HEALING DYNAMICS OF CLINICAL PARAMETERS AFTER SUB GINGIVAL INSTRUMENTATION FOR THE TREATMENT OF PERIODONTITIS: IS THERE EVIDENCE ON THE TIMING OF PERIODONTAL EVALUATION?

Paternò Holtzman Lucrezia (1), Valente Nicola Alberto (2), Vittorini Orgeas Gianluca (3), Copes Luca (4), Clementini Marco (4)

Affiliazione:

(1) Department of Periodontology and Prosthodontics, George Eastman Dental Hospital, Policlinico Universitario Umberto I, Rome, Italy

(2) Department of Periodontology, Università degli Studi di Cagliari and Department of Periodontology, State University of New York at Buffalo

(3) Department of Periodontology, Università Cattolica del Sacro Cuore School of Dentistry, Rome, Italy.

(4) Department of Periodontology, Vita-Salute San Raffaele University, Milan, Italy

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Corresponding author:

Dr. Lucrezia Paternò Holtzman

Viale Regina Elena 278 B

mail: lucreziaph@gmail.com

Abstract

Aim: to investigate the healing dynamics of clinical parameters after step 2 (subgingival instrumentation) periodontal therapy and search for evidence regarding the best timing for periodontal re-evaluation.

Methods: A PICO question was defined and searches were performed of the PubMed, EMBASE, Ovid MEDLINE and Web-of-Science databases. The inclusion criteria were RCT reporting periodontal clinical parameters between at least 2 follow-up time points with a minimum initial follow-up of 1 month. Standard meta-analyses were performed using PPD and CAL changes between follow-up time points and baseline.

Results: Thirty-one papers fulfilled the inclusion criteria and were included in qualitative analysis and meta-analysis. Weighted mean PPD reductions from baseline at 1-2, 3-4 and 5-6 months were respectively 1.5mm (CI 0.83; 2.09),1.4mm (CI 0.76; 1.94) and 2mm (CI 1.4; 2.67) for initially shallow (4-5mm) pockets, and 2.4mm (CI 0.60;4.09), 2.4mm (CI 1.21; 3.60) and 2.8mm (CI 1.77; 3.84) for initially deep (≥6mm) pockets.

Conclusions: This analysis demonstrated that PPD reduction for shallow and deep pockets occurs mainly within 1-2 months. However, reduction increases of 0.5 mm can occur up to 6 months after therapy.

INTRODUCTION

The EFP recently published clinical practice guidelines aiming to provide recommendations for practitioners for the treatment of stage I-III periodontitis (Sanz et al., 2020). These are based on a stepwise approach to therapy which includes a sequence of interventions (or steps) applied in an incremental fashion. While step one aims to guide behavioral changes and assist the patient in supragingival biofilm control, step two focuses on subgingival instrumentation (i.e. removal of subgingival plaque and calculus). A recent systematic review (Suvan et al., 2019) evaluated the efficacy of sub-gingival instrumentation in the treatment of periodontitis and concluded that it is efficacious in achieving the clinical endpoints of periodontal therapy (probing depth reduction, reduction of inflammation and reduced number of diseased sites). Furthermore, the systematic review reported that the efficacy of this therapy is independent of the type of instrumentation used (sonic/ultrasonic versus manual) and the timing of delivery of therapy (quadrant-wise fashion or a single session).
The effect of the second step of therapy should be assessed though a periodontal re-evaluation: if the endpoints of therapy (no periodontal pockets >4 mm with bleeding on probing or no deep periodontal pockets [≥6 mm]) have not been achieved, the third step of therapy (surgical treatment or repeated instrumentation) should be considered. On the other hand, if the clinical goals have been met, the patient is inserted into a supportive periodontal care program, aimed to maintain periodontal health stability (Sanz et al., 2020)

The ideal moment to re-evaluate the periodontium after subgingival instrumentation remains unclear (Segelnick and Weinberg, 2006) and various timepoints have been suggested in the literature. Proye et al. (1982) reported changes in attachment levels and probing depths within 3 weeks, and no major changes were found after this time-point. The authors reported that changes in the first week were related mainly to recession, while the following changes were due to gain in attachment levels. Caton et al. (1982) observed that the results in terms of improvement of the clinical parameters, obtained at 4 weeks, were stable at 8 and 16 weeks after periodontal subgingival instrumentation (root planing). Other authors however suggest a longer time interval between instrumentation and re-evaluation. Cercek et al. (1983), evaluating the response to non-surgical supra- and subgingival instrumentation, concluded that clinical changes occurred until 8 months following the procedure (Cercek et al., 1983). Kaldahl et al. (1988) also advocated a longer healing time, noting clinical changes up to one year after instrumentation.

From a histologic point of view, the timing of re-evaluation should be dictated by precise healing times of the epithelial and connective tissue components of the dento-gingival junction. Junctional epithelium heals within 1-2 weeks (Stahl et al 1972).
In the connective tissue compartment, formation of a new collagen matrix and its maturation requires a longer time and was reported to last up to several months (Biagini et al. 1988). Based on this information, it would be logical to re-evaluate the periodontal condition after these events have taken place.

From clinical, and histological standpoints, it appears that different time intervals after subgingival instrumentation have been proposed in the literature as appropriate to re-evaluate the periodontal condition.
The clinical practice guidelines clearly state the importance of a periodontal re-evaluation, that should be performed once the periodontal tissues have healed" (Sanz et al., 2020). However, the exact moment in which this assessment should be carried out after step 2 is not explicitly stated. Therefore the aim of the present systematic review is to investigate the healing dynamics

of clinical parameters after subgingival instrumentation for the treatment of periodontitis and search for evidence regarding the best timing for periodontal re-evaluation in periodontitis patients treated with subgingival instrumentation. Furthermore, the selection of an appropriate time-point is of paramount importance because it reduces the risk of overtreatment (which could occur if step 3 were performed too soon) while minimizing the risk of undertreatment (which would be possible if step 3 were performed too late allowing the periodontal condition to deteriorate).

MATERIALS AND METHODS

This review has been registered at the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews and has been assigned the number CRD42020223552.

PICO Criteria Definitions

Population: Patients suffering from periodontitis
Intervention: Mechanical sub gingival debridment
Comparison: Effect of mechanical sub gingival debridment at different time-points of follow up
Outcome: Change in clinical parameters (PPD, CAL, BoP)

Focused Question

In patients suffering from periodontitis treated with mechanical sub gingival debridment, when do periodontal clinical parameters become stable and show no additional improvement?

