

*Is PS better than NSPT with regards to reduction of PPD and CAL when the endpoints are observed over more than 1 year, provided that the patient maintains an adequate oral hygiene following therapy?*

Nisha Maharajasingam & Jovana Rosic

Supervisor: Professor Hans Ragnar Preus



Master Thesis Odontology

Faculty of Dentistry  
Section of Periodontology  
University of Oslo

May 2017

## **Introduction**

Periodontal disease is a common collective term that includes all destructive plaque-associated periodontal infections initiated by accumulation and maturation of the pathogenic microflora in the biofilm on teeth. (1,2) One of the most frequently occurring forms of periodontal diseases is chronic periodontitis, which is characterized by progressive destruction of the periodontal ligament and alveolar bone with periodontal pocket formation and/or recession of gingiva (3). The progression of this pathological, destructive process is most often associated with increased presence of subgingival biofilm and calculus (4), and the resulting destruction is generated by the immunological response to this bacterial biofilm (5). The treatment of this destructive process therefore aims at arresting the inflammatory process and to restore gingival health so that the immunologically motivated destructive process subsides (6). This is achieved by systematically and mechanically removing the pathogens (biofilm) that provoke the inflammatory process and contribute to the destruction of the periodontal membrane and alveolar bone (6). The reestablishment of a local microflora and environment compatible with periodontal health is therefore the goal for these efforts (6)

The most common form of periodontal treatment is non-surgical periodontal therapy (NSPT) (7). This implies the removal of gingival infection by diligently removing the accumulated calculus and biofilm from the root surfaces by mechanical scaling and root planing (8). These treatment modalities can be implemented by any dentist or hygienist, and complications associated with NSPT's are few. Most, if not all, studies have shown high success rates with NSPT in treatment of mild to moderate periodontitis (7,9).

However, in comparatively few cases, the periodontal destruction is not halted by these measures (10), and the reason for this is still an item for debate (9,10). The main reason for failing NSPT is insufficient removal of calculus and biofilm during the scaling and root planing

(11). This may be due to insufficient technique on part of the dentist or insufficient access to the subgingival compartments due to anatomy, or pockets so deep, that closed scaling and root planing is too technically challenging (9,11). It is also suggested that failing NSPT may be caused by persistent presence of specific microorganisms in the subgingival biofilm following such therapy, but this is not in the scope of the present review (9).

In those cases where treatment failure of NSPT is believed due to insufficient access to the subgingival compartments, periodontal surgery (PS) has been suggested as an alternative. PS comprises techniques where the mechanical debridement may be conducted under direct eyesight (12). These are techniques like gingivectomy, where the pockets are surgically excised (13) before mechanical debridement, or different forms of flap surgery where a periodontal flap is raised by various incision techniques (14). In both cases, it becomes possible to mechanically debride the root surfaces thoroughly under visual control and thereby achieve total debridement of the accessed areas.

Periodontal surgery is an invasive therapy, and brings with it possible complications like the risk of greater post-operative bleedings, infections, or pain (15), esthetically challenging anatomical results (6,14), considerations towards the patient's other diseases and/or medications (6,14) as well as psycho-somatic reactions (6,14). PS has also been criticized because the nature of the technique is a subjective measure on the operator's part, of when to perform such therapy, i.e. the dentist him/herself subjectively decides that NSPT will not be effective.

Many factors will influence the effect of any form of periodontal therapy. First of all, the patient's plaque control, prior to and following the intervention is of the essence (16). Indeed the post-operative self-performed oral hygiene is often compromised due to postsurgical anatomical changes like gingival recession and greatly increased interdental spaces – sometimes so large that regular hygiene remedies are ineffective (6). Another factor is the time after PS one

evaluate the result of therapy before it may be expected to wear off. One should expect that surgical therapy, with all its negative aspects, should at least last for 5 years following therapy. For this one needs proper, thoroughly controlled, long term intervention studies. Thus, the research community carries a special responsibility not to endorse surgical intervention in periodontal treatment, unless long-term evidence exists that such therapy considerably alters the course of disease to the better.

