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**Title:** Efficacy of access flap procedures compared to subgingival debridement in the treatment of periodontitis. A systematic review and meta-analysis.

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## ABSTRACT

**Aim:** This systematic review aimed to answer the following focused questions: 1) “In patients with periodontitis, how effective are access flaps (AFs) as compared to subgingival debridement in attaining probing depth (PD) reduction?”; 2) “In patients with periodontitis, does the type of AF impact PD reduction?”.

**Material and Methods:** Randomized clinical trials were searched in three databases. Besides PD, information concerning clinical attachment level (CAL) and other relevant outcomes was also collected. Meta-analyses were performed whenever possible and results were categorized based on the initial PD.

**Results:** Thirty-six publications were included. AFs resulted in a significantly greater PD reduction in deep pockets (>6 mm or  $\geq 6$  mm), as compared to subgingival debridement, in short- [n=4; weighted mean difference (WMD)=0.67 mm; 95% confidence interval (CI) 0.37,0.97; p<0.001] and long-term studies (n=4; WMD=0.39 mm; 95% CI 0.09,0.70; p=0.012), while in moderately deep pockets (4-6 mm, 5-6 mm or 4-5 mm) only in short-term studies (n=4; WMD=0.34; 95% CI 0.21,0.46; p<0.001). In shallow pockets (1-3 mm or 1-4 mm), AFs led to greater CAL (n=7; WMD=-0.43 mm; 95% CI -0.56,-0.28; p<0.001). There was not enough evidence to answer question PICO 2.

**Conclusions:** AFs resulted in greater PD reduction in the treatment of deep and moderate pockets.

## **Clinical Relevance**

**Scientific rationale for study:** Severe periodontitis (stages III and IV) is one of the most prevalent non-communicable chronic diseases affecting humans. Since in this clinical situation subgingival debridement may not be enough to control the disease, it is worthy to assess if a surgical access is needed.

**Principal findings:** The effectiveness of the mode of therapy is going to be dependent on the initial probing depth (PD). Surgery has shown benefits in terms of PD reduction when treating initially moderate and deep pockets. When combining the results for PD reduction and clinical attachment level (CAL) gain, subgingival debridement seems to be the choice at moderately deep pockets and access surgery at initially deep pockets.

**Practical implications:** In order to attain proper pocket reduction, access flaps might be more efficacious when aimed to treat initially deep pockets. However, subgingival debridement provides higher CAL gain in moderately deep pockets and less clinical attachment loss in shallow sites. Long-term results seem to be related with other factors different than the type of debridement provided (surgical or non-surgical), such as hygiene measures or maintenance protocols, as differences between therapies tend to disappear throughout time.

## Introduction

The role of subgingival biofilm in the initiation and progression of periodontal diseases has been clearly established (Roberts & Darveau, 2015). Thus, adequate individual plaque control practices, and professional elimination of supra- and subgingival plaque and calculus are essential for the successful treatment of periodontitis (Graziani, Karapetsa, Alonso, & Herrera, 2017). In this context, cause-related periodontal therapy aims to mechanically remove subgingival biofilm and to control inflammation, either with non-surgical or surgical approaches, in order to arrest further attachment loss by reducing probing depth (PD), as sites with  $PD \leq 4$  mm are associated with lower risk of disease progression and tooth loss (Matuliene et al., 2008b).

Non-surgical periodontal therapy consists on subgingival debridement. Traditionally, this approach has been done by means of subgingival scaling and root planing (SRP). Although, theoretically, these are well-differentiated procedures, they are performed clinically at the same time (Aimetti et al., 2014; Graziani et al., 2017; Laleman et al., 2017).

A consistent amount of evidence has indicated that subgingival debridement is effective in reducing bleeding on probing (BOP) and PD, and gaining clinical attachment level (CAL) (Sanz, Alonso, Carasol, Herrera, & Sanz, 2012; Smiley et al., 2015; Van der Weijden & Timmerman, 2002). However, it is technically demanding, and complete calculus removal is difficult to achieve (Jepsen, Deschner, Braun, Schwarz, & Eberhard, 2011). Indeed, in vitro studies have shown that after therapy 3% to 80% of instrumented root surfaces harboured some residual calculus (Buchanan & Robertson, 1987; Caffesse, Sweeney, & Smith, 1986a; Geisinger, Mealey, Schoolfield, & Mellonig, 2007; Rabbani, Ash, & Caffesse, 1981). More hard deposits are generally detected in deep sites ( $PD > 5$  mm) and at molars (particularly in furcation areas), than at single-rooted teeth (Caffesse, Sweeney, & Smith, 1986b; Rateitschak-Pluss, Schwarz, Guggenheim, Duggelin, & Rateitschak, 1992; Waerhaug, 1978), what limits the efficacy of closed subgingival debridement as definitive therapy (Heitz-Mayfield, Trombelli, Heitz, Needleman, & Moles, 2002; Serino, Rosling, Ramberg, Socransky, & Lindhe, 2001).

Access flaps were introduced to improve the efficiency of subgingival debridement by gaining direct access to the root surface, root concavities and furcations in sites with residual pockets irrespective of the pattern of bone resorption. In these conservative surgeries, there is no active removal of alveolar bone and no or minimal resection of soft tissues, as the treatment strategy focuses on enhancing the cleaning of the colonized root surface to achieve shallower pockets, greater CAL gain and lower levels of BOP. Graziani et al. (Graziani, Karapetsa, Mardas, Leow, & Donos, 2018) classified

conservative surgical procedures into open flap debridement (Kirkland, 1931), minimally resective flaps [e.g. the modified Widman flap (MWF) (Ramfjord & Nissle, 1974)], and flaps aimed at conserving interdental soft tissues [e.g. papilla preservation techniques (Checchi & Schonfeld, 1988; Dello Russo, 1981; Michaelides & Wilson, 1996; Takei, Han, Carranza, Kenney, & Lekovic, 1985)]. The first two approaches achieve a reduction in PD by a combination of gingival recession and CAL gain along time. In the minimally resective flaps, a marginal soft tissue resection is also performed in order to eliminate the epithelium of the periodontal pocket and the inflamed tissue from the inner part of the flap. On the contrary, papilla preservation techniques are particularly indicated in the treatment of intrabony defects with the objective of maximizing CAL gain by enhancing blood clot stability and thus, reducing tissue contraction. As reported in a previous systematic review, the magnitude of clinical improvement may be related to the surgical flap design (Graziani et al., 2012). In this sense, greater CAL gain and less recession were observed when papilla preservation techniques were applied in the surgical treatment of intrabony defects. Moreover, the adjunctive use of magnification and microsurgical instruments may also improve visibility of subgingival deposits and calculus removal. Currently, there is a paucity of literature on the use of magnification in non-surgical periodontal treatment (Nibali, Pometti, Chen, & Tu, 2015; Nibali, Yeh, Pometti, & Tu, 2018; Ribeiro et al., 2011).

Ideally, the least invasive treatment with the better biological cost-effectiveness ratio should be used to restore periodontal health. Furthermore, patients' perspective of therapy may differ from traditional clinical endpoints. Assessment of pain and discomfort experienced during and after therapy should complement conventional clinical measures (Hujoel, 2004).

Therefore, the aim of the present systematic review was to answer the following two PICO questions: "In patients with periodontitis (population), how effective are access flaps (intervention) as compared to subgingival debridement (comparison) in attaining PD reduction (primary outcome)?" (PICO 1) and "In patients with periodontitis (population), does the type of access flaps (intervention and control) impact PD reduction (primary outcome)?" (PICO 2).

## **Material and methods**

### **Protocol development and focused question**

The protocol of this systematic review was made a priori, agreed upon all authors and registered in the PROSPERO International Prospective Register of Systematic Reviews hosted by the Centre for

Reviews and Dissemination, University of York, National Institute for Health Research (United Kingdom; CRD42019123077). This systematic review was reported according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement (Moher, Liberati, Tetzlaff, & Altman, 2009).

#### Eligibility criteria

##### Inclusion criteria (PICOS)

- Population: patients older than 18 with chronic or aggressive periodontitis based on the criteria described by Armitage (Armitage, 1999);
- Interventions: any type of access flap (PICO 1) or any access flap different to conventional MWF (PICO 2);
- Comparisons: subgingival debridement (PICO 1) or conventional MWF (PICO 2);
- Outcomes: changes in PD;
- Study design: randomized controlled clinical trials (RCTs) with at least 6 months of follow up and a minimum of 10 patients per treatment group. Only RCTs were included to be able to make direct comparisons and, if possible, to be included in the meta-analyses.

##### Exclusion criteria

- Studies aiming at apically position the flaps;
- Studies using resective approaches;
- Studies aiming at using regenerative technologies in intra-osseous defects;
- Studies focusing only on furcated teeth.

##### Type of intervention and comparisons

Studies were selected that included interventions for cause-related periodontal therapy. To answer question PICO 1 interventions in the test group included any access flap such as traditional open flap debridement [OFD, (Kirkland, 1931)], MWF or microsurgical access procedures, whereas interventions in the control group included subgingival debridement with or without adjunctive therapies, irrespective of the instrument used for the mechanical removal of biofilm. To answer question PICO 2 intervention in the test group included any AF different to conventional MWF, whereas interventions in the control group included conventional MWF.

##### Type of outcomes

The primary outcome for assessing the efficacy of the treatment of periodontitis was PD reduction.