Search Strategy

The reporting of this systematic analysis adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher et al., 2010).
Relevant articles published up to June 7th, 2020 were searched using the relevant keywords and respective Boolean logic operators (AND, OR, NOT) used in the following databases: PubMed, EMBASE, Ovid MEDLINE, Web of Science. The relevant keywords were combined as follow for the search: (("periodontitis"[All Fields]) AND (("therapy"[All Fields]) OR ("non surgical therapy"[All Fields]) OR ("ultrasonic"[All Fields]) OR ("manual"[All Fields]) OR ("mechanical"[All Fields]) OR ("laser"[All Fields]) OR ("antibiotics"[All Fields]) OR ("antiseptic"[All Fields])) NOT (("endodontics"[All Fields]) OR ("apical"[All Fields])) AND((humans[Filter]) AND (alladult[Filter])) AND ((humans[Filter]) AND (english[Filter]) AND (alladult[Filter]))) Filters: Humans, English, Adult: 19+ years
Two independent reviewers (LPH and NAV) screened all of the titles, abstracts and then the full text of the studies according to the inclusion and exclusion criteria. Disagreements were resolved by discussion with a third reviewer (MC)

Inclusion criteria

- Studies investigating non-surgical therapy for periodontitis in healthy (i.e. not affected by systemic diseases) patients.
- Randomized controlled trials (RCTs).
- Studies reporting at least probing pocket depth PPD (mm) between at least 2 follow-up time points with a minimum initial follow-up of 1 month

- At least 10 patients included.
- Patient level analysis.
- Studies using a quadrant-wise or full-mouth delivery of subgingival therapy.
- Studies employing mechanical or power-driven instruments, or a combination of both.
- English language.

Exclusion criteria

- Periodontal non-surgical therapy for gingivitis, necrotizing periodontitis and periodontitis as manifestation of systemic diseases.
- No reporting of standard deviation or standard error.
- Prospective cohort studies, Retrospective studies, Case series, Case reports.
- Split mouth design of the study.
- Site level analysis.
- Subsequent articles reporting information on the same cohort of patients.
- Studies in which patients received additional subgingival re-instrumentation after the initial session of therapy.
- Additional therapy (local or systemic antimicrobials, laser, host modulators, laser or antimicrobial photodynamic therapy) combined with subgingival instrumentation.
- Studies with a single follow-up appointment.
- Studies including implants.
- Studies including surgical therapy of periodontal defects.
- Studies focusing specifically on infrabony defects/ furcation defects.
- Studies presenting data only in graph form.
- Studies lacking a clear periodontal diagnosis.
- Studies with insufficient sample size (less than 10 patients).

Quality Assessment

Two authors (GVO and LC) independently assessed the studies in terms of the inclusion, relevance, eligibility, and risk of bias following the Cochrane Collaboration tool (Higgins et al., 2011).

Data Extraction and Collection Process

Following the screening process, two reviewers (LPH and NAV) independently extracted the data of the selected articles using data extraction tables. Disagreements were resolved by discussion with a third reviewer (MC). The primary outcome (PPD) and secondary outcomes (CAL, BOP) were reported in the table as mean and standard deviation according to time ranges (1-2 months, 3-4 months, 5-6 months) and baseline PPD, either as an absolute value or as a change between the different time points depending on how they were reported in the study.

Statistical analysis

Data were organized into evidence tables, and a descriptive summary was performed to determine the quantity of data and study variations (i.e. study subjects, treatment and results). Following article selection, Cohen's kappa coefficient (*k*) was performed to assess inter-examiner agreement.
Continuous data (changes of PD and CAL) mean values and standard deviations were grouped according to baseline PPD (all, shallow (4-5 mm) or deep (≥6 mm)). These were pooled into random-effects meta-analyses and expressed as initial and final averages to calculate weighted mean differences (WMD) with their associated 95% confidence intervals (CI). Standard meta-analyses were performed using PPD and CAL changes between baseline and 1-2 month, 1-2 month and 3-4 months, 3-4 months and 5-6 months, respectively. As none of the selected RCTs addressed this evaluation, it was decided a posteriori to analyse PPD and CAL changes at different follow up time points respect to baseline. Statistical heterogeneity was explored .The significance of discrepancies in the estimates of the treatment effects from the different trials was assessed by means of Cochrane's Q statistic ($p<0.$) for heterogeneity and the $I2$ index (Higgins, Thompson, Deeks, & Altman, 2003). Forest plots were used to illustrate the outcomes of the different analyses. Publication bias was evaluated through Funnel plots (function: metafunnel) and Egger s test for small-study effects (Egger, Davey Smith, Schneider, & Minder, 1997). All analyses were performed with Stata (Stata Statistical Software: Release 15, StataCorp LLC, College Station, TX, USA)

RESULTS

Search results and selection of included studies

A total of 4401 references, published up to June 2020, were identified by the electronic search in MEDLINE (by PubMed), in the Cochrane Collaboration databases and in Scopus. Seven citations from the manual search and the grey literature search were identified. After creating a single list and removal of 75 duplicates, 4326 records remained for title-abstract screening; independent screening of titles and abstracts resulted in elimination of 3869 articles, therefore 457 articles remained for full-text evaluation. A high level of agreement was found between the reviewers at both screening stages ($K > 0.9$). After full text screening, 426 references were discarded. The final number of articles included in the review was 31 (list of excluded references and reasons for exclusion can be found in **Fig.1**); all 31 references (**table 1**) were consequently included in both qualitative analysis and meta-analysis.

Characteristics of included studies

Disease definition

In 27 studies, periodontitis was defined as chronic (or adult), ranging from mild generalized to severe generalized, while in 4 (Andere 2017, Do Vale 2016, Talete 2016, Emingil 2012) the authors included aggressive periodontitis.
In terms of extent of disease, all studies included generalized forms while only 1 reference (Vitt et al 2) also included local forms. Disease severity was described with a wide range of qualifying terms (e.g. “early” “mild”, moderate”, “severe” and advanced”) and periodontal parameters (e.g. CAL, PPD and FMBS).

Study population/selected samples
Cumulatively, 653 patients were treated with subgingival instrumentation.
The mean age of participants ranged from 27.5 to 56.8 years with a cumulative mean of 45.71. In terms of tobacco use, 16 studies excluded smokers while 2 included only smokers. In the remaining 13 studies both categories were represented with various proportions.

Outcome assessment
All selected studies used a full-mouth approach to assess clinical outcome variables, either by evaluating all sites, or a group of sites according to a part of the mouth (e.g. a quadrant) or according to a clinical criterion (e.g. PPD > 4 mm). The clinical parameters were reported as follows: PPD in all 31 articles, CAL in 30 papers, FMBS in 26 and GI in 5 studies; the number of sites measured per tooth was 4–6 among all the selected publications. Due to the limited number of studies, it was not feasible to conduct a meta-analysis.

Type of interventions
Non-surgical mechanical Therapy
All included papers reported non-surgical mechanical instrumentation as the only active therapy in all patients. Different approaches with regard to both timing (quadrant-wise or various types of full mouth approach) and instrumentation (power-driven or manual) were included.

Maintenance Phase
Among all studies, the vast majority enrolled subjects in a supportive periodontal therapy program (step 4), while 2 papers reported no details on the type of maintenance they provided.

Risk of bias Quality assessment
Summarized results of the assessment of risk of bias are illustrated in **Fig.2**
Overall, 21 studies were judged to be at low risk of bias, 1 at high risk of bias and 8 presented with some concerns. These were related to the randomization process or to deviation from the intended interventions.

Quantitative synthesis
Due to insufficient data, it was not feasible to conduct a meta-analysis for studies reporting a direct comparison between changes in PPD at 1-2 months, 3-4 months or 5-6 months. For this reason, a meta-analysis was conducted only for studies reporting changes in PPD between various (1-2 months, 3-4 months and 5-6 months) time-points and baseline (i.e. before therapy was delivered).