Many of the current studies are inconclusive in showing the value of the chosen treatment, and the amount of proper studies comparing NSPT and surgical interventions are poor due to short follow up, few patients, insufficiently described clinical interventions and notoriously not reporting the important oral hygiene prior to and following the intervention.

The purpose of this systematic review was to gather data from studies that have compared surgical and nonsurgical interventions in patients with chronic periodontitis in order to see if there is evidence that PS is a better choice of therapy than NSPT. Surgical intervention were defined as “flap surgery”, not limited to specific areas like furcations and not with the intent to regenerate bone using additives of any kind.

**Focused question:** Is PS better than NSPT with regards to reduction of PPD and CAL when the endpoints are observed over more than 1 year, provided that the patient maintains an adequate oral hygiene following therapy?

#### **Materials and methods**

An advanced search in the online libraries Medline (Ovid), PubMed and Cochrane Controlled Trials Register (Central CCTR) with the search terms “periodontal or periodontitis”, «dental scaling», “scaling and root planing”, “SRP” combined with “Periodontal surgery” and «surgical flaps» within the time frames 1975 – 2016 produced a total number of 244 articles.

To be eligible for inclusion in the present analysis we first applied the same criteria as had been used in other systematic reviews and meta-analysis on the specific question. These were:

1. Randomized controlled clinical trials (RCT) and based on patients diagnosed with chronic marginal periodontitis. Trials based on patients diagnosed with other diagnoses, like aggressive periodontitis, were excluded.
2. Changes in clinical attachment level (CAL) and the reduction in pocket depth (PD) from baseline to the end of the study was set as the main criteria for evaluating the treatment outcome.
3. The studies had to be performed on human beings.
4. Scaling and mechanical debridement had to be performed using manual instrumentation.
5. The outcome of the studies should compare the clinical outcome after surgical therapy compared to that of dental scaling (SRP).

After reading titles and abstracts from all the harvested 244 titles, 213 articles were discarded. These studies included those with surgical pocket elimination techniques like gingivectomy, use of fillers and regeneration procedures as well as surgery performed in furcation areas or selected bony pockets with the intent to regenerate bone, debridement solely focused on furcations or specific anatomical structures or single rooted teeth as well as studies including antibiotic therapy or studies performed on teeth that later were planned for extraction to evaluate outcome. All uncertainty regarding the eligibility for inclusion was discussed among the authors until agreement was reached. After this primary evaluation, 31 (8,17-48) articles and 4 systematic reviews (49-52) remained for further scrutiny, all of which described and compared scaling and root planing (SRP) with either the sole treatment of a surgical intervention, or with SRP combined with a surgical treatment. The 4 systematic reviews (49-52) had accepted articles from 5 Randomized Clinical Studies, all of which had been evaluated in the present study as well.

