

Locally delivered simvastatin and rosuvastatin in the treatment of chronic periodontitis: A systematic review and meta-analysis

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ABSTRACT: Purpose: This systematic review and meta-analysis evaluated the effectiveness of locally delivered simvastatin and rosuvastatin in the treatment of chronic periodontitis. **Methods:** A thorough literature review was performed utilizing PubMed, Scopus, Google Scholar, and ClinicalTrials.gov for studies published until June 2025. Titles, abstracts, and full texts of the eligible studies were obtained and reviewed. Data were subsequently extracted from the chosen studies and analyzed accordingly. **Results:** A total of 30 RCT studies with 1,211 participants were included. Our study showed that the local delivery of simvastatin and rosuvastatin significantly improved pocket depth [Weighted Mean Difference (WMD) 95% confidence interval (CI)] = -0.83, -1.31 respectively, $P < 0.001$), clinical attachment level (-1.20, -1.59, $P < 0.001$), gingival index (-0.60, -1.42, $P < 0.001$), modified sulcus bleeding index (-0.61, -0.36, $P < 0.001$), plaque index (-0.38, $P < 0.001$), and relative attachment level (-0.54, -0.89, $P < 0.001$). However, there was no significant association between the plaque index and the use of rosuvastatin (-0.20, $P < 0.05$). (*Am J Dent* 2026;39:125-133).

CLINICAL SIGNIFICANCE: The local delivery of simvastatin and rosuvastatin along with scaling and root planing significantly reduced pocket depth and improved clinical attachment level, gingival index, modified sulcus bleeding index, and relative attachment level. Further clinical trials are still required to support the results of the current meta-analysis.

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Introduction

Chronic periodontitis is an inflammatory condition initiated by a dysbiotic microbial biofilm that progressively destroys the tooth-supporting apparatus, including the periodontal ligament and alveolar bone. This inflammatory condition, often triggered by oral pathogens within a biofilm or plaque, leads to the progressive destruction of periodontal tissues.¹⁻³ Untreated cases often end up with greater tooth mobility and eventual tooth loss, leading to a major public health concern and a highly prevalent disease worldwide.^{4,5} Periodontopathogenic bacteria, the hosts' innate and adaptive immune responses, genetic predisposition, and unfavorable environmental factors all interact dynamically to cause periodontitis.⁶ Periodontitis is known to have systemic effects in addition to its localized ones on the oral cavity. Chronic periodontitis has a significant impact on a person's general health and quality of life, as evidenced by a growing body of research that connects it to several systemic conditions, including diabetes mellitus and cardiovascular diseases.⁷⁻¹⁰ Scaling and root planing (SRP), a non-surgical mechanical debridement procedure that aims to dismantle the microbial biofilm matrix and remove calculus deposits, is the gold standard for treating chronic periodontitis.^{10,11} The intricate structure of furcation spaces and the invasive potential of some bacteria into gingival epithelial cells and sub-epithelial connective tissue, however, can limit the effectiveness of SRP alone, especially when treating deep periodontal pockets and advanced disease stages. This can result in bacterial regrowth and reinfection, so the investigation of adjunctive therapeutic agents is necessary.^{12,13} Additionally, smokers, who have a major risk factor for periodontitis, frequently do not respond as well to non-surgical periodontal

therapy as non-smokers, showing less decrease in post-operative probing depth (PD) and clinical attachment level (CAL) gain.¹⁴ To overcome the limitations of mechanical therapy and enhance treatment outcomes, particularly in challenging cases like smokers or deep pockets, various adjunctive local drug delivery (LDD) systems have been developed. In comparison to systemic administration, LDD has several advantages, including the ability to achieve higher drug concentrations at the target site with lower dosages, fewer systemic side effects, and sustained release of the therapeutic agent into the periodontal pockets, all of which improve patient acceptability and compliance.^{15,16}

Statins, primarily known as inhibitors of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase for their cholesterol-lowering effects, have garnered a lot of study interest in periodontal therapy due to their pleiotropic effects. Important anti-inflammatory, antioxidant, immunomodulatory, and osteoinductive qualities are among these effects, which go beyond lipid reduction.^{17,18} By encouraging vascular endothelial growth factor (VEGF) and bone morphogenetic protein-2 (BMP-2), statins can promote osteoblast differentiation, supporting tissue repair and bone formation. They also exert anti-inflammatory effects by suppressing inflammatory mediators like C-reactive protein, interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α).¹⁹⁻²¹ Among them, simvastatin and rosuvastatin have been investigated for their potential to enhance periodontal regeneration and improve clinical outcomes when delivered locally as an adjunct to SRP, forming the basis of this investigation. Simvastatin (SMV), a lipid-lowering drug of the statin group, has demonstrated anti-inflammatory and anabolic effects on bone.^{22,23} Despite its advantages, SMV is poorly water-soluble, which

Table 1. Search Strategy for present systematic review and meta-analysis.