Weighted mean PPD reduction at different time-points for all initial PPD values (Fig.3)

Analysis of all treated pockets revealed a weighted mean PPD reduction of 1.5 mm (CI 1.02; 2.03) within the first 1-2 months after treatment (4 studies, 5 treatment groups), and of 1.6 mm (CI 1.02; 2.03) at 3-4 months (7 papers, 8 treatment groups). Weighted mean PPD reduction after 5-6 months post-treatment was 1.4 mm (CI 0.98;1.72).
Heterogeneity was low for all time-points (I2=0% for 1-2 months and 5-6 months, 17.6% for 3-4 months).

Weighted mean PPD reduction for initially shallow (PPD 4-5mm) pockets (Fig.4)

In the first 2 months after instrumentation a weighted mean PPD reduction of 1.5 mm (CI 0.83; 2.09) was achieved (2 articles, 3 treatment groups). Weighted mean PPD reduction of 1.4 mm with respect to baseline (CI 0.76; 1.94) was observed after 3-4 months (6 papers, 7 treatment groups). Additional PPD reduction was observed after 5-6 months, with a weighted mean PPD reduction of 2 mm (CI 1.41; 2.67) achieved from analysis of 6 studies (11 treatment groups).
Heterogeneity was low (I2<1%) for all comparisons.

Weighted mean PPD reduction for initially deep (PPD ≥ 6 mm) pockets (Fig.5)

For initially deep (PPD≥ 6 mm) sites, a weighted mean PPD reduction of 2.4 mm (CI 0.60;4.09) was observed (2 articles, 3 groups) within 1-2 months. The same weighted mean reduction was found after 3-4 months (2.4 mm, CI 1.21; 3.60) on data from 6 papers (7 treatment groups). At 5-6 months a weighted mean reduction of 2.8 mm (CI 1.77; 3.84) was revealed (7 papers, 9 treatment groups).
Heterogeneity (I2=0%) was low for all comparisons.

Weighted mean CAL gain at different time-points for initially shallow (PPD 4-5mm) pockets

Weighted mean CAL gain after 1-2 months post-therapy was 1.4 mm (CI 1.20; 1.69) (2 treatment groups of the same study). The weighted mean gain at 3-4 months remained substantially the same (1.2 mm, CI 0.68; 1.63) and was based on 5 studies, 6 treatment groups). At 5-6 months the weighted mean gain was observed to be 1.5 mm (CI 1.11; 1.94), extracted from 5 studies (10 treatment groups).
Heterogeneity was low (I2 0% for both 1-2 and 5-6 months and 15.2% for 3-4 months).

Weighted mean CAL gain at different time-points for initially deep (PPD≥ 6 mm) pockets

Within the first 2 months post-treatment, weighted mean CAL gain was 2.3 mm (CI 1.47; 3.48) based on 2 groups of the same article. After 3-4 months the value remained substantially the same (2.1 mm, CI 1.08; 3.06) (5 articles, 6 groups). The value of CAL gain remained substantially unchanged at 5-6 months (2.4 mm, CI 1.57; 3.16), based upon 5 studies and 8 groups.
Heterogeneity was again low (I2=0) for all comparisons.

Weighted mean FMBS reduction (%) at different time-points for all initial PPD values

Due to lack of studies addressing this time-point, it was impossible to evaluate reduction in FMBS at 1-2 months. The weighted mean reduction was 40% (CI 0.25; 0.56) after 3-4 months post-treatment (5 studies). The FMBS reduction after 5-6 months was 46.5% (CI 0.35; 0.58) based on 6 studies, 7 treatment groups.

DISCUSSIONS

In the present systematic review the PPD reduction for shallow sites was 1.4 mm after 3-4 months and was in agreement with the value reported by Suvan et al. for the same time-point (1.5 mm). The same authors found that at 6-8 months the PPD reduced by 1.6 mm, while in the present study the value is similar though slightly greater (2 mm). For deep sites findings were again in agreement with those of Suvan et al., (2.6 mm at 3-4 months versus 2.4 mm in the present study; 2.6 mm at 6-8 months versus 2.8 mm in the present study at 5-6 months).

The primary outcome of the present systematic review is reduction of mean PPD over time. When observing PPD reduction for all initial probing depths, this value appears to change very little if not at all between time-points, suggesting that when all PPD values are considered together the parameter is stable already 1-2 months post-instrumentation. On the other hand, when shallow pockets (4-5 mm) are observed, the healing dynamic differs and PPD values continue to decrease after 5-6 months from therapy, with a further reduction of 0.5 mm between 3-4 and 5-6 months. The same is true for deep pockets (initial PPD $\geq$ 6 mm), where a further reduction of 0.4 mm could be observed between 3-4 and 5-6 months.

The present data seems to indicate that in systemically healthy patients presenting with varying degrees of periodontal disease there is value in waiting 5-6 months after step 2 therapy prior to performing re-evaluation. One possible explanation could be found in the histologic changes that take place after sub gingival instrumentation. Healing of the periodontium involves healing of both the epithelial and connective tissue compartments. The junctional epithelium was found to be re-epithelialized two weeks after sub gingival instrumentation (Waerhaug et al 1978). Healing also occurs in the connective tissue compartment which involves its change from a tissue heavily infiltrated with inflammatory cells to one that is healthier and more collagen fiber-rich. This transition also has repercussions on the resistance offered by the tissue to the probe (and therefore on clinical parameters): when the connective tissue is inflamed, the probe easily penetrates into the connective tissue past the junctional epithelium, whereas when the inflammatory cells are replaced by collagen fibers the tissue is firmer and offers a greater resistance to probing (Fowler et al., 1982; Armitage 1982). A time interval of 30 to 60 days was reported as necessary for functionally oriented connective tissue fibers to be formed (Biagini et al. 1988), but reorganization of collagen fibers appears to occur beyond this time-point (Polimeni et al., 2006). Based on this evidence, re-evaluation should be scheduled once the healing of the connective tissue is complete.

The present study has shown that there is a paucity of studies presenting data for consecutive follow-ups after step 2 therapy, which would allow direct observation of changes in periodontal parameters over time. Due to the lack of data it was not possible to directly compare changes between consecutive time-points and all meta-analyses were performed for changes between different time-points and baseline.

This represents a limitation of the present study because periodontal stability could only be deducted from indirect comparisons between consecutive time-points and baseline.

CONCLUSION

Within the limitations of the present review, a comprehensive search and analysis of the available literature based on RCTs investigating the healing dynamics after subgingival instrumentation for the treatment of periodontitis demonstrated that PPD reduction for all, shallow (4-5 mm) or deep (≥6 mm) pockets occurs mainly within 1-2 months. However, reduction increases by a weighted average of 0.5 mm up to 6 months after therapy.

Based on the present data, it appears reasonable to postpone periodontal re-evaluation until at least 6 months post-therapy in healthy patients affected by periodontal disease treated with mechanical instrumentation (both sonic/ultrasonic and manual). This appears true irrespective of initial PPD.
Further studies should determine the effect on healing times (and thus timing of re-evaluation) of adjunctive treatments, such as host modifiers, lasers and local/systemic antimicrobials among others.