The following secondary outcomes were studied:

- CAL change,
- Changes in gingival or bleeding indices and plaque indices,
- Tooth loss,
- Mean number of residual pockets (PD > 3 mm and/or PD > 3 mm with BOP or PD > 4 mm and/or PD > 4 mm with BOP) at the end of therapy,
- Percentage of closed pockets (PD ≤ 3 mm or PD ≤ 4 mm) out of the total number of pockets at baseline (PD > 3 mm or PD > 4 mm),
- Percentage of cases with need for re-treatment,
- Harms and adverse effects such as swelling, root sensitivity, gingival recession, etc.,
- Patient-reported outcome measures (PROMs), such as pain, discomfort, satisfaction, etc.

### **Information sources and search**

#### Electronic search

Three electronic databases were used as sources in the search for studies satisfying the inclusion criteria: (1) The National Library of Medicine (MEDLINE via PubMed); (2) Cochrane Central Register of Controlled Trials; and (3) Scopus. These databases were searched for studies published until February 8th, 2019. The search was limited to human subjects and to studies reported in English. No more languages were considered due to the limited time for the preparation of this systematic review.

#### Manual search

All reference lists of the selected studies and previously published systematic reviews were checked for cross-references. The following journals were hand-searched from year 2008 to 2018: Journal of Clinical Periodontology, Journal of Periodontology, The International Journal of Periodontics and Restorative Dentistry and Journal of Periodontal Research.

#### Search strategy

The following search terms were used in PubMed:

#### Population

[MeSH terms]: (adult periodontitis[mh] OR chronic periodontitis[mh] OR aggressive periodontitis[mh] OR early onset periodontitis[mh] OR juvenile periodontitis[mh])

OR

[Text Words, Title]: periodontitis[tw]

Intervention

[MeSH terms]: surgical flap[mh] OR surgical flaps[mh]

OR

[Text Word, Title]: access flap[tw] OR access flaps[tw] OR open flap debridement[tw] OR open flap debridements[tw] OR modified Widman flap[tw] OR modified Widman flaps[tw] OR Widman flap[tw] OR Widman flaps[tw] OR Kirkland flap[tw] OR Kirkland flaps[tw]

The search was combined as Population AND Intervention.

The search strategy applied for the Cochrane was '(adult periodontitis OR chronic periodontitis OR aggressive periodontitis OR early onset periodontitis OR juvenile periodontitis OR periodontitis) AND (surgical flap OR surgical flaps OR access flap OR open flap debridement OR modified Widman flap OR Widman flap OR Kirkland flap) AND (dental scaling OR root scaling OR root scalings OR scaling, dental OR scaling, root OR scaling, subgingival OR scaling, supragingival OR scalings, root OR subgingival scaling OR supragingival scaling OR debridement, nonsurgical periodontal OR debridement, periodontal OR debridement, periodontal pocket OR debridements, nonsurgical periodontal OR debridements, periodontal OR debridements, periodontal pocket OR scaling and root planing OR subgingival debridement) AND (clinical trials, randomized OR controlled clinical trials, randomized OR randomized controlled trial)'

The search strategy used in SCOPUS was as follows (paradontitis OR parodontitis OR peridontitis OR periodontitis OR "periodontal disease" OR "dental loss" OR "furcation defects" OR "paradontal disease" OR paradontopathy OR paraodontopathy OR parodontopathy OR "parodontal disease" OR "parodontium disease" OR "parodontive tissue disease" OR "peridontal disease" OR "peridontal tissue disease" OR "peridontium disease" OR "periodontal atrophy" OR "periodontal Attachment loss" OR "periodontal diseases" OR "periodontal infection" OR "periodontium disease" OR periodontopathy ) AND ("surgical flaps" OR "surgical flap" OR "access flap" OR "access flaps" OR "open flap debridement" OR "modified widman flap" OR "widman flap" OR "kirkland flap" OR "modified widman flaps" OR "widman flaps" OR "kirkland flaps" ) with the limit to dental and medical journals (LIMIT-TO (SUBJAREA "MEDI") OR LIMIT-TO ( SUBJAREA,"DENT"))).

### **Screening methods**

Two reviewers (F.C. and A.M.) screened independently the titles and abstracts. The same reviewers selected full manuscripts of studies meeting the inclusion criteria, or those with insufficient data in the title and abstract to make a clear decision. Any disagreement was resolved by discussion with a third reviewer (I.S.). The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the full-text analysis was calculated.

### **Data extraction**

Two different reviewers (I.S. and E.M.) performed duplicate data extraction. When data were incomplete or missing, authors of studies were contacted for clarification. If agreement could not be reached, data were excluded until further clarification was available. When the results of a study were published more than once, the data were used upon necessity. If a study was comparing more than two arms, the data from the groups of interest were extracted.

### **Quality assessment (risk of bias in individual studies)**

A quality assessment of the included RCTs was performed according to the Cochrane Collaboration risk of bias tool for randomized trials (Rob2 updated in October 2018) (Higgins et al., 2016) and the CONSORT statement (Moher et al., 2012). Five main quality domains were assessed: randomization process, deviation from the intended intervention including blinding of participants and personnel (performance bias) and blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), measurement of the outcome, and selective outcome reporting (reporting bias). These parameters were rated to be in low risk of bias if all the criteria were met.

### **Risk of bias across studies**

The publication bias was evaluated using a Funnel plot and the Egger's linear regression method for the primary outcome. A sensitivity analysis of the meta-analysis results was also performed for this outcome (Tobias & Campbell, 1999).

### **Data analyses**

To summarize studies, they were combined in order to perform meta-analyses (MAs) reporting weighted mean differences (WMDs) and 95% confidence intervals (CI) to compare the effect of subgingival debridement and AFs (PICO 1), and of different types of AFs (PICO 2) for the primary and secondary outcomes. For a better interpretation of the clinical effect of each procedure, PD and CAL were reported together. Subgroup analyses were performed on the selected outcome variables using

the study follow-up [short ( $\leq 12$  months) or long ( $> 12$  months)] and the initial probing depth (PD) as explanatory variables. Furthermore, the absolute effect of each intervention was reported through weighted mean effects (WMEs) with their respective 95% CI. The statistical heterogeneity among studies was assessed using the Q test based on chi-square statistics (Cochran, 1954) as well as the  $I^2$  index (Higgins, Thompson, Deeks, & Altman, 2003) in order to know the percentage of variation in the global estimate that is attributable to heterogeneity. Study specific estimates were pooled with both the fixed and random-effect models (DerSimonian & Laird, 1986). If a significant heterogeneity was found, then the random-effect model results were presented. A Forest Plot was created to illustrate the effects of the different studies and the global estimation. STATA® (StataCorp LP, Lakeway Drive, College Station, Texas, USA), and OpenMeta [Analyst] intercooled software was used to perform all analyses. Statistical significance was defined as a p value  $< 0.05$ .

## **Results**

### **Search**

Figure 1 depicts the flow chart summarizing the results of the search. The search rendered 2117 titles, which, after evaluating their titles and abstracts, resulted in 56 articles for full text analysis. After this analysis, 36 articles were included for data extraction, representing 18 investigations, since eight groups of papers reported the results of the same material at different time points, or different outcomes from the same population. Agreement for title and abstract screening was 98.68% [ $\kappa=0.72$ ; 95% CI (0.62-0.82)] and 91.07% [ $\kappa=0.80$ ; 95% CI (0.64-0.96)] for full text. The reasons for excluding the remaining studies are detailed in Supplementary Table 1.

### **Description of selected studies**

Table 1 depicts the methodological characteristics of the selected studies. Out of the 18 investigations, 15 RCTs had a split-mouth design and 3 a parallel design (Ribeiro et al., 2011; Serino et al., 2001; Trombelli, Simonelli, Schincaglia, Cucchi, & Farina, 2012). Ten studies compared two different arms and 8 investigations three or more treatment approaches. The first PICO question (AFs versus subgingival debridement) was studied in 13 investigations and the second PICO question (comparison between different AFs) in 6 RCTs. One study provided data and results for both PICO questions (Lindhe & Nyman, 1985). There were 4 investigations evaluating the treatment of localized intrabony defects (Renvert, Nilvéus, Dahlén, Slots, & Egelberg, 1990; Renvert, Nilveus, & Egelberg, 1985; Ribeiro et al., 2011; Trombelli et al., 2012; Wennström, Wennström, & Lindhe, 1986) and one additional publication reporting the results for intrabony defects from an investigation treating the whole mouth (Isidor, Attström, & Karring, 1985).

Most of the studies performed subgingival debridement prior to surgery (12 out of 18), as part of the initial periodontal therapy, and received a second round of subgingival debridement in the control group during the surgical phase, except in the study performed in Minnesota, in which quadrants assigned to the control group received only one round of subgingival debridement (Pihlstrom, McHuon, Oliphant, & Ortiz-Campos, 1983; Pihlstrom, Oliphant, & McHugh, 1984; Pihlstrom, Ortiz-Campos, & McHugh, 1981). In the remaining 6 investigations, subgingival debridement was performed as part of the surgical phase, but not before (Lindhe & Nyman, 1985; Lindhe et al., 1982; Polansky, Haas, Lorenzoni, Wimmer, & Pertl, 2003; Serino et al., 2001; Wennström et al., 1986; Westfelt et al., 1985).

Some studies presented the results in relation to the initial PD. While most of the studies that categorized initial pockets used the ranges 1-3 mm, 4-6 mm and >6 mm (Becker et al., 1988; Hill et al., 1981; Lindhe & Nyman, 1985; Lindhe et al., 1982; Pihlstrom et al., 1981; Westfelt et al., 1985), the study from Kaldahl et al. (Kaldahl, Kalkwarf, Patil, Molvar, & Dyer, 1996) sub-grouped for 1-4 mm, 5-6 mm and >6 mm initial pockets, and the study from Serino et al. (Serino et al., 2001) presented data for 1-3 mm, 4-5 mm and >5 mm initial pockets.

