups<sup>47</sup>. Therefore, neither the  
327 differences between the groups nor the overall results were calculated. Furthermore, the meta-  
328 analyses should be interpreted cautiously because of the small number of the included studies in  
329 each group and the high degree of heterogeneity between them.

330 This current review concludes that a need exists for a long-term, double blind RCT with large  
331 sample size and split-mouth technique are required to eliminate patient-related bias. In addition, all  
332 potential confounders should be taken into account. Finally, it would be helpful if the definition,  
333 diagnosis and the outcomes of the disease were standardised, to be able to conduct more precise  
334 reviews, meta-analyses and the evidence-based surgical treatment of these patients.

335

336

337

338 **Conclusion**

339 This systematic review shows that a surgical approach to mechanical debridement alone may result  
340 in improved clinical outcomes, with no evidence to show the benefits of apically-repositioned flap  
341 procedures. No additional clinical benefits were found from the use of surface decontaminants  
342 (chemicals or lasers) or additional systemic antibiotics. A single study demonstrated a significant  
343 improvement following implantoplasty. Bone augmentation improved radiographic bone levels; the  
344 use of additional membrane/s, however, did not result in any additional benefit. The high degree of  
345 heterogeneity and the small number of controlled studies make it difficult to identify which  
346 procedure is superior to any other.

347

348 **Funding**

349 None

350

351 **Conflict of Interest**

352 The authors confirm that there are no conflicts of interest to declare.

353

354 **Ethical approval**

355 None required

356

357

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512

513 **Table 1** Keywords used for the electronic search

<b>Dental Implantology</b>	<b>Peri-implant disease</b>	<b>Procedure</b>	<b>Technique</b>
Tooth Implantation	Periimplantitis	Management	Surgery
Dental Implants	Peri-implantitis	Treatment	Surgical
Tooth implants	Peri-implant disease	Therapy	Surgical approach
Oral Implants	Peri-implant defect		Open flap
Endosseous implants	Peri-implant infection		Access flap
Osseointegrated implants	Peri-implant inflammation		Resective
	Peri-implant bone loss		Regenerative
			Bone regeneration
			Bone augmentation

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516 **Figure legends:**

517 **Figure 1** Publishing rate of papers on (a) peri-implant disease and (b) peri-implantitis treatment in  
518 the period 2001-2015.

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520 **Figure 2** PRISMA flow chart for study selection.

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522 **Figure 3** Proportion of (a) surgical intervention investigated and (b) surface decontamination  
523 methods used in the included studies.

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525 **Figure 4** The relationship between observed outcomes and time for (a) BOP and (b) PPD <sup>28, 29, 49</sup>.

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527 **Figure 5** Forest plot for (a) probing pocket depth (PPD) reductions and (b) radiographic bone level  
528 (RBL) changes.