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Table 1 A

(A) ***Characteristics of included studies, study design, population, intervention***

Main Author	Country	Settings	Population	Smoking habits	Mean age	Age range	% of Women	Type of tooth	Diagnosis	Treatment	Maintenance	Clinical parameters
AlAhmari et al. 2019	Saudi Arabia	University	43	A. mixed B. none	44.7	N.R.	0	all	Chronic	Full mouth manual	N.R.	PD, CAL, BOP, PI
Andere et al. 2017	Brazil	University	20	none	31.25	N.R.	95	all	Aggressive	Full mouth ultrasonic	Supragengival + OHI	BOP, PPD, CAL, REC
Celik et al. 2019	Turkey	University	19	none	38.4	25 - 58	50	all	Chronic	Manual + ultrasonic	Supragengival + OHI	PI, PD, CAL, BOP
Chopra et al. 2016	India	University	59	none	36.70	N.R.	49.15	all	Chronic	Manual + ultrasonic	N.R.	PPD, CAL, BOP
Cosyn et al. 2006	Belgium	University/ private	13	mixed	51	N.R.	61.54	all	Chronic	2 session manual + ultrasonic	Supragengival + OHI	SBI, PD, BOP, PI. CAL, REC
Cosyn et al. 2006	Belgium	University	**6**	none	51	N.R.	50	all	Chronic	Full mouth manual + ultrasonic	Supragengival + OHI	BOP, PI, PD, CAL, GI
Cosyn et al. 2007	Belgium	University	16	none	52	N.R.	56.25	all	Chronic	Full mouth ultrasonic + manual	Supragengival + OHI	PD, CAL, BOP, PI, SBI
Cosyn et al. 2013	Belgium	University	18	mixed	44	N.R.	44.44	all	Chronic	Ultrasonic	Supragengival + OHI	PlI, BOP, PPD, CAL
do Vale et al. 2016	Brazil	University	14	none	28.57	N.R.	64.28	all	Aggressive	Full mouth ultrasonic	Supragengival + OHI	FMPS, BOP, PPD, CAL, REC
Emingil et al. 2012	Turkey	University	16	mixed	29.56	N.R.	50	all	Aggressive	Quadrant wise	Supragengival + OHI	PD, CAL, BOP

Main Author	Country	Settings	Population	Smoking habits	Mean age	Age range	% of Women	Type of tooth	Diagnosis	Treatment	Maintenance	Clinical parameters
Guilherme M. Zanatta et al. 2006	Brazil	University	30	mixed	40.5	27-62	N.R.	all	Chronic	A. Quadrant wise B. Ultrasonic full mouth	Supragengival + OHI	BOP, PPD, CAL, REC, PlI
Gürkan et al. 2006	Turkey	University	13	mixed	46.77	35 - 59	30.8	all	Chronic	Quadrant wise	Supragengival + OHI	PD, CAL, PBI and PI
Ioannou et al. 2009	Greece	University	40	mixed	50	N.R.	60.3	all	Chronic	A. Ultrasonic quadrant B. Manual quadrant wise	Supragengival + OHI	PlI, PD, CAL, GBI
Koshy et al. 2005	Japan	University	24	none	51.21	34 – 66	62.05	A. all B. all C. anterior D. anterior E. molar F. molar	Chronic	A. Full mouth ultrasonic B. Quadrant wise ultrasonic C. Full mouth ultrasonic D. Quadrant wise ultrasonic E. Full mouth ultrasonic F. Quadrant wise ultrasonic	Supragengival + OHI	PlI, BOP, PPD, CAL
Laleman et al. 2015	Turkey	University	24	none	47	39 - 58	41.7	all	Chronic	Full mouth 2 stages manual + ultrasonic	OHI	PD, BOP, GI, PI, REC
Machion et al. 2004	Brazil	University	23	all	40.45	N.R.	56	anterior	Chronic	N.R.	OHI	PI, BOP, PD, GR and RAL

Main Author	Country	Settings	Population	Smoking habits	Mean age	Age range	% of Women	Type of tooth	Diagnosis	Treatment	Maintenance	Clinical parameters
Mohammad et al. 2005	USA	University	12	none	83	77 - 90	92	N.R.	Chronic	N.R.	OHI	PD, BOP, CAL
Monzavi et al. 2016	Iran	University	25	none	50.3	35 – 55	52	all	Chronic	Full mouth manual + ultrasonic	Supragengival + OHI	PI, PD, CAL, BOP
Nogueira-Filho et al. 2010	Brazil	University	10	none	37.3	N.R.	66.7	all	Chronic	Full mouth	Supragengival + OHI	PD, CAL, BOP, PI
Oteo et al. 2010	Spain	University	13	mixed	46.9	37 - 65	38.5	all	Chronic	Full mouth 2 stages	OHI	PD, CAL, BOP
Palmer et al. 1998	UK	University	27	mixed	50.5	N.R.	N.R.	all	Chronic	Ultrasonic	Supragengival + OHI	PlI, BOP, PPD, CAL
Pera et al. 2012	Brazil	University	15	none	43.4	35 - 55	46.7	all	Chronic	Full mouth manual	Supragengival + OHI	PD, CAL, BOP, PI
Pradeep & Kathariya et al. 2011	India	University	19	none	37.3	29 – 48	52.6	all	Chronic	Ultrasonic	OHI	PD, CAL, GI
Rusu et al. 2017	Romania	University	17	mixed	48.29	40 - 60	41.17	all	Chronic	Full mouth 2 stages manual + ultrasonic	Supragengival + OHI	BOP, PPD, CAL
Saglam et al. 2014	Turkey	University	15	none	40.83	32 - 56	46.7	all	Chronic	Full mouth manual + ultrasonic	OHI	PD, CAL, BOP, PI, GI
Sakellari et al. 2010	Greece	University	29	mixed	48.75	37 - 75	48	all	Chronic	Full mouth 2 stages manual + ultrasonic	OHI	PD, CAL, BOP
Sanz-Sanchez et al. 2015	Spain	University	21	mixed	56.8	39 - 71	78.19	all	Chronic	2 session ultrasonic	Supragengival + OHI	BOP, PPD, CAL, REC, PlI

Main Author	Country	Settings	Population	Smoking habits	Mean age	Age range	% of Women	Type of tooth	Diagnosis	Treatment	Maintenance	Clinical parameters
Taiete et al. 2016	Brazil	University	18	none	27.5	N.R.	67	all	Aggressive	Full mouth manual + ultrasonic	Supragengival + OHI	FMBS, FMPS, PPD, GMP, rCAL,
Theodoro et al. 2018	Brazil	University	17	all	46.2	N.R.	28.6	all	Chronic	Full mouth manual + ultrasonic	OHI	PD, CAL, BOP
Üstün et al. 2018	Turkey	University	20	none	45.80	35 - 58	40	all	Chronic	Full mouth	Supragengival + OHI	CAL, PD, PI and GI
Vitt et al. 2019	Belarus	University	19	mixed	45.4	N.R.	42.10	all	Chronic generalized or local	Manual + ultrasonic	Supragengival + OHI	PlI, BOP, PPD