The resulting systematic review pooled data from 503 patients at baseline, from which 428 were analyzed at the end of the investigation. Patients were followed for a mean period of  $41.50 \pm 39.90$  months (range: 6 to 156 months).

#### **Risk of bias in individual studies**

Rob2 tool was used to score the randomized clinical trials (Table 2). Serious methodological inadequacies associated to bias were found in almost all the studies for at least one domain. Only the study by Ribeiro et al. (Ribeiro et al., 2011) was at low risk of bias. The most frequent domains with risk of bias were incomplete reporting of the randomization process (sequence generation and allocation concealment) and examiner blinding (Supplementary table 2).

#### **Risk of bias across studies**

No significant publication bias was observed for the primary outcome measure (PD reduction) when considering studies reporting the mean PD change (Lindhe et al., 1982; Polansky et al., 2003; Serino et al., 2001), or for studies reporting the PD change according to the initial PD distribution ( $p > 0.10$ ).

The sensitivity analysis showed that the exclusion of a single study did not substantially alter any estimate.

### **Effects of interventions**

PD reduction and CAL change (PICO 1: access flap versus subgingival debridement)

Table 3 depicts the meta-analyses comparing PD and CAL change between access flaps and subgingival debridement. The WME within each group for PD reduction and CAL change is depicted in Table 4.

#### All pockets

Access flap showed significant greater PD reduction when all categories of initial PD were combined irrespectively of the follow-up (n=3; WMD=0.71 mm; 95% CI 0.44, 0.98; p<0.001). On the contrary, when combining all initial PD categories, subgingival debridement showed significant CAL gain, whereas access flap showed no change. The difference between both groups in terms of CAL change was significant (n=3; WMD= -0.26 mm; 95% CI -0.39, -0.14; p<0.001). For studies focusing only on intra-bony defects, the PD reduction was significantly greater in the surgery group (n=4; WMD= 0.49 mm; 95% CI 0.11, 0.86; p=0.01), although no differences were observed in terms of CAL gain (n=4; WMD= 0.07 mm; 95% CI -0.29, 0.44; p=0.691).

#### Shallow pockets (1-3 mm or 1-4 mm) (Figures 2 and 3)

Non-significant changes were observed in the test or control groups in terms of PD reduction in shallow pockets. Although PD reduction was significantly greater in the group receiving surgery at the short-term (n=4; WMD=0.13 mm; 95% CI 0.07, 0.18; p <0.001), this difference became non-significant at the long-term (n=4; WMD= -0.02 mm; 95% CI -0.09, 0.05; p= 0.648). For this pocket category both groups showed significant clinical attachment loss at the long-term (not at short-term for subgingival debridement), which was greater in the surgery group at all time points (n=7; WMD= -0.43mm; 95% CI -0.56, -0.28; p<0.001; prediction interval -0.81, -0.04; at the short term and n=6; WMD= -0.27mm; 95% CI -0.34, -0.20; p<0.001, at the long term respectively). For studies reporting the change in the frequency distribution of shallow pockets in the long-term, the use of access flap provided an additional increase of 11.60%, which was statistically significant (95% CI 6.76, 16.45; p<0.001).

#### Moderately deep pockets (4-6 mm, 5-6 mm or 4-5 mm) (Figures 2 and 3)

Both groups showed significant PD reduction in moderately deep pockets. As it happened with shallow pockets, PD reduction was significantly greater in the access flap group at the short-term (n=4; WMD= 0.34 mm; 95% CI 0.21, 0.46; p<0.001). This additional reduction in PD for AFs over subgingival debridement amounted for 29.6%. Whereas the subgingival debridement group showed significant CAL gain only at the short-term, the changes were not significant in the surgery group. When comparing both treatment modalities, the subgingival debridement group showed greater CAL gain in the short- and the long-terms, although this difference tended to mitigate with time (n=7; WMD= -0.34 mm; 95% CI -0.46, -0.22; p<0.001, and n=6; WMD= -0.12 mm; 95% CI -0.22, -0.01; p= 0.032, respectively). For studies reporting the change in the frequency distribution of moderately deep pockets in the long-term, the use of access flap provided an additional increase of 9.49%, which was statistically significant (95% CI 4.88, 14.10; p<0.001).

#### Deep pockets (> 6 mm or ≥6 mm) (Figures 2 and 3)

Although both groups showed significant PD reduction in this pocket category, this reduction was significantly greater in areas receiving surgery in the short- and long-terms (n=4; WMD= 0.67 mm; 95% CI 0.37, 0.97; p<0.001, and n=4; WMD= 0.39 mm; 95% CI 0.09, 0.70; p=0.012, respectively). The additional PD reduction for AFs over subgingival debridement amounted for 27.5% in the short term and 25.3% in the long term. As it happened with moderately deep pockets, the differences tended to be smaller with time. On the contrary, no significant differences among groups were observed for CAL gains at the short- and long-terms (n=7; WMD= 0.19 mm; 95% CI -0.04, 0.43; p=0.111, and n=6; WMD= 0.07 mm; 95% CI -0.15, 0.29; p=0.524, respectively). No differences among groups could be found for the change in the frequency distribution of this PD category.

#### Molar versus non-molar teeth

Only three studies compared the difference in treatment response between molar and non-molar teeth. In the study from Lindhe et al. (Lindhe et al., 1982), it was observed that in surgically treated sites, PD reduction was significantly greater (for initial pockets of ≥4 mm) in single-rooted than in multi-rooted teeth. However, in the subgingival debridement group, the PD reduction was similar in both types of teeth. CAL loss was seen in sites with initial PD <4 mm irrespectively of the type of tooth. Similarly, CAL gain was observed for sites with initial PD >6 mm, without differences between groups or between the type of tooth. In the study from Philstrom et al. (Pihlstrom et al., 1984) it was observed that for initial pockets of 4-6 mm, molars showed greater PD and CAL irrespectively of the assigned treatment; and that for initial pockets >7 mm, AF resulted in less PD on non-molars than on molars, without significant differences for CALs, neither for tooth type nor for the method of therapy.

Additionally, one study reported the results differentiating four tooth and site groupings: interproximal sites of single rooted teeth, facial and lingual sites of single rooted teeth, non-furcation sites of molar teeth and furcation sites of molar teeth (Kaldahl, Kalkwarf, Patil, & Molvar, 1990). While no differences were observed for PD reductions or CAL gains in shallow sites, PD reduction and CAL gain were greater in single rooted teeth at moderately deep and initial deep pockets.

PD reduction and CAL change (PICO 2: different access flaps)

Three studies compared the MWF to the Open Flap Debridement. No meta-analyses were performed for PD or CAL changes due to the heterogeneity found for these outcomes (mean changes, changes in proportions, data expressed as figures, sub-grouping by initial PD, etc.). While two of these studies did not find any significant difference among both flap procedures (Lindhe & Nyman, 1985; Svoboda, Reeve, & Sheridan, 1984), one study reported better results for conventional MWF in terms of PD reduction and CAL gain (Reddy et al., 2014). Additionally, one study compared the MWF using conventional blades to the MWF using a micro-dissection needle or an electro-cautery tip (Chandra, Savitharani, & Reddy, 2016) and another investigation compared the MWF using conventional instruments to the use of microsurgical instruments (Perumal, Ramegowda, Lingaraju, & Raja, 2015). In both studies there was significant PD reduction and CAL gain without significant differences among interventions. Finally, one study compared the use of the single-flap approach to the double-flap approach in the surgical treatment of intra-bony defects with significant better results in terms of PD reduction and CAL gain for the single-flap approach (Trombelli et al., 2012).

### **Secondary outcomes**

Changes in gingival or bleeding indices and in plaque indices (Supplementary Table 3)

Bleeding on probing was assessed in 10 investigations (Isidor & Karring, 1986; Kaldahl et al., 1996; Kalkwarf, Kaldahl, Patil, & Molvar, 1989; Lindhe & Nyman, 1985; Perumal et al., 2015; Renvert, Garrett, Nilvéus, Chamberlain, & Egelberg, 1985; Renvert et al., 1990; Ribeiro et al., 2011; Serino et al., 2001; Trombelli et al., 2012; Wennström et al., 1986; Westfelt et al., 1985). Due to the high heterogeneity of studies analyzing this outcome (PICO 1, PICO 2, studies focused exclusively on the treatment of intra-bony defects, etc.) no meta-analysis was performed. In general, both treatment groups showed similar and significant BOP reductions that slightly worsened with time in long-term studies. In one study the reduction of BOP was only significant in test group (Trombelli et al., 2012).

The gingival index was used to assess inflammation in 8 investigations either as the Löe and Silness index (Becker et al., 2001; Becker et al., 1988; Isidor & Karring, 1986; Lindhe & Nyman, 1985; Lindhe

et al., 1982; Reddy et al., 2014; Svoboda et al., 1984), the papillary bleeding index from Saxer et al. (Polansky et al., 2003) or as the gingival index from Lobene (Chandra et al., 2016). In summary, both treatment groups showed a significant reduction in mean inflammation scores and an increase in the percentage of sites without inflammation (score=0) with no differences among groups.