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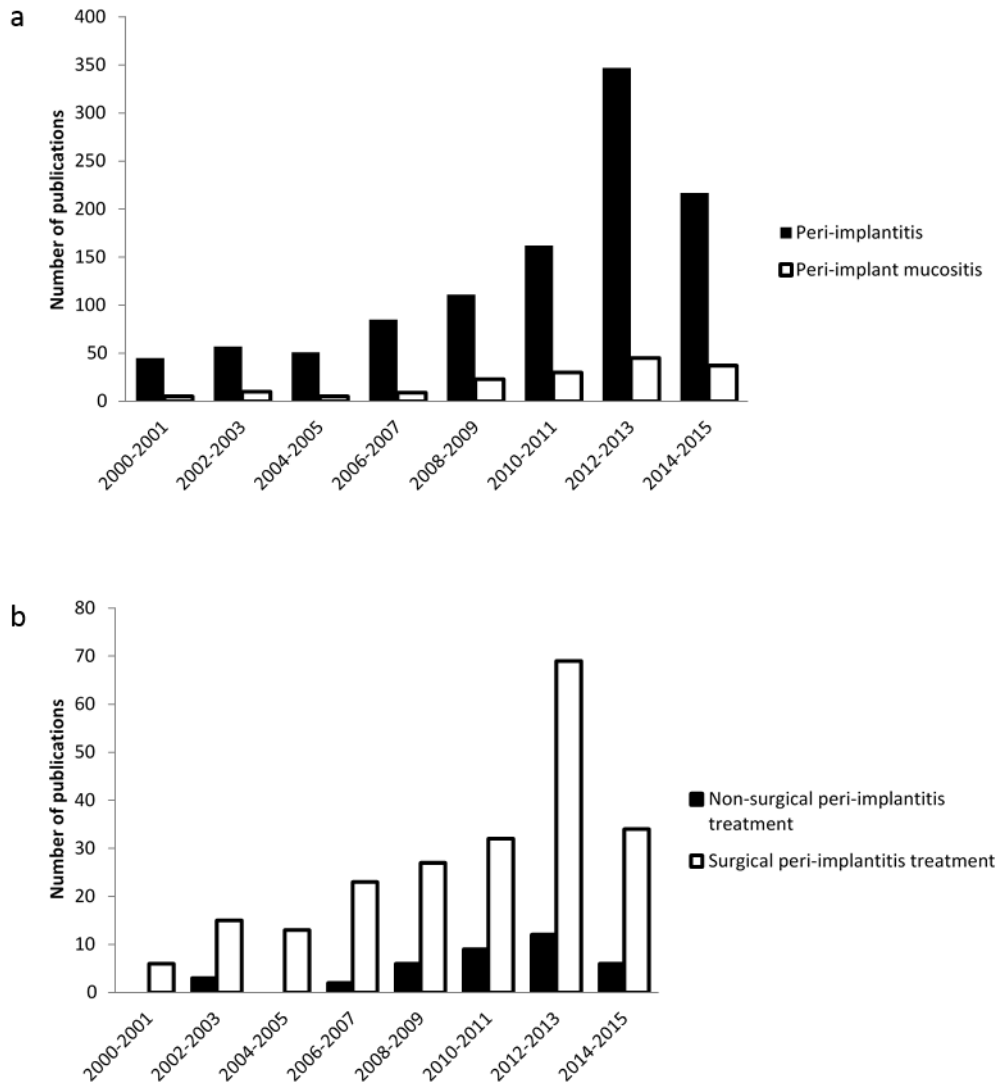
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537 Figure 1:

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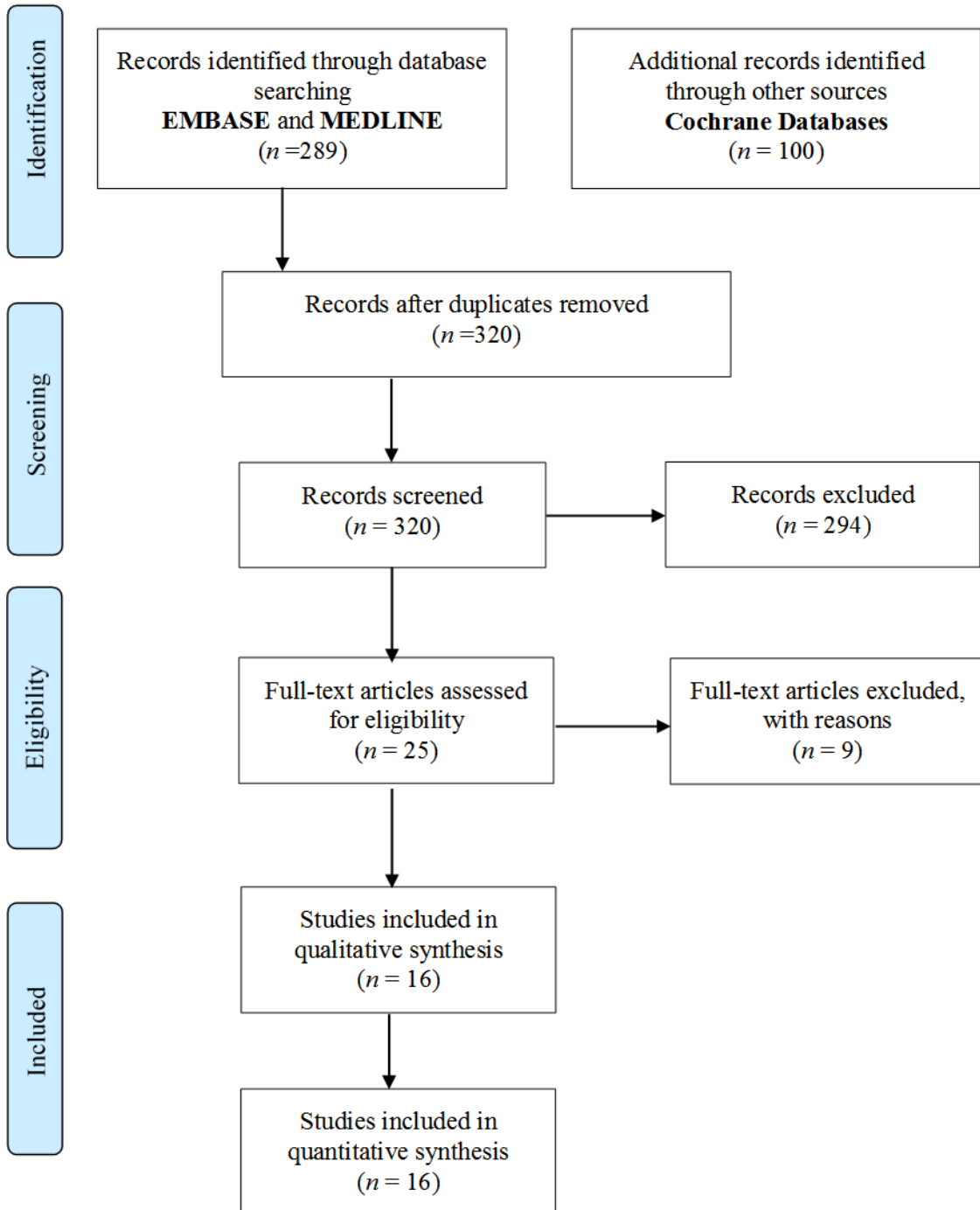
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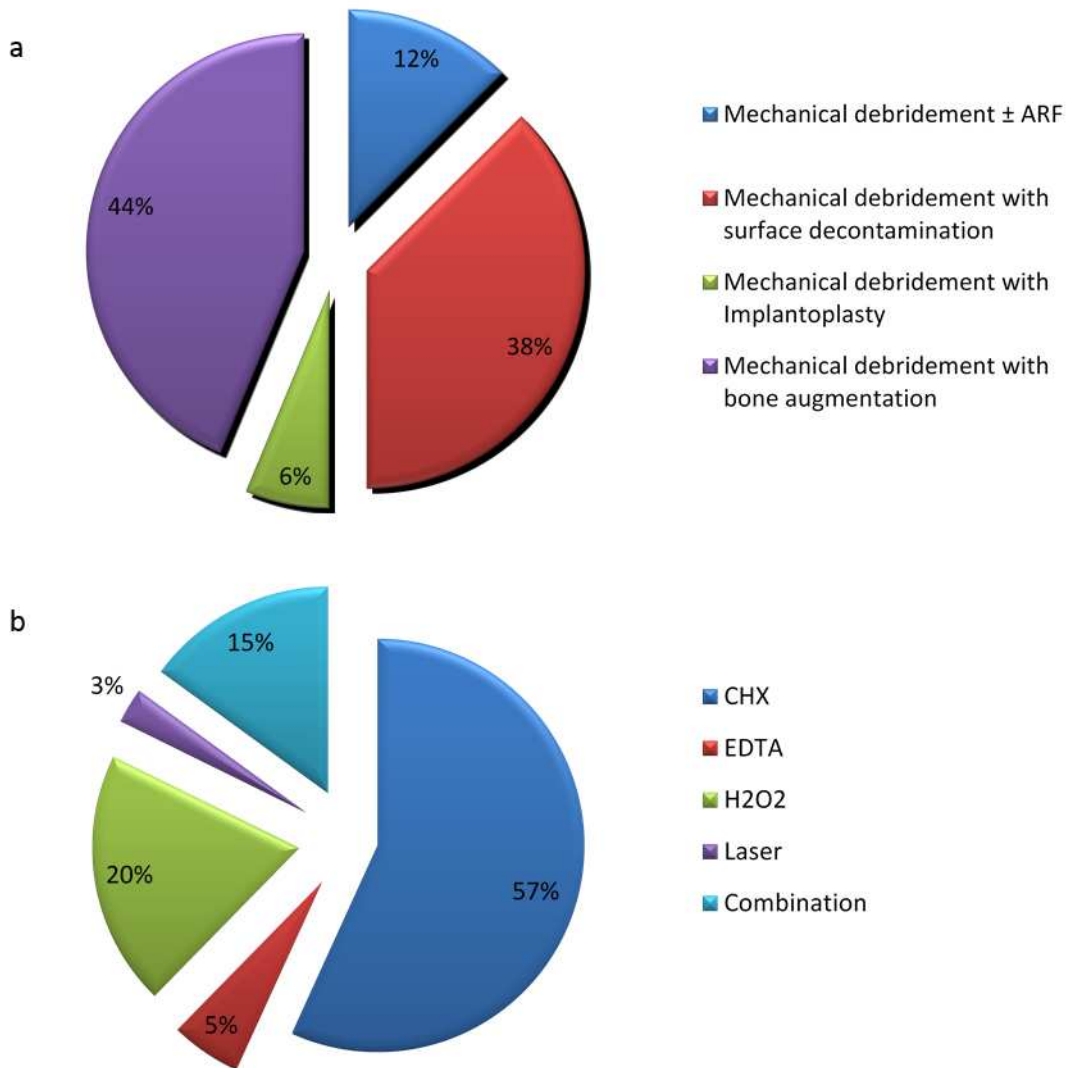