Table 1 B *Clinical outcomes*

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
AlAhmari et al. 2019	1, 3 months	a) 1 month = 0.7 3 months = 0.6 b) 1 month = 2.2 3 months = 2.5	a) N.R. b) N.R.	a) N.R. b) N.R.	a) 1 month = 0.8 3 months = 1.1 b) 1 month = 2 3 months = 2.3	a) N.R. b) N.R.	a) N.R. b) N.R.	a) 1 month = 4.7 3 months = 2.6 b) 1 month = 43.9 3 months = 40.9	a) N.R. b) N.R.
Andere et al. 2017	3, 6 months	3 months = 0.7 6 months = 0.67	3 months = 1.92 6 months = 1.84	3 months = 3.04 6 months = 3.00	3 months = 0.63 6 months = 0.60	3 months = 1.79 6 months = 1.72	3 months = 2.97 6 months = 2.88	3 months = 36 6 months = 36	N.R.
Celik et al. 2019	3, 6 months	N.R.	3 months = 1.8 6 months = 1.9	3 months = 2.4 6 months = 2.7	N.R.	3 months = 1.8 6 months = 1.8	3 months = 2.5 6 months = 2.8	3 months = 46 6 months = 45.7	N.R.
Chopra et al. 2016	1, 3 months	1 month = 1.50 3 months = 1.91	N.R.	N.R.	1 month = 2.01 3 months = 1.60	N.R.	N.R.	1 month = 40.1 3 months = 57.6	1 month =0.67 3 months = 0.92
Cosyn et al. 2006	1, 3, 6, and 9 months	1 month = 1.18 3 months = 1.27 6 months = 1.22	N.R.	N.R.	N.R.	N.R.	N.R.	1 month =48 3 months = 48 6 months = 47	N.R.
Cosyn et al. 2006	1 and 3months	1 month = 0.54 3 months = 0.74	N.R.	N.R.	1 month = -0.05 3 months = 0.09	N.R.	N.R.	1 month = 25 3 months = 27	N.R.

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
Cosyn et al. 2007	1, 3, 6 months	1 month = 0.79 3 months = 0.95 6 months = 0.96	N.R.	N.R.	1 month = 0.08 3 months = 0.26 6 months = 0.39	N.R.	N.R.	1 month = 30 3 months = 28 6 months = 30	N.R.
Cosyn et al. 2013	1 and 3 months	1 month = 0.96 3 months = 1.02	N.R.	N.R.	1 month = 0.56 3 months = 0.48	N.R.	N.R.	1 month = 32 3 months = 32	N.R.
do Vale et al. 2016	1, 3, and 6 months	1 month = 1.85 3 months = 2.2 6 months = 2.05	N.R.	N.R.	1 month = 1.15 3 months = 1.33 6 months = 1.18	N.R.	N.R.	N.R.	N.R.
Emingil et al. 2012	1, 3, 6 months	1 month= 1.47 3 months = 1.54 6 months = 1.68	1 month = 2.04 3 months = 2.35 6 months = 2.51	1 month = 4.1 3 months = 4.4 6 months = 4.76	1 month = 1.39 3 months = 1.53 6 months = 1.58	N.R.	N.R.	1 month = 54.01 3 months = 55.75 6 months = 59.55	N.R.
Guilherme M. Zanatta et al. 2006	1 and 3 months	a) 1 month = 1.83 3 months = 2.51 b) 1 month = 2.16 3 months = 2.58	a) 1 month = 1.65 3 month = 2.20 b) 1 month = 1.98 3 months = 2.19	a) 1 month = 2.61 3 months = 4,37 b) 1 month = 3.51 3 months = 4.36	a) 1 month = 1.41 3 months = 1.87 b) 1 month = 1.62 3 months = 1.99	a) 1 month = 1.32 3 months = 1.61 b) 1 month = 1.57 3 months = 1.74	a) 1 month = 1.92 3 months = 3.01 b) 1 month = 2.95 3 months = 3.19	a) N.R. b) N.R.	a) N.R. b) N.R.

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
Gürkan et al. 2006	3, 6 months	3 months = 3.46 6 months = 3.31	3 months = 1.53 6 months = 1.46	3 months = 2.78 6 months = 2.57	3 months = 2 6 months = 1.85	3 months = 1.01 6 months = 0.78	3 months = 1.74 6 months = 1.76	N.R.	N.R.
Ioannou et al. 2009	3, 6 months	a) 3 months = 0.53 6 months = 0.44 b) 3 months = 0.88 6 months = 0.88	a) 3 months = 1.23 6 months = 1.28 b) 3 months = 1.55 6 months = 1.53	a) 3 months = 2.16 6 months = 2.28 b) 3 months = 2.71 6 months = 3.14	a) 3 months = -0.38 6 months = -0.29 b) 3 months = 1.14 6 months = 1.14	a) 3 months = 0.79 6 months = 0.75 b) 3 months = 1.25 6 months = 1.25	a) 3 months = 1.89 6 months = 1.96 b) 3 months = 2.06 6 months = 2.55	a) N.R. b) N.R.	a) N.R. b) N.R.
Koshy et al. 2005	1, 3, and 6 months	a) 6 months = 1.74 b) 6 months = 1.5 c) N.R. d) N.R. e) N.R. f) N.R.	a) 6 months = 3.21 b) 6 months = 3.06 c) 6 months = 2.97 d) 6 months = 2.84 e) 6 months = 2.62 f) 6 months = 2.48	a) N.R. b) N.R. c) 6 months = 4.24 d) 6 months = 3.8 e) 6 months = 3.81 f) 6 months = 3.9	a) 6 months =1.2 b) 6 months = 1 c) N.R. d) N.R. e) N.R. f) N.R.	a) 6 months = 2.26 b) 6 months = 1.99 c) 6 months = 2.08 d) 6 months = 1.89 e) 6 months = 1.74 f) 6 months = 1.56	a) N.R. b) N.R. c) 6 months = 3.3 d) 6 months = 2.83 e) 6 months = 3.02 f) 6 months = 2.64	a) 6 months = 61.9 b) 6 months = 49.18 c) N.R. d) N.R. e) N.R. f) N.R.	a) N.R. b) N.R. c) N.R. d) N.R. e) N.R. f) N.R.