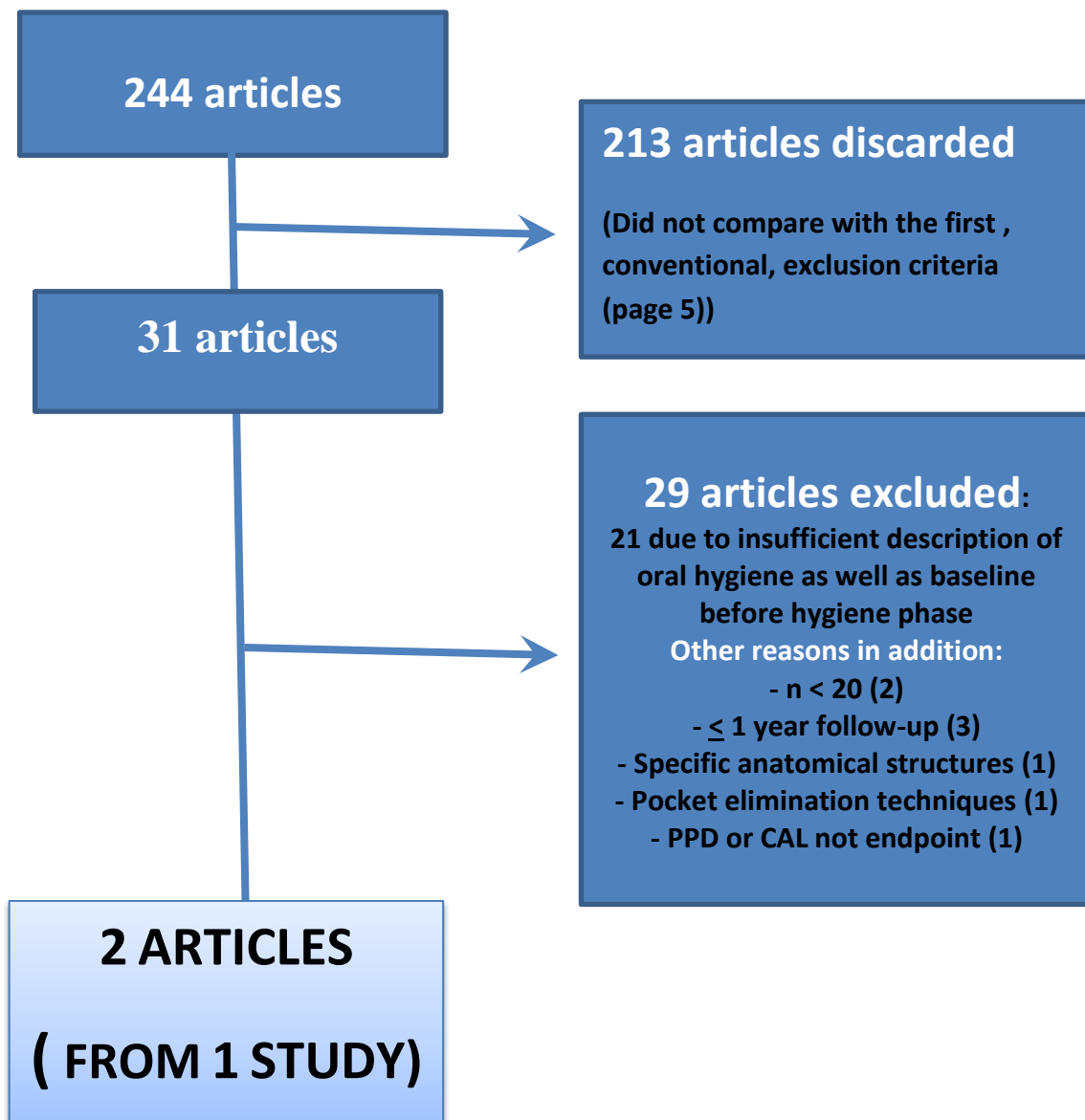
At this point a set of more stringent criteria was set for inclusion.

1. Studies with short observation time ( $\leq 1$  year) were eliminated since less than a year of follow up is too short time for evaluating treatment outcome of periodontal therapy. Even 1 year of follow-up seems too short for evaluation.
2. The number of participants in all groups – regardless number of comparison arms – had to be acceptable ( $n > 20$ ).
3. Further, studies without any description of an oral hygiene phase prior to therapy and no report of the PD or CAL following the hygiene phase/prior to therapy.

## **Exclusion process and results**

Twenty-one articles were excluded due to insufficient description of oral hygiene and/or reporting no PD or CAL measurements after the hygiene phase/prior to intervention which was the primary exclusion criterion (8,17-38). In addition, 8 articles were excluded; 1 study was based on single rooted teeth (39). 2 articles had  $n < 20$  (40,41), 1 article described the effect of gingivectomy as well as being of 1 year or less duration (42), 3 articles had 1 year or less follow up (43,44,45), 1 study had endpoints based on bleeding or suppuration (46). Among the first 21 articles to be excluded (due to sketchy description of the oral hygiene phase and not recording the PPD and CAL after this phase) also other reasons for exclusion were noted like having one year or less of follow-up, gingivectomy, or describing the effect of surgery on special teeth or anatomical structures. These were also obviously excluded, and should have been evaluated in the first round of exclusion, but escaped the readers' attention at that time.