Plaque indices were assessed in 13 out of the 18 included investigations, either as the plaque index from Silness & Loe (Becker et al., 2001; Chandra et al., 2016; Isidor & Karring, 1986; Lindhe & Nyman, 1985; Lindhe et al., 1982; Reddy et al., 2014; Svoboda et al., 1984) or as the percentage of surfaces harbouring plaque (Kaldahl et al., 1996; Renvert et al., 1990; Ribeiro et al., 2011; Serino et al., 2001; Wennström et al., 1986; Westfelt et al., 1985). In general, both treatment groups showed a significant reduction in mean plaque scores and an increase in the percentage of sites without plaque (score=0) with no differences among groups.

#### Tooth loss

Tooth loss was reported in 7 investigations (Isidor & Karring, 1986; Kaldahl et al., 1990; Pihlstrom et al., 1984; Ramfjord et al., 1987; Renvert et al., 1990; Serino et al., 2001; Wennström et al., 1986), with a range between 0 and 2.43% in periods from 60 to 156 months. Tooth loss was due to periodontal and non-periodontal related causes and the most frequent teeth extracted were molars.

Percentage of residual pockets (PD>3 mm or PD>4 mm with or without the assessment of BOP) or closed pockets (PD<3 mm or PD<4 mm with or without the assessment of BOP)

At the end of the therapy, none of the included studies in this systematic review evaluated the percentage of closed or open pockets using a composite outcome that included BOP in the equation together with PD. The percentage of residual sites with PD>3 mm after treatment varied from 17 to 49% in the access flap group, and 20 to 62% in the subgingival debridement group (Becker et al., 2001; Lindhe & Nyman, 1985; Lindhe et al., 1982; Serino et al., 2001; Wennström et al., 1986).

#### Harms, adverse effects and patient reported outcomes (PROMs)

Harms and adverse effects related to the technique were not reported in any of the studies. The most common complications reported during follow-up were the incidence of further attachment loss and the need for re-treatment. The weighted mean incidence of sites exhibiting attachment loss  $\geq 2$  mm or  $\geq 3$  mm by intervention group and by initial PD is depicted in Table 5. Due to the high heterogeneity found when reporting this outcome, no meta-analyses could be done to compare the risk for future attachment loss between both interventions. Just four studies reported the percentage of patients or

teeth in need for re-treatment during the study follow-up, with values between 0% and 14% in the access flap group, and from 8% to 29% in the subgingival debridement group (Kaldahl, Kalkwarf, Patil, Dyer, & Bates Jr, 1988; Pihlstrom et al., 1984; Ramfjord et al., 1987; Serino et al., 2001).

Finally, PROMs were reported in four investigations. One study used a questionnaire to rate seven domains (Kaldahl et al., 1996), two studies used the visual analogue scale to rate pain (Chandra et al., 2016; Perumal et al., 2015) and one study evaluated the percentage of cases with hypersensitivity (Reddy et al., 2014). In general, no differences could be observed between groups.

## **Discussion**

The results of this systematic review, based on 36 publications reporting data from 18 investigations, indicate a high variability in terms of treatment protocols and on how the outcomes were reported, so the results should be interpreted with caution. This systematic review focused on the clinical performance of subgingival debridement and AF and on the comparison of different surgical approaches for flap debridement in the treatment of periodontitis. The primary outcome was PD reduction. The results of the meta-analysis showed that for all pockets greater PD reduction is expected when doing an AF. In particular, AF has shown to offer consistent benefits over subgingival debridement in deep pockets on the short- and long-term. Due to lack of studies it was impossible to draw definitive conclusions for the comparative efficacy of different surgical approaches.

Both treatments resulted in PD reduction in shallow sites with limited clinical relevance. Despite the fact that PD reduction was greater in sites treated with AF, both therapies resulted in CAL loss at the short- and long-term (0.2-0.8 mm). Nevertheless, subgingival debridement might have an advantage, since treatment can be limited to moderately deep and initial deep pockets, whereas surgery needs to include in many situations shallow sites adjacent to pockets (PD $\geq$ 4 mm). These findings confirmed those of a previous systematic review on the same topic (Heitz-Mayfield, Trombelli, Heitz, Needleman, & Moles, 2002).

In moderately deep pockets both treatment modalities showed significant PD reduction that was greater for AF in the short-term. However, these differences disappeared and both procedures were comparable in terms of PD reduction after one year. CAL gain was only significant in the subgingival debridement at the short-term and the differences between groups, although limited, were statistically significant at short- and long-term. The subgingival debridement group showed a decrease in CAL gain without major changes in PD in the long-term, indicating that with time gingival

recession increased. Based on these results, non-surgical periodontal therapy may be considered the ideal treatment option to restore periodontal health in patients affected by moderately deep pockets only (Badersten, Nilvéus, & Egelberg, 1981).

In deep pockets greater PD reduction was achieved by means of access therapy on the short- and long-term. However, this difference was progressively reduced over time and the added effect of access therapy was <0.5 mm in the long-term. Moreover, no differences were found in terms of CAL change between the procedures neither at short- nor long-term. We might consider that these results may be attributable to a greater gingival recession in the sites treated by means of AF. Recession in fact contributes to PD reduction and allows direct access to root surfaces during oral hygiene procedures. This could be beneficial to maintain periodontal stability over time due to improved plaque control. However, in order to draw robust conclusions, data regarding residual PD rather than PD reduction would have been desirable. Furthermore, a study reporting for plaque accumulation after different treatments did not observe statistically significant differences between AF and SRP (Kaldahl, Kalkwarf, Patil, & Molvar, 1990).

The main objective of periodontal treatment is to control inflammation and thereby arrest attachment and tooth loss. This is achieved in part by reducing the severity and the number of pockets, creating an accessible environment for oral hygiene. These goals should be maintained over time to warrant periodontal stability (Pini Prato, Di Gianfilippo, & Wang, 2019). Interestingly, AF was more successful increasing the number of shallow sites (11.6%). However, it is unclear if this might translate into a better stability in the long-term, since both treatments resulted in a consistent percentage of sites exhibiting further CAL loss. Even though AF was better at increasing the percentage of shallow sites compared to subgingival debridement, this might not have been enough to avoid disease progression at patient level. Unfortunately, we could not compare both treatments approaches since standard deviations were not provided in most of the studies reporting on attachment loss. Furthermore, both treatments were associated to a comparatively low frequency of tooth loss (0-2.5%) in respect to people who discontinued periodontal treatment (Becker, Berg, & Becker 1979; Harrel & Nunn, 2001).

Ideally a better outcome for periodontal treatment would be “pocket closure”, a composite variable including PD and BOP, since residual PD and BOP have been consistently associated to an increased odds for tooth loss and disease progression at site- and patient-level (Claffey & Egelberg, 1995; Matuliene et al., 2008a, 2008b). However, none of the included studies reported the changes in terms

of “open/closed pockets”, which prevented us to select it as primary outcome. Additionally, we were not able to compare the frequency of residual pockets due to inconsistencies found on how this outcome was reported.

Only two studies (Lindhe et al., 1982; Pihlstrom et al., 1984) compared the efficacy of subgingival debridement and AFs between molars and non-molars. In general, a better performance on single-rooted teeth was observed for both treatments. This difference may be explained by accessibility and anatomical factors, such as the increased bucco-lingual dimension, the presence of anatomical abnormalities, and the position in the arch, which could impair the efficacy of subgingival debridement, especially when deep pockets are present (Caffesse, Sweeney, & Smith, 1986b; Rateitschak-Pluss, Schwarz, Guggenheim, Duggelin, & Rateitschak, 1992; Waerhaug, 1978). In this context it is also important to remark that the most frequent lost teeth were molars.

We found a limited number of studies comparing different AFs for the treatment of periodontitis and thus, no definitive conclusions can be drawn regarding a higher efficacy of any particular technique. It seems that traditional techniques such as MWF and OFD are equivalent. We also tried to evaluate if there was an impact of minimally invasive approaches in comparison to traditional approaches in the surgical treatment of periodontitis. However, this has only been demonstrated in intrabony defects, where minimally invasive techniques performed better than conventional procedures, suggesting that surgical procedures aiming at primary flap closure may protect the surgical area and the blood clot in the early healing phases (Graziani et al., 2012). Moreover, when the analysis was limited to intrabony defects, we found greater PD reduction in sites receiving access flap, although without differences in terms of CAL gain in the long term. The fact that these differences were maintained on the long term suggests that AF may be superior to subgingival debridement in the treatment of intrabony defects. When different surgical approaches were compared, the Single Flap Approach (SFA) performed better than the Double Flap Approach (DFA) in terms of PD reduction and CAL gain (Trombelli et al., 2012).

It is important to remark that in most of the studies, subgingival debridement was performed as part of the initial therapy and repeated in the assigned quadrant after randomization. Re-treatment of residual pockets after initial phase by means of subgingival debridement may result in further PD reduction, although with a smaller effect than after the first instrumentation (Tomasi, Koutouzis, & Wennstrom, 2008). Performing subgingival debridement as part of the initial non-surgical cause-related therapy could have affected the results by reducing the additional benefit of the surgical

procedures. Anyway, it should be considered that this approach simulates better the situation of the patients treated in the daily practice, in which re-instrumentation of residual pockets is a critical component of supportive periodontal therapy.

Similarly, it must be underlined that in the present review only a limited number of studies performed subgingival debridement with magnification. Nowadays loupes and operative microscope are commonly used in high standard dental practice and may enhance the effect of subgingival debridement, overcoming its limitations in terms of accessibility and precision. In fact, it has been demonstrated that subgingival debridement under magnification has excellent clinical performance (Ribeiro et al., 2011; Nibali, Pometti, Chen, & Tu, 2015).