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
Laleman et al. 2015	1, 2, 3, 6 months	3 months = 1.34 6 months = 1.62	3 months = 1.54 6 months = 1.82	3 months = 2.41 6 months = 3.43	3 months = 0.70 6 months = 0.75	3 months = 0.92 6 months = 0.98	3 months = 1.39 6 months = 1.82	3 months = 57 6 months = 60	1 month = 52.9 3 months = 48.3 6 months = 40.1
Machion et al. 2004	45 days, 3 and 6 months	45 days= 1.5 3 months = 1.62 6 months = 1.76	N.R.	N.R.	N.R.	N.R.	N.R.	45 days = 28 3 months = 35 6 months = 36	N.R.
Mohammad et al. 2005	3, 6, 9 months	N.R.	3 months = 0.63 6 months = 0.67	3 months = 0.75 6 months = 0.81	N.R.	3 months = 0.33 6 months = 0.33	3 months = 0.20 6 months = 0.23	3 months = 13.7 6 months = -5.9	
Monzavi et al. 2016	1 and 3months	1 month = 0.42 3 months = 0.63	N.R.	N.R.	1 month = 0.93 3 months= 1.55	N.R.	N.R.	1 month = 60 3 months = 52	N.R.
Nogueira-Filho et al. 2010	7, 15, 30, 60 and 90 days	1 month = 1.07 3 months = 1.1	N.R.	N.R.	1 month = 1.07 3 months = 1.3	N.R.	N.R.	N.R.	N.R.
Oteo et al. 2010	1, 3, 6 months	1 month = 0.22 3 months = 0.42 6 months = 0.27	N.R.	N.R.	1 month = 0.03 3 months = 0.65 6 months = 0.24	N.R.	N.R.	1 month = 22.08 3 months = 21.88 6 months = 18.31	N.R.
Palmer et al. 1998	2 months, 6 months	N.R.	N.R.	N.R.	2 months = 0.36 6 months = 0.51	N.R.	N.R.	N.R.	N.R.
Pera et al. 2012	3, 6 months	3 months = 1.7 6 months = 2.2	3 months = 1.8 6 months = 2.2	3 months = 2.7 6 months = 3.7	3 months = 1.4 6 months = 1.6	3 months = 1.4 6 months = 1.7	3 months = 2.1 6 months = 2.7	N.R.	N.R.

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
Pradeep & Kathariya et al. 2011	1, 3, 6, 9 months	1 month = 0.69 3 months = 1.16 6 months = 1	N.R.	N.R.	1 month = 0.51 3 months = 0.93 6 months = 0.86	N.R.	N.R.	N.R.	1 month = 1.71 3 months = 1.72 6 months = 1.5
Rusu et al. 2017	3, 6 months	3 months = 1.45 6 months = 1.43	N.R.	N.R.	3 months = 1.44 6 months = 1.33	N.R.	N.R.	3 months =38.91 6 months = 41.69	N.R.
Saglam et al. 2014	1, 3, 6 months	1 month = 0.7 3 months = 0.8 6 months = 0.8	N.R.	N.R.	1 month = 0.7 3 months = 0.8 6 months = 0.9	N.R.	N.R.	1 month = 55 3 months = 67 6 months = 52	1 month = 0.6 3 months = 0.8 6 months = 0.6
Sakellari et al. 2010	3, 6 months	3 months = 2.61 6 months = 2.05	N.R.	N.R.	3 months = 1.23 6 months = 1.4	N.R.	N.R.	3 months = 41 6 months = 33	N.R.
Sanz-Sanchez et al. 2015	3, 6 months	3 months = 0.41 6 months = 0.45	N.R.	N.R.	3 months = 0.32 6 months = 0.29	N.R.	N.R.	3 months = 24 6 months = 30	N.R.
Taiete et al. 2016	3 and 6 months	3 months = 2.2 6 months = 2.1	3 months = 1.6 6 months = 1.5	3 months = 2.9 6 months = 3	3 months = 1.4 6 months = 1.5	3 months = 1 6 months = 0.9	3 months = 2 6 months = 2.2	N.R.	N.R.
Theodoro et al. 2018	3, 6 months	3 months = -0.65 6 months = 0.34	3 months = 0.66 6 months = 0.68	3 months = 2.04 6 months = 2.40	3 months = 0.17 6 months = 0.21	3 months = 0.52 6 months = 0.68	3 months = 2.19 6 months = 2.38	3 months = 7.36 6 months = 7.56	N.R.
Üstün et al. 2018	1, 3 and 6 months	1 month = 1.095 3 months = 1.76 6 months = 1.945	N.R.	N.R.	1 month = 0.705 3 months = 0.885 6 months = 1.12	N.R.	N.R.	1 month = 27.2 3 months = 36.25 6 months = 44.6	1 month = 0.585 3 months = 0.735 6 months = 0.765

Main Author	Follow up Evaluations	PPD change all	PPD change 4-5 mm	PPD change ≥ 6 mm	CAL change all	CAL change 4-5 mm	CAL change ≥ 6 mm	BOP change	GI change
Vitt et al. 2019	2 weeks, 1, 4, 6 and 12 months	N.R.	1 month = 0.6 4 months = 0.3 6 months = 0.2	1 month = 0.9 4 months = 0.5 6 months = 0.2	N.R.	N.R.	N.R.	1 month = 9 4 months = 10 6 months = 11	N.R.