One or more of these criteria resulted in exclusion of 29 articles, leaving this review to report on 2 articles (47,48), which were reports from 2 and 5 years from the same study.



## Discussion

Numerous studies have been conducted to reveal if PS is better than NSPT in the therapy of periodontal disease. Based on these numerous articles, several systematic reviews (49-52) have been published. In these reviews altogether articles from 5 intervention studies were included concluding that PT being the most effective in pockets with PPD  $\geq$  7mm, but that the effect wears off after 1 - 2 year. In shallower pockets, the PT and NSPT seemed to be equally effective. As stated above, these are all among the studies that have been evaluated in the present study..

Systematic reviews and meta-analyses are advanced scientific endeavors and require a large amount of time, effort and advanced statistics on the combined results of the included studies in order to answer the focused question. The focused question of the different systematic reviews (49-52) can be summarized as “Is periodontal surgery (PS) better than non-surgical periodontal therapy with regards to reduction of PPD and CAL?” The systematic reviews (49-52) concluded that only very few studies have the quality and design needed and therefore the large picture is that only few intervention studies over the years deserves to be analyses in a systematic review. However, in their effort and very advanced analyses and statistics the authors of all these systematic reviews (49-52) and meta-analyses have all bypassed the most important factor in periodontal therapy, *the hygiene phase*. Therefore, the focused question of the present study has added two important features; “Is periodontal surgery (PS) better than non-surgical periodontal therapy with regards to reduction of PPD and CAL *when 1) the endpoints are observed over more than one year 2) provided that the patient maintains an adequate oral hygiene following therapy*”. In the present review, criteria to accommodate the two new issues of the new focused question were applied to include studies with a design to answer the question at hand. The findings left only one study (2 articles) that complied with these inclusion criteria and this study



revealed no difference in the results of the two therapy modalities.

Twenty-one of 31 articles were excluded due to the fact that they had their baseline before a sketchy described oral hygiene phase, and not after this most crucial phase. In any periodontal therapy, the oral hygiene of the patient is *of the essence*. The state of the periodontal tissues can have an effect on the reliability of the measurements (53-55) as well as they can affect the final outcome by affecting the PPD and CAL proper. Surprisingly, this important factor is almost never reported in intervention studies. Essentially all trials on periodontal therapy (any therapy) base their claims of clinical benefits on baseline data that have been recorded before any form of oral hygiene has taken place (56,57). This implies that the therapeutic effects of the oral hygiene improvement itself are ingrained in the results of the scaling routines tested. Clinical studies on the effect of oral hygiene improvement *per se* on the periodontal parameters are few. One study (58) indicated that a modest reduction in bleeding scores following oral hygiene procedures did not affect the probing pocket depths or the clinical attachment levels, whereas Tagge et al. (59) found that oral hygiene improvement exerted considerable reducing effects on both bleeding scores and pocket depths. Another argument for recording the periodontal baseline measurements of PPD and CAL after the completion of an oral hygiene phase is the well-known fact that the pretreatment recordings of PPD and CAL can be substantially exaggerated due to probe penetration into inflamed and collagen-depleted connective tissue (54,60,61), just as tissue edema may contribute to inflated pretreatment PPD recordings. If results are based on pretreatment PPD and CAL values, the changes observed will inevitably be inflated. Unless all trial participants respond equally to the oral hygiene phase, which they obviously never do, this study design could also distort the results and conclusions with respect to the effects of the intervention tested. To our knowledge, few studies on periodontitis intervention include information on PPD or CAL, or plaque or bleeding scores

following the oral hygiene phase, but before the mechanical instrumentation of the roots. When they also fail to report on plaque scores following the intervention the clinician is not able to distinguish the effects of insufficient daily oral hygiene from the results of insufficient instrumentation of the roots.