The available evidence suggests that the effects of non-surgical therapy are expressed over an extended period of time and that traditional re-evaluation at 3 months may mask the real potential of non-surgical treatment. In this sense, the healing potential of subgingival debridement has shown to last more than 9 months, depending on the maintenance protocol and patient compliance (Badersten, Nilveus, & Egelberg, 1984). All the studies included in this systematic review followed a strict maintenance protocol, which varied from intervals between every 2 weeks to every 6 months, including or not subgingival instrumentation. This may explain the positive results found in the studies included, and the tendency to present similar results irrespectively of treatment modality (Axelsson & Lindhe, 1981; Lindhe, Westfelt, Nyman, Socransky, & Haffajee, 1984). Nevertheless, we must emphasize that the maintenance protocols used in many of the included studies might be difficult to extrapolate to the daily clinical practice.

In the present review, caution is required before interpreting the principal findings due to the high heterogeneity between studies, mainly concerning the strategy of initial therapy, patient selection, teeth included in the analysis, the modalities and frequency of supportive periodontal treatment and the length of follow-up. Furthermore, most studies are out-dated and had a high risk of bias. One of the limitations of this review derives from the different treatment strategies, with some studies performing non-surgical subgingival debridement as part of the initial phase and others moving directly to surgery in the patients or quadrants assigned. No superiority of any strategy could be concluded, as long as subgroup meta-analysis was not possible due to lack of data. This may hamper the recommendations made on the basis of this review regarding the most appropriate timing for access flaps. Another important limitation is that in order to be more inclusive in the sub-group analysis, we combined studies using different initial PD categories. The shallow pockets from the

“Nebraska studies” (1-4 mm) (Kaldahl et al., 1988; Kaldahl et al., 1996) were pooled together with the 1-3 mm pockets of other included studies. Similarly, the deep pockets from Serino et al. ( $\geq 6$  mm) (Serino et al., 2001) were pooled together with the results for the  $\geq 7$  mm pockets of other investigations. This could have influenced the real effect of treatment, even though no significant heterogeneity was observed in most of the meta-analysis. Moreover, the inclusion of studies with at least 10 patients per treatment group in order to report more robust results forced us to exclude three studies, which although very unlikely, could have influenced the results. However, the effort of pooling together studies with similar characteristics, allow us to describe the clinical performance of different modalities of periodontal treatment in different clinical conditions. This enlightens the fact that periodontal therapy should be tailored and personalized to accomplish patient-centered treatment needs focused on specific clinical conditions.

Within the limitations of the present systematic review (including the high risk of bias of the included studies) it can be concluded that:

- AF achieved larger PD reduction when compared to subgingival debridement in initially deep pockets ( $>6$  mm or  $\geq 6$  mm). In this pocket category, no differences were detected between treatment groups for CAL gain.
- In moderately deep pockets (4-6 mm, 5-6 mm or 4-5 mm), AF achieved greater PD reduction in the short term. However, subgingival debridement resulted in higher CAL gain.
- In shallow pockets (1-3 mm or 1-4 mm), AF resulted in significantly greater clinical attachment loss.
- None of the included studies reported outcomes in terms of a composite variable including PD and BOP. Just a few studies reported the percentage of residual pockets after therapy, not allowing comparing subgingival debridement and AFs for this outcome variable. Future studies should overcome this deficiency.
- Regarding the comparison of different AFs, no clear conclusions can be made due to the limited studies available.

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## Figure Legends

**Figure 1:** Flow chart depicting the article selection process.

**Figure 2:** Short term ( $\leq 12$  months) changes in probing depth (PD) and clinical attachment level (CAL) by initial PD.

**Figure 3:** Long term ( $> 12$  months) changes in probing depth (PD) and clinical attachment level (CAL) by initial PD.

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**Table 1.** Methodological characteristics of the included studies

Authors/Year	Study Design & PICO question	Number of patients baseline (final) Age range (mean)	Longer follow-up reported (in parenthesis, previous follow-ups reported)	Intervention	Other interventions not included in this SR	Outcomes	Setting, location, and funding	Comments (Teeth included in the study, data subgrouping by PD or CAL, other study characteristics)
Lindhe et al. (1982a,b; 1984)	RCT Split mouth PICO 1	15 (11) 32-57 (47.9) years	60 months (24 months)	<i>Initial therapy:</i> OHI <i>Test:</i> MWF <i>Control:</i> SRP  <i>Maintenance protocol:</i> OHI with supra and subgingival debridement every 2 weeks the first 6 months, every 3 months from 6 to 24 months. 4-6 months supragingival cleaning from 24 to 60 months	None	PI GI Δ PD Δ CAL	University, Sweden, supported by governmental research funding	All teeth included <i>PD subgrouping:</i> Initial PD 1-3mm Initial PD 4-6mm Initial PD >6 mm non-molars molars 5-years data: frequency distributions of Δ CAL in patients with plaque score ≤10% and ≥50%
Pihlstrom et al. (1981, 1983, 1984)	RCT Split mouth PICO 1	17 (10) 22-59 (43) years	78 months (48 months)	<i>Initial therapy:</i> OHI+SRP <i>Test:</i> MWF <i>Control:</i> no further therapy <i>Maintenance protocol:</i> OHI with supra- and subgingival instrumentation every 3-4 months	None	PI CI GI Δ PD Δ CAL	University, USA, funding not reported	All teeth included <i>PD subgrouping:</i> Initial PD 1-3mm Initial PD 4-6mm Initial PD >6mm
Svoboda et al. (1984)	RCT Split-mouth PICO 2	12 (12) 34-60 (44) years	6 months	<i>Initial Therapy:</i> OHI + SRP + OA (when needed) <i>Test:</i> OFD <i>Control:</i> MWF <i>Maintenance protocol:</i> Not specified	None	PI GI Δ PD Δ CAL Δ REC Mobility Rx BL	University, USA, funding not reported	Only anterior teeth included (canine-canine) All type of defects treated without distinction between horizontal or vertical defects
Lindhe & Nyman (1985)	RCT Split mouth	15 (15) 42-59 (50) years	12 months	<i>Initial therapy:</i> OHI <i>Test 1:</i> MWF	None	PI GI	University, Sweden,	All teeth included <i>PD subgrouping:</i>

	PICOs 1 & 2			<i>Test 2:</i> OFD <i>Control:</i> SRP <i>Maintenance protocol:</i> prophylaxis every 2 weeks the first 3 months, and every 3 months from 3 to 12 months follow-up		BoP Δ PD Δ CAL Microbial analysis	supported by governmental research funding	Initial PD 1-3mm Initial PD 4-6mm Initial PD >6mm All type of defects treated without distinction between horizontal or vertical defects
Westfelt et al. (1985)	RCT Split mouth PICO 1	16 (16) 35-65 years	6 months	<i>Initial therapy:</i> OHI <i>Test:</i> MWF <i>Control:</i> SRP <i>Maintenance protocol:</i> prophylaxis every 2 weeks	<i>Test 2:</i> Gingivectomy <i>Test 3:</i> AF <i>Test 4:</i> AF with bone recontouring <i>Test 5:</i> MWF with bone recontouring	PI BoP Δ PD Δ CAL	University, Sweden, supported by governmental research funding	All teeth included <i>PD subgrouping:</i> Initial PD 1-3mm Initial PD 4-6mm Initial PD >6 mm
Isidor et al. (1984, 1985) Isidor & Karring (1986)	RCT Split mouth PICO 1	17 (16) 28-52 (40) years	60 months (6 and 12 months)	<i>Initial therapy:</i> OHI+SRP (without LA) <i>Test:</i> MWF <i>Control:</i> SRP (with LA) <i>Maintenance protocol:</i> prophylaxis every 2 weeks	<i>Test 2:</i> Reverse bevel flap	PI GI BoP Δ PD Δ CAL REC Rx BL	University, Denmark, funding not reported	Only non-molar teeth included Angular bony defects separately reported (Isidor et al. 1985)
Wennström et al. (1986)	RCT Split mouth PICO 1	16 (16) 14-29 (19.7) years	60 months	<i>Initial Therapy:</i> OHI <i>Test:</i> MWF <i>Control:</i> SRP (twice in 3 weeks) <i>Maintenance protocol:</i> Professional tooth cleaning every 4 weeks for 6 months. Later, professional tooth cleaning every 3 months for 2 years. During the last 3 years the patients were seen only by their regular dentists	None	PI GI BoP Δ PD Δ CAL Δ REC RxBL Microbial analysis	University, Sweden, supported by governmental research funding	All teeth included Juvenile and post-juvenile periodontitis. Focus on intrabony defects (PD≥5mm + presence of intrabony defects on radiographs)