FIGURE 1 ***PRISMA flowchart.***

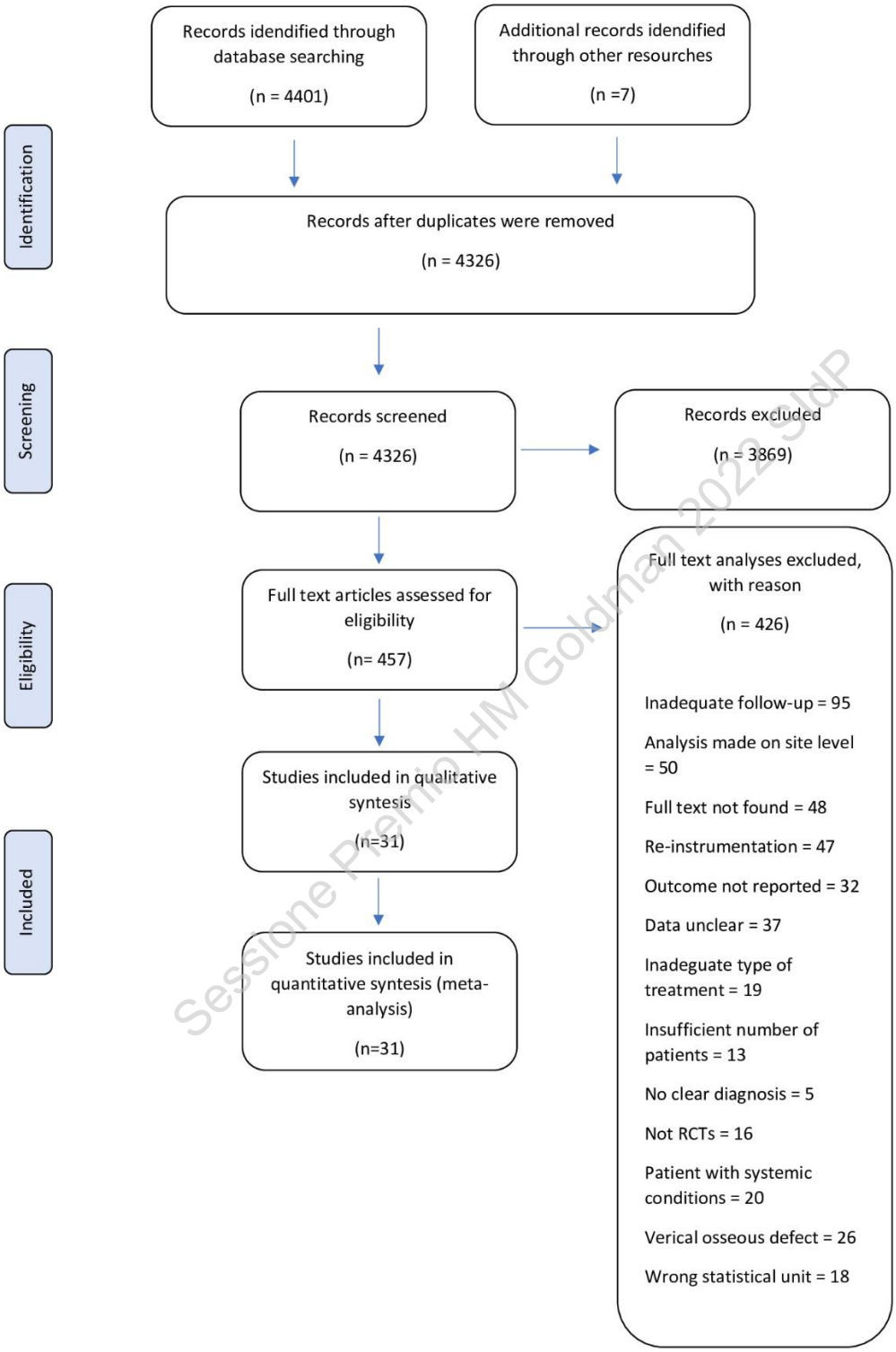


FIGURE 2 ***Risk of bias analysis.***

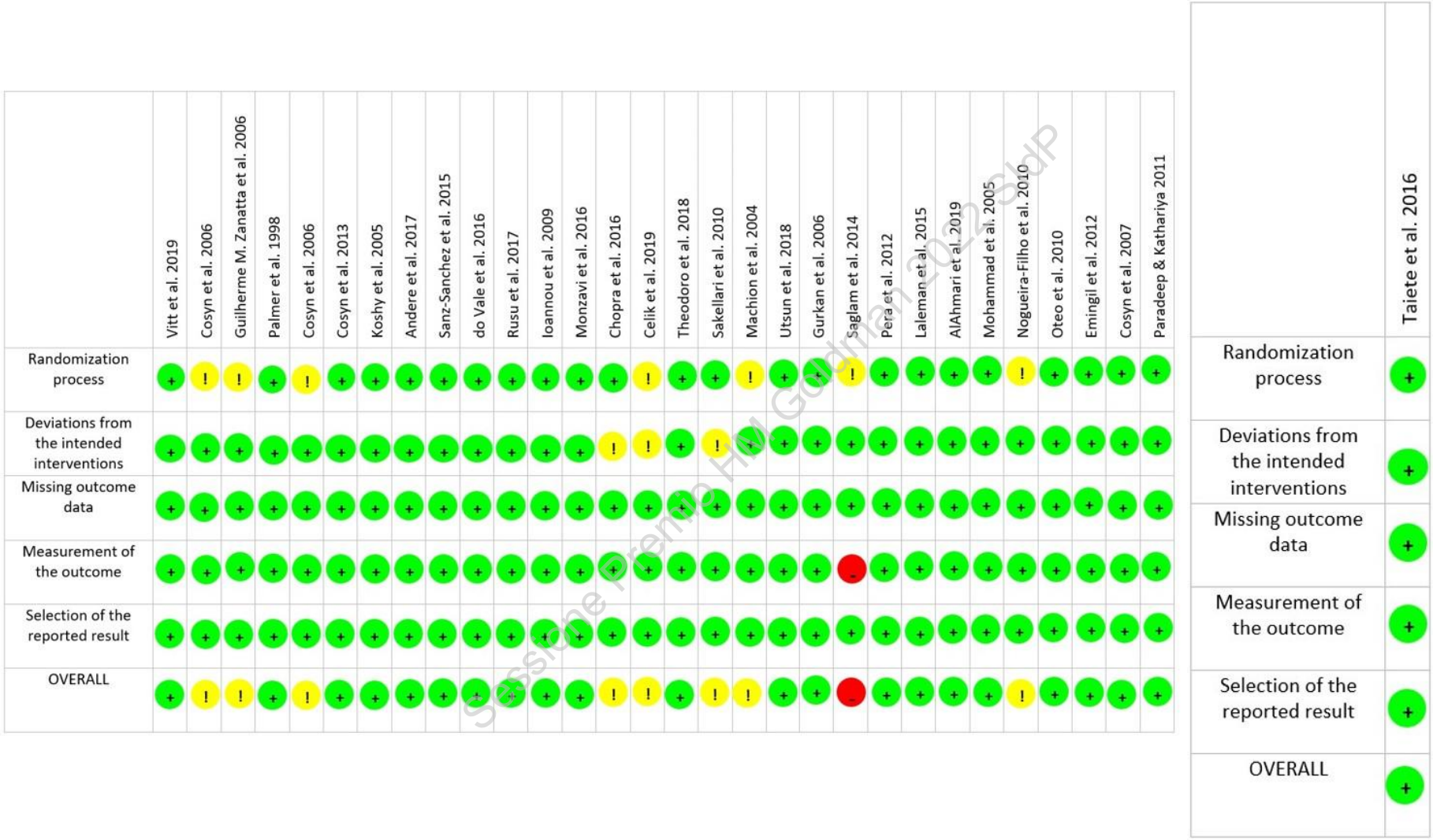
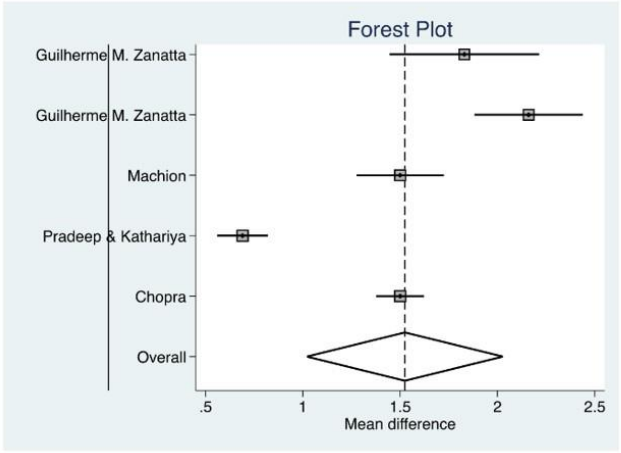
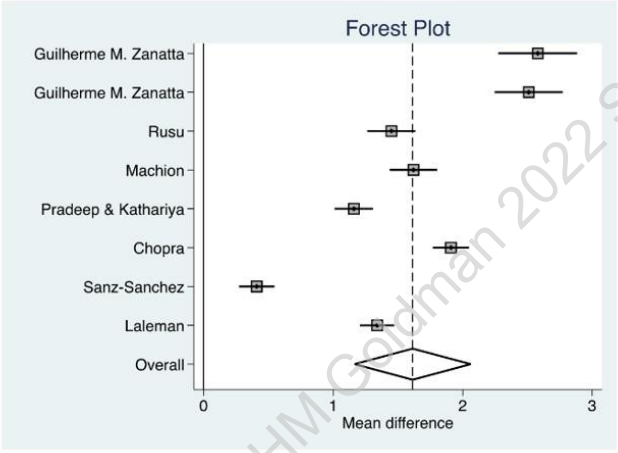