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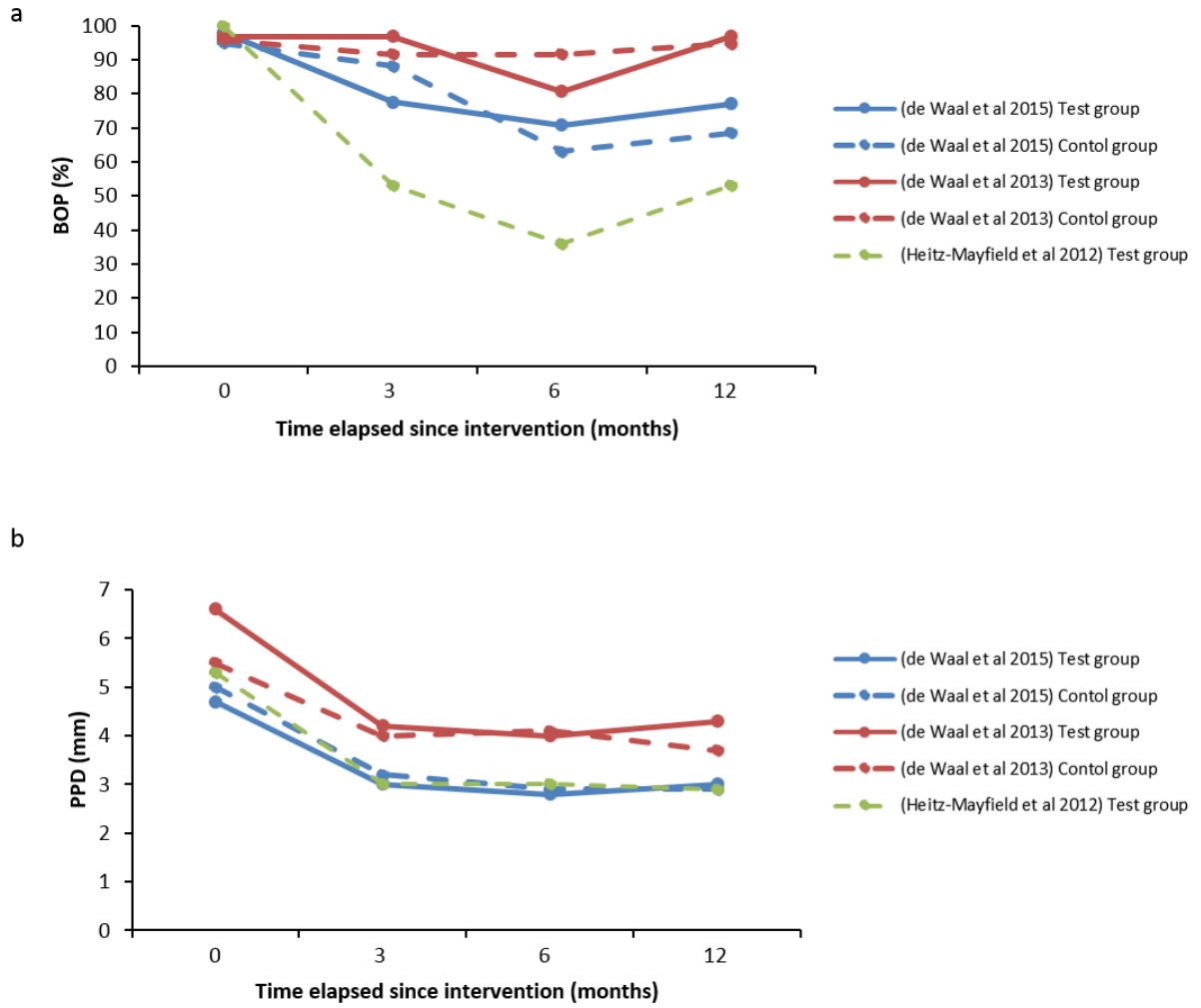
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