Renvert et al. (1985, 1990a,b)	RCT Split mouth PICO 1	14 (12) 32-67 (NR) years	60 months (6 months)	<i>Initial Therapy:</i> OHI + SRP <i>Test:</i> OFD <i>Control:</i> SRP <i>Maintenance protocol:</i> After 6 weeks, polishing was performed. From 6 weeks up to 6 months, patients were seen every 6 weeks for tooth cleaning. From 6 to 60 months, tooth cleaning was performed every 6 months	None	PI BoP Δ PD Δ CAL Probing bone level	University, not specified, funding not reported	All teeth included Focus on intrabony defects (2 separate proximal sites with radiographic intrabony lesions + PD≥6 mm)
Hill et al. (1981) Ramfjord et al. (1987) Burgett et al. (1992)	RCT Split mouth PICO 1	90 (72) 24 - 68 (45) years	60 months (24 months)	<i>Initial therapy:</i> OHI+SRP+OA (OA only when needed) <i>Test:</i> MWF <i>Control:</i> SRP <i>Maintenance protocol:</i> polishing every week for 3-4 weeks, and prophylaxis with re-SRP (when needed) every 3 months	<i>Test 2:</i> Surgical pocket elimination <i>Test 3:</i> Subgingival curettage	PI CI GI Mobility Δ PD Δ CAL Tooth loss	University, USA, supported by governmental research funding	All teeth included <i>PD subgrouping:</i> Initial PD 1-3mm Initial PD 4-6mm Initial PD >6 mm
Kaldahl et al. (1988, 1990a, 1990b, 1990c) Kalkwarf et al. 1989 Kalkwarf (1992) Kaldahl (1996a, 1996b)	RCT Split mouth PICO 1	82 (51) NR (43.5) years	84 months (24 and 36 months)	<i>Initial therapy:</i> OHI+CS (1 quadrant) +SRP (3 quadrants) <i>Test:</i> MWF <i>Control:</i> SRP (no further treatment after initial therapy) <i>Maintenance protocol:</i> OHI+ supra- and subgingival debridement (when needed)	<i>Test 2:</i> OS <i>Control 2:</i> CS	PI BoP Sup Δ PD Δ CAL REC PROMS	University, USA, supported by governmental research funding	All teeth included CS group follow-up discontinued at 2 years: teeth in CS group that showed ≥3mm CALoss from baseline during maintenance, were scaled and root planed and incorporated in SRP group <i>PD subgrouping:</i> Initial PD 1-4mm Initial PD 5-6mm Initial PD >6 mm
Becker et al. (1988, 2001)	RCT Split mouth PICO 1	16 (16) 30-57 (42) years	60 months (12 months)	<i>Initial therapy:</i> OHI+SRP (without LA) + OA <i>Test:</i> MWF	<i>Test 2:</i> OS	PI GI Δ PD	Private practice, USA, funding	Only posterior teeth included (premolars and molars) <i>PD subgrouping:</i>

				<i>Control:</i> SRP (with LA) <i>Maintenance protocol:</i> prophylaxis weekly for 6 weeks, and SRP and polishing every 3 months		Δ CAL REC Mobility Furcation lesions Tooth loss	not reported	Initial PD 1-3mm Initial PD 4-6mm Initial PD >6 mm
Serino et al. (2001)	RCT Parallel PICO 1	64 (45) NR	156 months	<i>Initial Therapy:</i> OHI <i>Test:</i> MWF <i>Control:</i> SRP <i>Maintenance protocol:</i> OHI and supra- and subgingival debridement every 3-4 months	None	PI BoP Δ PD Δ PAL Rx BL Tooth loss	University, Sweden, supported by governmental research funding and by company	Only non-molar teeth included <i>PD subgrouping:</i> Initial PD 1-3 mm Initial PD 4-5 mm Initial PD >5 mm
Polansky et al. (2003)	RCT Split-mouth PICO 1	29 (29) 38-75 (54.6) years	12 months	<i>Initial Therapy:</i> OHI + supragingival scaling <i>Test:</i> MWF <i>Control:</i> SRP <i>Maintenance protocol:</i> supra- and subgingival (when needed) debridement every 3 months	Control 2: no further treatment after initial therapy (CS)	PI PBI Δ PD Δ CAL Mobility	University, Austria, funding not reported	Canines and premolars receiving telescopic crowns
Ribeiro et al. (2011)	RCT Parallel PICO 1	29 (27) 35-57 (45.43) years	6 months	<i>Initial Therapy:</i> OHI + SRP <i>Test:</i> MIST <i>Control:</i> SRP with microscope and micro instruments <i>Maintenance protocol:</i> supragingival prophylaxis every 15 days for the first month and monthly for 6 months	None	PI BoP Δ PD Δ CAL Δ REC PROMS Chair-time	University, Brazil, supported by governmental research funding and by foundation	Only single-rooted teeth included Focus on intrabony defects [≥1 single-rooted tooth with PD≥5 mm + BoP, CAL≥5 mm and radiographic evidence of an intrabony defect (depth ≥4 mm and width≥2 mm)]
Trombelli et al. (2012)	RCT Parallel PICO 2	28 (28) 36-62 (49) years	6 months	<i>Initial Therapy:</i> OHI + SRP <i>Test:</i> Single Flap Approach <i>Control:</i> Double Flap Approach	None	BoP Δ PD Δ CAL	University, Italy, supported by	All teeth included Focus on intrabony defects (presence of ≥1 site with PD≥6

				Maintenance protocol: OHI + Supragingival plaque removal every month for 3 months, and at intervals according to personal needs thereafter		Δ REC	governmental research funding	mm and radiographic depth ≥3 mm)
Reddy et al. (2014)	RCT Split mouth PICO 2	13 (13) 22-60 (NR) years	6 months	Initial Therapy: OHI + SRP Test: OFD Control: MWF Maintenance protocol: Not specified	None	GI PI PD CAL REC GCI Mobility Furcation lesions DH	University, India, self-supported	Only posterior teeth included (premolars and molars) All type of defects treated with distinction between horizontal and vertical defects
Perumal et al. 2015	RCT Split-mouth PICO 2	13 (13) 30-50 (NR) years	9 months	Initial Therapy: OHI + SRP Test: MWF (microsurgical approach) Control: MWF (conventional approach) Maintenance protocol: Not specified	None	GI PD RAL REC EHI Pain	University, India, self-supported	All teeth included All type of defects treated without distinction between horizontal or vertical defects
Chandra et al. (2016)	RCT Split mouth PICO 2	22 (19) 25-45 (34.8) years	6 months	Initial Therapy: OHI + SRP + SPT Test 1: MWF with Microdissection needle Test 2: MWF with electrocautery tip Control: MWF with conventional scalpel Maintenance protocol: not specified	None	PI GI PD CAL PH EHI Blood loss Pain	University, India, self-supported	All teeth included All type of defects treated without distinction between horizontal or vertical defects

SR: systematic review; PD: probing depth; CAL: clinical attachment level; RCT: randomized controlled trial; OHI: oral hygiene instructions; MWF: modified Widman flap; SRP: scaling and root planing; PI: plaque index; GI: gingival index; CI: calculus index; OA: occlusal adjustment; OFD: open flap debridement; REC: recession; Rx BL: radiographic bone level; BoP: bleeding on probing; AF: access flap; LA: local anesthesia; NR: not reported; CS: coronal scaling; OS: osseous surgery; Sup: suppuration; PROMS: patient reported outcome measures; CAL Loss: clinical attachment loss; MIST: minimally invasive surgical technique; GCI: gingival contour index; DH: dentinal hypersensitivity; RAL: relative attachment level (measured from a stent to the bottom of the pocket); EHI: early healing index; SPT: supportive periodontal therapy; PH papilla height

**Table 2.** Cochrane tool for the qualitative assessment of randomized clinical trials

Authors/Year	Randomization Process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Ramfjord et al. (1975)	?	?	-	-	?	-
Lindhe et al. (1982a)	?	?	+	-	?	-
Lindhe et al. (1982b)	?	?	+	-	?	-
Lindhe et al. (1984)	?	?	+	-	?	-
Pihlstrom et al. (1981)	?	+	+	-	?	-
Pihlstrom et al. (1983)	?	+	+	-	?	-
Pihlstrom et al. (1984)	?	+	+	+	?	?
Svodoba et al. (1984)	?	?	-	-	?	-
Lindhe & Nyman (1985)	?	?	-	-	?	-
Westfelt et al. (1985)	?	?	-	-	?	-
Isidor et al. (1984)	?	?	-	-	?	-
Isidor et al. (1985)	?	?	+	-	?	-
Isidor & Karring (1986)	?	?	+	-	?	-
Wennstrom et al. (1986)	?	?	+	-	?	-
Renvert et al. (1985)	?	?	+	-	?	-
Renvert et al. (1990)	?	?	+	-	?	-
Hill et al. (1981)	?	?	-	-	?	-
Ramfjord et al. (1987)	?	?	-	-	?	-
Burgett et al. (1992)	?	?	+	-	?	-
Kaldahl et al. (1988)	?	+	+	+	?	?
Kalkwarf et al. (1989)	?	+	+	+	?	?
Kaldahl et al. (1990a)	?	+	+	+	?	?
Kaldahl et al. (1990b)	?	+	+	+	?	?
Kaldahl et al. (1990c)	?	+	+	+	?	?
Kalkwarf et al. (1992)	?	+	+	-	?	-
Kaldahl et al. (1996a)	?	+	+	+	?	?
Kaldahl et al. (1996b)	?	+	+	+	?	?
Becker et al. (1988)	?	?	+	-	?	-
Becker et al. (2001)	?	?	+	-	?	-
Serino et al. (2001)	?	?	+	-	?	-
Polansky et al. (2003)	?	?	-	-	?	-
Ribeiro et al. (2011)	+	+	+	+	+	+
Trombelli et al. (2012)	?	+	+	+	?	?
Reddy et al. (2014)	?	?	-	-	?	-
Perumal et al. (2015)	?	?	-	-	?	-
Chandra et al. (2016)	+	?	+	+	+	?

+: low risk of bias; -: high risk of bias; ? : some concerns.