FIGURE 3 ***Weighted mean PPD reduction for all initial PPD values at different time-points.***

BASELINE VS 1-2 MONTHS



BASELINE VS 3-4 MONTHS



BASELINE VS 5-6 MONTHS

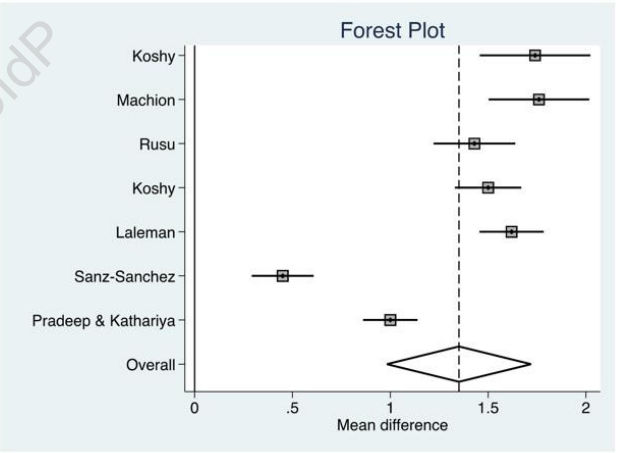


FIGURE 4 ***Weighted mean PPD reduction for shallow pockets (PPD 4-5 mm) at different time-points.***

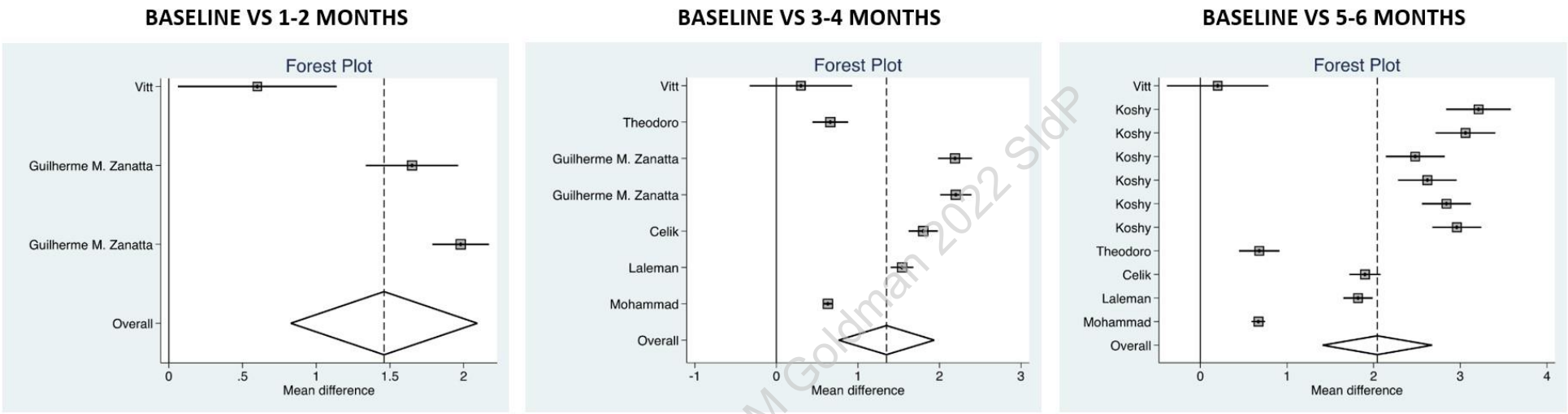
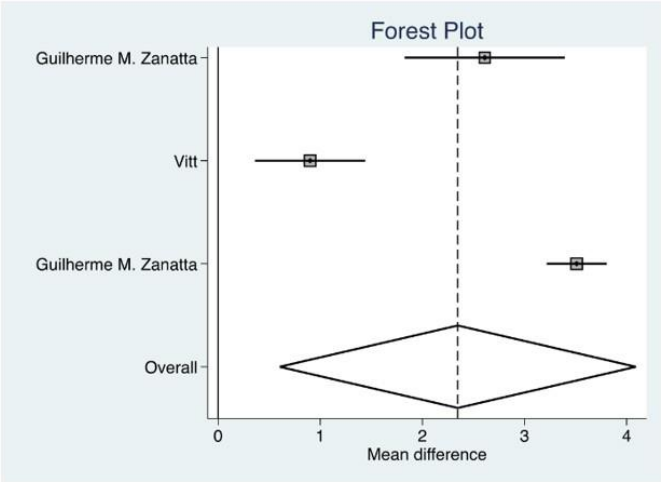
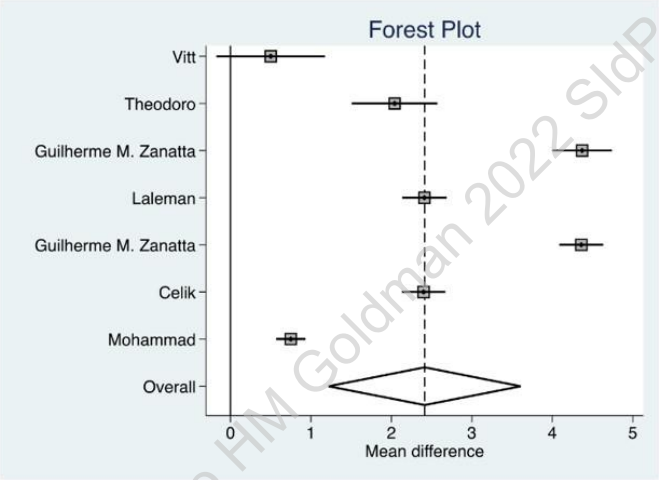


FIGURE 5 ***Weighted mean PPD reduction for deep pockets (PPD ≥ 6 mm) at different time-points.***

BASELINE VS 1-2 MONTHS



BASELINE VS 3-4 MONTHS



BASELINE VS 5-6 MONTHS

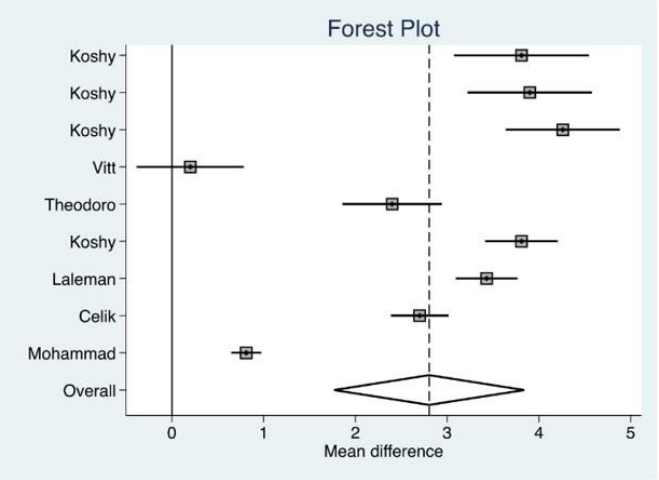


FIGURE 6 ***Histogram depicting PPD changes over time.***