The 4 meta-analyses mentioned above (49-52) showed a significant difference in favor of surgery on deep pockets ( $\geq 7$ mm). This does not come as a surprise since deeper pockets are technically more difficult to perform NSPT in than shallower pockets. On the other hand, the fact that PT is chosen in patients with deeper PPD (i.e. PPD > 7mm), analyses of treatment outcomes according to the baseline depth of the periodontal lesions may illustrate the well-known observation that the observed treatment ‘benefit’ is highest in the deepest lesions whereas shallow lesions do not benefit. While a floor effect (62) may indeed be present, particularly regarding the shallower lesions, it is not unlikely that a considerable portion of the observed ‘benefit’ in deeper lesions results from regression towards the mean, and therefore represents a statistical phenomenon (“regression towards the mean”) rather than a real biological effect (63).

Clinically, periodontal therapy has been reported effective if the mechanical therapy has been conducted with skill and with a systematic approach. One must expect that this has been the case in all of the studies in this review. However, in several of these studies the surgery was conducted by more than one operator, leaving a possibility that their surgical skills or techniques be different. Both CAL and BOP are subjective measures and can thus vary greatly from operator to operator and from day to day if the operators performing the measurements are not calibrated. In many of the trials reported in the systematic reviews, the intervention procedures were not well enough described. Only two of the 31 trials evaluated in our study had the same operator performing the measurements from the beginning and throughout (32,40). Calibration procedures had not been performed, since this would have been an impossible task. However,

even if difficult, the clinical design of such studies deserves to be criticized since such studies should be conducted with only one operator.

Fourteen of the 31 reports, including the two final trials (47,48) included in this study, were split-mouth designs, which preclude double blinding. Areas that have undergone a surgical intervention can usually be clinically distinguished from those receiving non-surgical treatment and the subject that has undergone the treatment is also affected in some degree by the given therapy. Having a surgical procedure performed in one quadrant may influence or compromise the plaque control in that or the other quadrants due to pain and generalized discomfort or size of interproximal spaces and thus difficulty with cleaning. Another weakness of the split-mouth designs in this particular setting is the ability of spill-over effects from one area of therapy to another (51), as f.ex. Chlorhexidine was also used after PS, but not after NSPT and which technique was applied first (PT or NSPT) was not reported in most cases either.

As specifically pointed out in the present study, many of the existing intervention studies report their results after very short follow-up time, i.e. at the most 1 year, but mostly considerably less. In the present review it has been revealed that the significant difference shown in the short-time follow up tends to fade after a couple of years. After 5 years follow up, the significant difference in PPD fades while the CAL still remains non-significant (40). After two years follow-up the significant difference fades out on CAL in 4-6 mm pockets and on PPD and CAL in  $\geq 7$ mm pockets, PPD in pockets at 4-6 mm stays significantly different and both CAL and PPD stay significantly different in shallow pockets (1-3mm) in favor of scaling (47).

**Conclusion:** By imposing 2 new obvious exclusion criteria that have not been used in systematic reviews before, on the common criteria used in intervention studies to evaluate NSPT vs. PS; i.e. follow-up  $>1$  year and baseline measurements after the hygiene phase, only one study and 2 articles were found representing 2 registration time points (2 and 5 years) in this

intervention study. None of these articles, from the same study, could distinguish the effect of NSPT from PS after five years. This does not mean that PS and NSPT is equally effective in *all* cases of periodontal therapy, only that the absolute majority of periodontal intervention studies regarding the comparison of mechanical, non-antibiotic therapies have not been designed well enough - especially regarding the effect of the pre-intervention oral hygiene phase - to address the aim of the intervention: periodontal surgery or non-surgical periodontal therapy – what is best?