**Table 3.** Summary of meta-analysis performed for probing depth (PD) and clinical attachment level (CAL) changes.

Initial PD category (mm)	Number of studies	WMD (mm or %)	95% CI		p-value for WMD	Heterogeneity		
						I <sup>2</sup> (%)	p value	Method
<b>Studies including all type of defects</b>								
<b>PD reduction (mean)</b>								
All	3	0.71	0.44	0.98	<0.001	63.6	0.064	IV
<b>Short term (≤ 12 months)</b>								
Shallow pockets	4	0.13	0.07	0.18	<0.001	34.2	0.207	IV
Moderate pockets	4	0.34	0.21	0.46	<0.001	40.5	0.169	IV
Deep pockets	4	0.67	0.37	0.97	<0.001	0	0.582	IV
<b>Long term (&gt;12 months)</b>								
Shallow pockets	4	-0.02	-0.09	0.05	0.648	0	0.739	IV
Moderate pockets	4	0.09	-0.01	0.18	0.063	0	0.897	IV
Deep pockets	4	0.39	0.09	0.70	0.012	41.4	0.163	IV
<b>CAL gain (mean)</b>								
All	3	-0.26	-0.39	-0.14	<0.001	36.4	0.208	IV
<b>Short term (≤ 12 months)</b>								
Shallow pockets	7*	-0.43	-0.56	-0.29	<0.001	55.6	0.036	DL
Moderate pockets	7*	-0.34	-0.46	-0.22	<0.001	6.6	0.378	IV
Deep pockets	7*	0.19	-0.04	0.43	0.111	0	0.664	IV
<b>Long term (&gt;12 months)</b>								
Shallow pockets	6	-0.27	-0.34	-0.20	<0.001	50.8	0.071	IV
Moderate pockets	6	-0.12	-0.22	-0.01	0.032	0	0.511	IV
Deep pockets	6	0.07	-0.15	0.29	0.524	0	0.983	IV

Proportions (long term)								
Change in % of shallow pockets	3*	11.60	6.76	16.5	<0.001	35.0	0.215	IV
Change in % of moderate pockets	3*	9.49	4.88	14.10	<0.001	0	0.472	IV
Change in % of deep pockets	3*	0.92	-1.27	3.11	0.413	33.6	0.222	IV
Studies including exclusively intra-bony defects								
PD reduction (mean)								
All pockets (short and long tem)	4	0.49	0.11	0.86	0.010	54.7	0.085	IV
CAL gain (mean)								
All pockets (short and long tem)	4	0.07	-0.29	0.44	0.691	0	0.405	IV

\* Lindhe et al. 1985 compared two different access flaps (Modified Widman Flap or Modified Kirkland Flap) versus subgingival debridement. WMD, weighted mean difference; CI, confidence interval; IV, inverse-variance weighted (fixed effect) model; DL, DerSimonian and Laird (random effect) model.

Positive values indicate a mean difference in favor of surgery.

**Table 4.** Weighted mean effect (WME) of scaling and root planing (SRP) and Access flaps according to the initial probing depth.

Initial PD category (mm)	Number of studies	WME (mm)				p value	Heterogeneity	
		IV	DL	95% CI			I <sup>2</sup>	p value
Studies including all type of defects								
PD Reduction								
Access Flap								
All (short and long tem)	3	-	1.70	0.89	2.52	<0.001	95.1	<0.001
SRP								
All (short and long tem)	3	-	1.04	0.55	1.5	<0.001	84.5	0.002
Short term (≤ 12 months)								
Access Flap								
Shallow pockets	4	-	0.26	0.10	0.43	<0.001	96.3	<0.001
Moderate pockets	4	1.53	-	1.44	1.62	<0.001	21.4	0.282
Deep pockets	4	2.94	-	2.76	3.13	<0.001	26.1	0.255
SRP								
Shallow pockets	4	-	0.13	-0.01	0.27	0.158	90.8	<0.001
Moderate pockets	4	-	1.08	0.81	1.35	<0.001	88.7	<0.001
Deep pockets	4	-	2.13	1.57	2.70	<0.001	79.2	<0.001
Long term (>12 months)								
Access Flap								
Shallow pockets	4	-	-0.03	-0.38	0.32	0.163	97.5	<0.001
Moderate pockets	4	-	1.23	0.85	1.62	<0.001	94.8	<0.001
Deep pockets	4	-	2.77	2.34	3.20	<0.001	73.1	<0.001
SRP								
Shallow pockets	4	-	0.01	-0.30	0.32	0.258	97.2	<0.001
Moderate pockets	4	-	1.15	0.82	1.47	<0.001	94.2	<0.001

Deep pockets	4	-	2.07	1.18	2.96	<0.001	92.7	<0.001
CAL gain								
Access Flap								
All (short and long tem)	3	-	-0.1	-0.32	0.12	0.460	71.4	0.030
SRP								
All (short and long tem)	3	0.14	-	0.04	0.24	<0.001	37.1	0.204
Short term ( $\leq 12$ months)								
Access Flap								
Shallow pockets	7	-	-0.64	-0.90	-0.38	<0.001	93.9	<0.001
Moderate pockets	7	-	0.22	-0.12	0.57	0.206	92.7	<0.001
Deep pockets	7	-	1.31	0.90	1.71	<0.001	85.7	<0.001
SRP								
Shallow pockets	6	-	-0.16	-0.38	0.06	0.396	91.6	<0.001
Moderate pockets	6	-	0.53	0.22	0.83	<0.001	91.9	<0.001
Deep pockets	6	-	1.16	0.67	1.65	<0.001	83.4	<0.001
Long Term (> 12 months)								
Access Flap								
Shallow pockets	6	-	-0.76	-1.07	-0.45	<0.001	96.6	<0.001
Moderate pockets	6	-	0.16	-0.23	0.55	0.663	94.8	<0.001
Deep pockets	6	-	1.25	0.81	1.70	<0.001	82.4	<0.001
SRP								
Shallow pockets	6	-	-0.43	-0.78	-0.08	<0.001	97.4	<0.001
Moderate pockets	6	-	0.36	-0.04	0.75	0.195	95.8	<0.001
Deep pockets	6	-	1.18	0.69	1.66	<0.001	84.2	<0.001
Studies including exclusively intrabony defects								
PD Reduction								
Access Flap								
All	4	3.20	-	2.75	3.65	<0.001	65.5	0.034

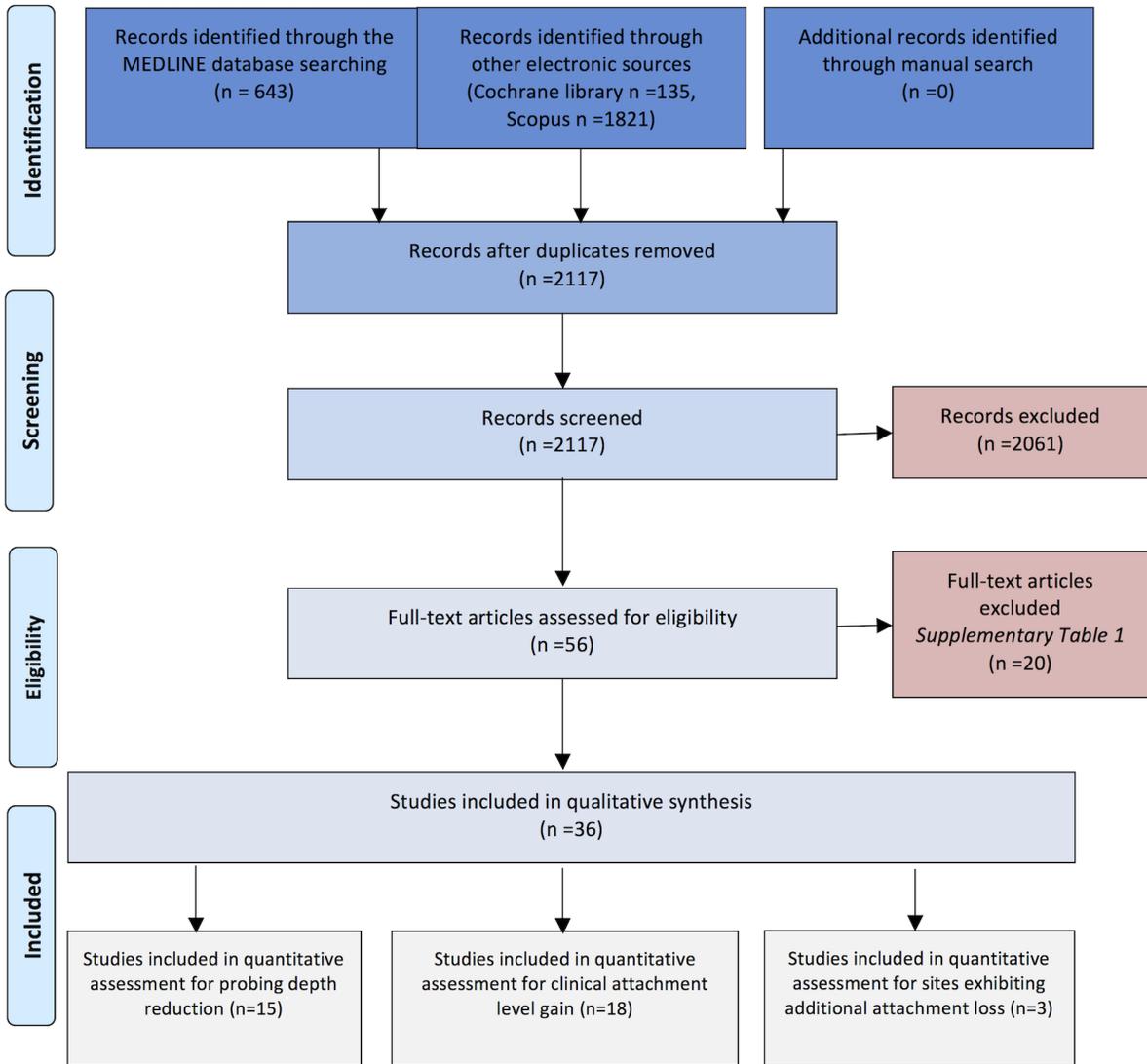
SRP									
All	4	2.75	-	1.88	3.61	<0.001	88.8	<0.001	
CAL gain									
Access Flap									
All	4	-	1.36	0.43	2.29	<0.001	92.3	<0.001	
SRP									
All	4	-	1.43	0.57	2.29	<0.001	73.8	<0.001	

PD, probing depth; IV, inverse-variance weighted (fixed effect) model; DL, DerSimonian and Laird (random effect) model; CI, confidence interval

**Table 5.** Meta-analysis performed for the percentage of sites exhibiting attachment loss (ALoss)  $\geq 2$  mm or  $\geq 3$  mm by intervention group and by initial probing depth (PD).

Initial PD category (mm)	Number of studies	WMI (%)				p value	Heterogeneity	
		IV	DL	95% CI			I <sup>2</sup>	p value
<b>AL <math>\geq 2</math> mm</b>								
<b>Access flap</b>								
Shallow pockets	2 <sup>a,b</sup>	-	25.4	5.6	45.2	0.012	98.2	<0.001
Moderate pockets	2 <sup>a,b</sup>	-	21.3	8.2	34.4	0.001	94.8	<0.001
Deep pockets	2 <sup>a,b</sup>	10.3	-	4.0	16.6	0.001	64.4	0.094
<b>SRP</b>								
Shallow pockets	2 <sup>a,b</sup>	-	19.6	0.0	40.6	0.066	99.0	<0.001
Moderate pockets	2 <sup>a,b</sup>	-	16.1	6.0	26.2	0.002	93.1	<0.001
Deep pockets	2 <sup>a,b</sup>	15.7	-	7.5	24.0	<0.001	0.0	0.574
<b>AL <math>\geq 3</math> mm</b>								
<b>Access flap</b>								
Shallow pockets	2 <sup>a,c</sup>	-	6.5	0.0	17.9	0.265	99.5	<0.001
Moderate pockets	2 <sup>a,c</sup>	-	6.0	0.0	14.6	0.169	98.1	<0.001
Deep pockets	2 <sup>a,c</sup>	2.1	-	1.6	2.6	<0.001	0.8	0.315
<b>SRP</b>								
Shallow pockets	2 <sup>a,c</sup>	-	4.9	0.0	13.3	0.255	99.3	<0.001
Moderate pockets	2 <sup>a,c</sup>		4.9	0.0	11.0	0.109	97.1	<0.001
Deep pockets	2 <sup>a,c</sup>	3.2	-	2.6	3.8	<0.001	0.0	0.535

WMI, Weighted mean incidence; IV, inverse-variance weighted (fixed effect) model; DL, DerSimonian and Laird (randome effect) model; CI, confidence interval  
<sup>a</sup>Ramfjord et al. (1987); <sup>b</sup> Becker et al. (2001); <sup>c</sup> Kaldahl et al. (1996)

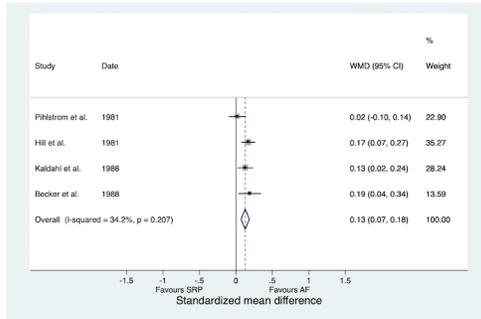


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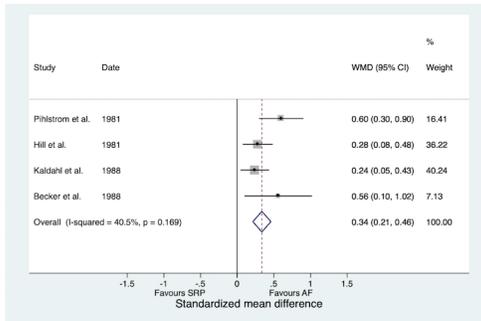
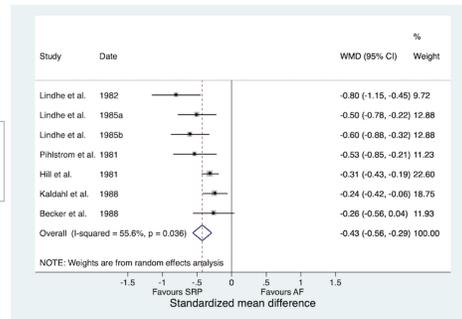
## Short term changes ( $\leq 12$ months) by initial PD

PD

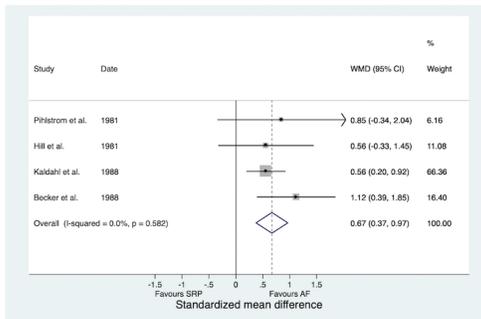
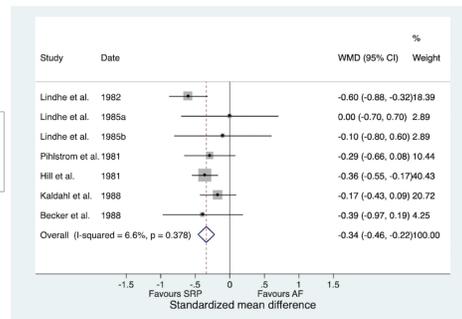
CAL



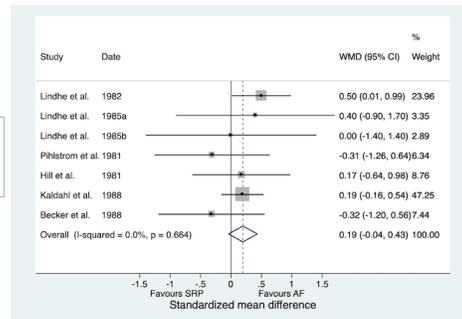
Shallow Pockets



Moderate Pockets



Deep Pockets

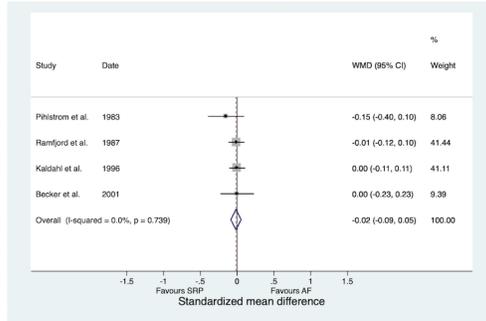


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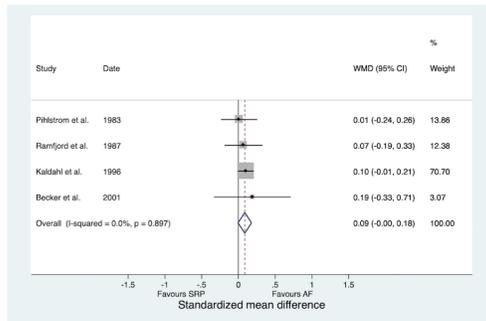
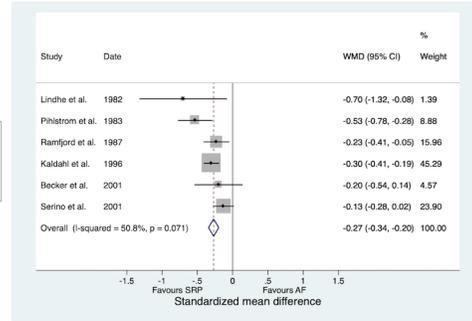
## Long term changes ( $\geq 12$ months) by initial PD

PD

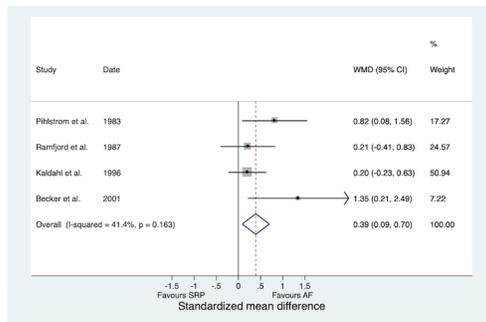
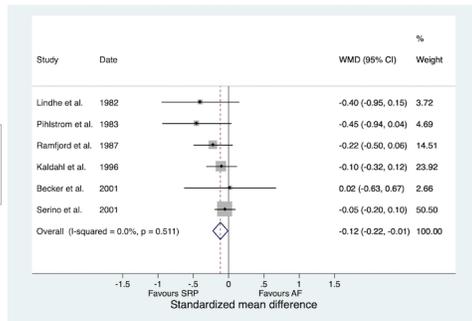
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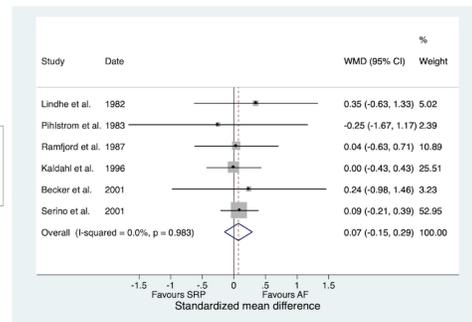
Shallow Pockets



Moderate Pockets



Deep Pockets



jcpe\_13259\_f3.tiff