## References

1. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *Lancet* 2005; 19:1809-1820.
2. Drisko CH. Nonsurgical periodontal therapy. *Periodontol 2000* 2001;25: 77-88.
3. 1999 International International Workshop for a Classification of Periodontal Diseases and Conditions. Papers. Oak Brook, Illinois, October 30-November 2, 1999. *Ann Periodontol* 1999;4: 1-112.
4. Mariotti A, Hefti AF. Defining periodontal health. *BMC Oral Health* 2015(Suppl 1):S6 doi: 10.1186/1472-6831-15-S1-S6.
5. Silva N, Abusleme L, Bravo D, Dutzan N, Garcia-sesnich J, Vernal R, Hernández M, Gamonal J. Host response mechanisms in periodontal diseases. *J Appl Oral Sci* 2015; 23: 329-355.
6. Heitz-Mayfield LJ, Lang NP. Surgical and nonsurgical periodontal therapy. Learned and unlearned concepts. *Periodontology 2000* 2013;62:218-231.
7. Cobb CM. Non-surgical pocket therapy: mechanical. *Ann Periodontol* 1996;1:443-490.
8. Caffesse RG, Sweeney PL, Smith BA. Scaling and root planing with and without periodontal flap surgery. *J Clin Periodontol* 1986;13: 205-210.
9. Slots J. Periodontology: past, present, perspectives. *Periodontol 2000* 2013;62:7-19..
10. Tariq M, Iqbal Z, Ali J, Baboota S, Talegaonkar S, Ahmad Z, Sahni JK. Treatment modalities and evaluation models for periodontitis. *Int J Pharm Investig* 2012; 2: 106–122.
11. Armitage GC. The complete periodontal examination. *Periodontology 2000* 2004;34: 22–33.
12. Haffajee AD, Teles RP, Socransky SS. The effect of periodontal therapy on the composition of the subgingival microbiota. *Periodontol 2000* 2006;42:219-258.
13. Ramfjord SP, Costich ER. Healing after simple gingivectomy. *J Periodontol* 1963;34:401-415
14. Rosling B, Nyman S, Lindhe J, Jern B. The healing potential of the periodontal tissues following different techniques of periodontal surgery in plaque-free dentitions. *J Clin Periodontol* 1976; 3: 233-250
15. Curtis JW Jr, Mclain JB, Hutchinson RA. The incidence and severity of complications and pain following periodontal surgery. *J Periodontol* 1985;56: 597-601.
16. Lindhe J, Nyman S. The effect of plaque control and surgical pocket elimination on the establishment and maintenance of periodontal health. A longitudinal study of periodontal therapy in cases of advanced disease. *J Clin Periodontol* 1975;2;67-79.
17. Schroer MS, Kirk WC, Wahl TM, Hutchens LH Jr, Moriarty JD, Bergenholz B. Closed versus open debridement of facial grade II molar furcations. *J Clin Periodontol* 1991;18:323-329.
18. Lindhe J, Westfelt E, Nyman S, Socransky SS, Haffajee AD. Long-term effect of surgical/non-surgical treatment of periodontal disease. *J Clin Periodontol* 1984;11: 448-458
19. Knowles J, Burgett F, Morrisson E, Nissle R, Ramfjord S, Comparison of results following three modalities of periodontal therapy related to tooth type and initial pocket depth. *J Clin Periodontol* 1980;7: 32- 47.
20. Lindhe J, Westfelt E, Nyman S, Socransky SS, Hejl L, Bratthall G. Healing following surgical/non-surgical treatment of periodontal disease. A clinical study. *J Clin Periodontol* 1982; 9: 115-128..
21. Aljateeli M, Koticha T, Bashutski J, Sugai JV, Braun TM, Giannobile WV, Wang HL. Surgical periodontal therapy with and without initial scaling and root planing in the management of chronic periodontitis: a randomized clinical trial. *J Clin Periodontol* 2014; 41:693-700.
22. Dosumu EB, Arowojolu MO, Savage KO. Alveolar bone regeneration pattern following surgical and non-surgical treatment in Juvenile Periodontitis. *West African J Med* 2002; 21:272-275.
23. Ramfjord SP, Knowles JW, Nissle RR, Burgett FG, Shick RA. Results following three modalities of periodontal therapy. *J Periodontol* 1975;46:522-526.
24. Ramfjord SP, Knowles JW, Nissle RR, Shick RA, Burgett FG. Longitudinal study of periodontal therapy. *J Periodontol* 1973;44:66-77.
25. Ramfjord SP, Nissle RR, Shick RA, Cooper H Jr. Subgingival curettage versus surgical elimination of periodontal pockets. *J Periodontol* 1968;39:167-175.

26. Burgett FG, Knowles JW, Nissle RR, Shick RA, Ramfjord SP. Short term results of three modalities of periodontal treatment. *J Periodontol* 1977;48:131-135.
27. Pihlstrom BL, Ortiz-Campos C, McHugh RB. A randomized four-year study of periodontal therapy. *J Periodontol* 1981;52:227-242.
28. Kaldahl WB, Kalkwarf KL, Patil KD, Molvar MP, Dyer JK. Long-term evaluation of periodontal therapy: I. Response to 4 therapeutic modalities. *J Periodontol* 1996; 67(2):93-102.
29. Wylam JM, Mealey BL, Mills MP, Waldrop TC, Moskowicz DC. The clinical effectiveness of open versus closed scaling and root planing on multi-rooted teeth. *J Periodontol* 1993;64: 1023-1028.
30. Parashis AO, Anagnou-Vareltzides A, Demetriou N. Calculus removal from multirooted teeth with and without surgical access. *J Clin Periodontol* 1993;20:63-68.
31. Ramfjord SP. Long-term assessment of periodontal surgery versus curettage or scaling and root planing. *Int J Tech Assess Health Care* 1990;6: 392-402.
32. Kalkwarf KL, Kaldahl WB, Patil KD, Molvar MP. Evaluation of gingival bleeding following 4 types of periodontal therapy. *J Clin Periodontol* 1996;67:93-102.
33. Kaldahl WB, Kalkwarf KL, Patil KD, Molvar MP, Dyer JK,. Evaluation of four modalities of periodontal therapy. Response to 4 therapeutic modalities.*J Periodontol* 1988;59:783-793.
34. Buchanan SA, Robertson PB. Calculus removal by scaling/root planing with and without surgical access. *J Periodontol* 1987;58:159-163.
35. Wennström A, Wennström J, Lindhe J. Healing following surgical and non-surgical treatment of juvenile periodontitis. *J Clin Periodontol* 1986;13:869-882.
36. Pihlstrom BL, McHugh RB, Oliphant TH, Ortiz-Campos C. Comparison of surgical and nonsurgical treatment of periodontal disease A review of current studies and additional results after 6 1/2 years. *J Clin Periodontol* 1983;10:524-541.
37. Pihlstrom BL, Ortiz-Campus C, McHugh RB. A randomized four-year study of periodontal therapy. *J Periodontol* 1981; 52: 227-242.
38. Isidor F, Karring T, Attström R.The effect of root planing as compared to that of surgical treatment. *J Clin Periodontol* 1984;11: 669–681
39. Kim TS, Schenk A, Lungeanu D, Reitmeir P, Eickholz P. Nonsurgical and surgical periodontal therapy in single-rooted teeth. *Clin oral invest* 2007;11:391-399.
40. Becker W, Becker BE, Caffesse R, Kerry G, Ochsenbein C, Morrison E, Prichard J. A longitudinal study comparing scaling, osseous surgery, and modified Widman procedures: results after 5 years. *J Periodontol* 2001;72:1675-84
41. Isidor F, Karring T. Attström R, Long-term effect of of surgical and non-surgical periodontal treatment. A 5-year clinical study.*J Periodont Res* 1986;21:462-472
42. Waite IM. A comparison between conventional gingivectomy and a non-surgical regime in the treatment of periodontitis. *J Clin Periodontol* 1976;3:173-185.
43. Pedrazzoli V, Kilian M, Karring T, Kirkegaard E. Effect of surgical and non-surgical periodontaltreatment on periodontal status and subgingival microbiota. *J Clin Periodontol* 1991;18: 598-604
44. Becker W, Becker BE, Ochsenbein C, Kerry G, Caffesse R, Morrison EC, Prichard J. A longitudinal study comparing scaling, osseous surgery and modified Widman procedures. Results after one year. *J Periodontol* 1988;59: 351-365.
45. Morrison EC, Ramfjord SP, Hill RW. Short-term effects of initial, nonsurgical periodontal treatment (hygienic phase). *J Clin Periodontol.* 1980;7:199-211
46. Kaldahl WB, Kalkwarf KL, Patil KD, Molvar MP., Evaluation of gingival suppuration and supragingival plaque following 4 modalities of periodontal therapy. *J Clin Periodontol* 1990, 17: 642–649.
47. Hill RW, Ramfjord SP, Morrison EC, Appleberry EA, Caffesse RG, Kerry GJ, Nissle RR. Four types of periodontal treatment compared over two years. *J Periodontol* 1981;52: 655-662.
48. Ramfjord SP, Caffesse RG, Morrison EC, Hill RW, Kerry GJ, Appleberry EA, Nissle RR, Stults DL. 4 modalities of periodontal treatment compared over 5 years. *J Clin Periodontol* 1987; 14:445-452

49. Berkey CS, Antczak-Bouckoms A, Hoaglin DC, Mosteller F, Pihlstrom BL. Multiple-outcomes meta-analysis of treatments for periodontal disease. *J Dent Res.* 1995;74:1030-1039.
50. Hung HC, Douglass CW. Meta-analysis of the effect of scaling and root planing, surgical treatment and antibiotic therapies on periodontal probing depth and attachment loss. *J Clin Periodontol* 2002;29:975-986.
51. Antczak-Bouckoms A, Joshipura K, Burdick E, Camilla Tulloch JF. Meta-analysis of surgical versus non-surgical methods of treatment for periodontal disease. *J Clin Periodontol* 1993;20: 259-268.
52. Heitz-Mayfield LJ, Trombelli L, Heitz F, Needleman I, Moles D. A systematic review of the effect of surgical debridement vs non-surgical debridement for the treatment of chronic periodontitis. *J Clin Periodontol* 2002; 29 Suppl 3: 92-102 (discussion 160-162)
53. Fowler C, Garrett S, Crigger M, Egelberg J. Histologic probe position in treated and untreated human periodontal tissues. *J Clin Periodontol.* 1982;9:373-385.
54. Larsen C, Barendregt DS, Slot DE, Van der Velden U, Van der Weijden F. Probing pressure, a highly undervalued unit of measure in periodontal probing: a systematic review on its effect on probing pocket depth. *J Clin Periodontol* 2009;36:315–322.
55. van der Velden U. Location of probe tip in bleeding and non-bleeding pockets with minimal gingival inflammation. *J Clin Periodontol.* 1982;9:421-427.
56. Preus HR, Dahlen G, Gjermo P, Baelum V. Microbiological observations following four treatment strategies among periodontitis patients maintaining a high standard of oral hygiene. A secondary analysis of a randomized controlled clinical trial. *J Periodontol* 2015;86: 856-865.
57. Preus HR, Gjermo P, Baelum V. A double-masked RCT comparing four periodontitis treatment strategies: 5-year clinical results. *J Clin Periodontol* 2017; *In Press*
58. Cercek JF, Kiger RD, Garrett S, Egelberg J. Relative effects of plaque control and instrumentation on the clinical parameters of human periodontal disease. *J Clin Periodontol* 1983; 10: 46-56.
59. Tagge DL, O’Leary TJ, El-Kafrawy AH. The clinical and histological response of periodontal pockets to root planing and oral hygiene. *J Periodontol* 1975; 46: 527-533.
60. Armitage GC, Svanberg GK, Löe H. Microscopic evaluation of clinical measurements of connective attachment levels. *J Clin Periodontol* 1977; 4: 173-190.
61. Robinson PJ, Vitek RM. The relationship between gingival inflammation and resistance to probe penetration. *J Periodont Res* 1979; 14: 239-243.
62. Preus HR, Sandvik L, Gjermo P, Baelum V. Baseline and change revisited: The effect of smoking on the outcome of periodontal treatment. *Eur J Oral Sci.* 2014;122:89-99
63. Tu YK, Gilthorpe MS. Key statistical and analytical issues for evaluating treatment effects in periodontal research. *Periodontol 2000* 2012;59:75-88.