Search engine	Search strategy	Additional filter / Date
PubMed	((simvastatin[Title/Abstract]) OR (rosuvastatin[Title/Abstract]))AND (periodont*[Title/Abstract]) AND ((local*[Title/Abstract]) OR (locally[Title/Abstract]))	June 5th, 2025
Scopus	(TITLE-ABS-KEY (simvastatin) OR TITLE-ABS-KEY (rosuvastatin)) AND (TITLE-ABS-KEY (periodont*) AND (TITLE-ABS-KEY (local*) OR TITLE-ABS-KEY (locally))	June 5th, 2025
Google scholar	allintitle: periodontitis local* rosuvastatin OR simvastatin allintitle: periodontitis locally rosuvastatin OR simvastatin	June 5th, 2025
Clinicaltrials.gov	Condition/disease: chronic periodontitis Intervention/treatment: simvastatin Condition/disease: chronic periodontitis Intervention/treatment: rosuvastatin	June 5th, 2025

limits its penetration through the gingival sulcus and results in low oral bioavailability.²³ Numerous randomized controlled trials (RCTs) have specifically investigated the efficacy of locally delivered simvastatin. These studies have consistently reported that the application of a simvastatin gel as an adjunct to scaling and root planing (SRP) results in statistically significant improvements in clinical parameters, including probing depth (PD) reduction, clinical attachment level (CAL) gain, and radiographic evidence of intrabony defect fill, when compared to SRP with a placebo.^{24,25} Studies^{14,26} with high-risk patient cohorts, including smokers and people with type 2 diabetes, have further supported the validity of these findings by showing improved therapeutic outcomes with adjunctive simvastatin. Rosuvastatin (RSV) is a synthetic, sulfur-containing, hydrophilic statin known for its high potency in inhibiting HMG-CoA reductase.²⁷⁻³⁰ Similar to SMV, RSV also exhibits important anti-inflammatory and osteoblastic differentiation properties.^{31,32} While all locally delivered statins, such as atorvastatin, rosuvastatin, and simvastatin, were better than SRP alone, a Bayesian network meta-analysis evaluating the statins themselves found no discernible differences. Rosuvastatin, however, may provide a slight edge in encouraging intrabony defect fill, according to the same analysis.³³ There is a growing body of research comparing the effectiveness of various locally administered statins. For instance, a study comparing 1.2% RSV and 1.2% atorvastatin (ATV) gels discovered that RSV significantly outperformed ATV in terms of PD reduction, CAL gain, and defect depth reduction.³⁴

Although there is preliminary evidence supporting the effectiveness of locally administered statins from individual randomized controlled trials, these studies are frequently hampered by methodological issues that cast doubt on the findings' generalizability. A strong approach to overcoming these obstacles can be found by a systematic review and meta-analysis.³⁵ Therefore, the objective of this systematic review and meta-analysis is to evaluate the clinical and radiographic efficacy of locally delivered simvastatin and rosuvastatin when used as adjuncts to scaling and root planing in the treatment of chronic periodontitis.

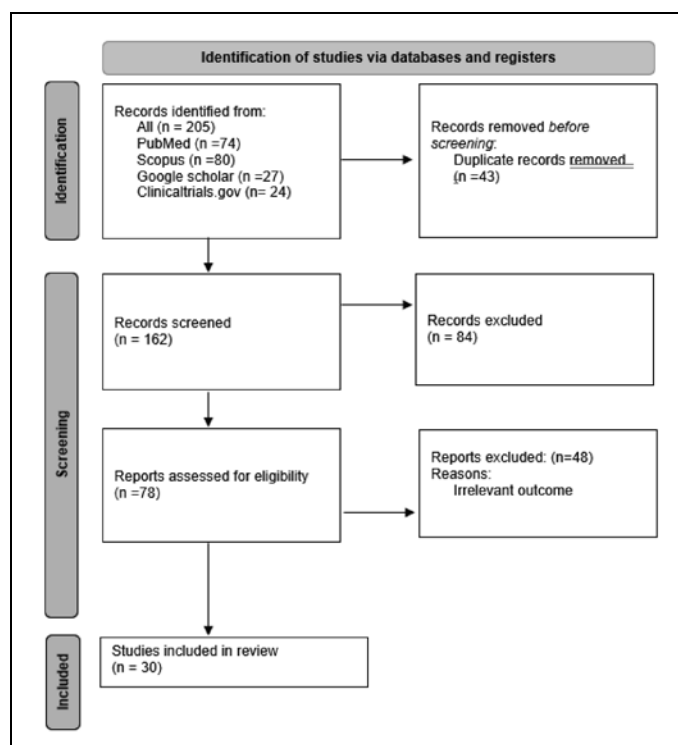


Fig. 1. Study identification, screening and inclusion process for this meta-analysis.

Materials and Methods

This systematic review and meta-analysis evaluated the therapeutic efficacy of locally administered Simvastatin and Rosuvastatin in the management of chronic periodontitis. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.³⁶

Search strategy - A thorough search of electronic databases, including PubMed, Scopus, Google Scholar, and ClinicalTrials.gov, was carried out up to June 5, 2025, to identify studies relevant to the review objective. The strategy was based on three clusters of Medical Subject Headings (MeSH) terms: one pertaining to local drug delivery, and the other two concerning simvastatin/rosuvastatin and chronic periodontitis. These clusters were combined using the Boolean operator "AND," and the search queries were tailored to match the syntax requirements of each individual database (Table 1, Fig. 1). No filters were applied regarding language, publication type, or time of publication. To ensure completeness, reference lists from previously published systematic reviews were also screened. All accessible studies were considered for inclusion. Each step of the screening process was independently performed by two reviewers, with any disagreements resolved through discussion.

Eligibility assessment - The initial screening involved independent evaluation of titles and abstracts by the authors to exclude studies unrelated to the effectiveness of locally delivered simvastatin or rosuvastatin in treating chronic periodontitis. Full texts of the remaining studies were then retrieved and closely examined alongside their reference lists to identify any additional eligible publications. Studies were included if they met the following criteria: (1) random-

Table 2. Baseline characteristics of included studies.

Author (year) ref	Study population	No. of participants	Intervention	Dose	Follow-up duration	Quality score
Pradeep et al (2013) ⁵⁹	CP	65	1.2% rosuvastatin gel	1.2mg	6 months	11/13
Agrawal et al (2016) ⁶⁰	CP	30	1.2% simvastatin gel	1.2mg	6 months	10/13
Jambhekar et al (2023) ⁶¹	Periodontitis	20	1.2% rosuvastatin gel+simvastatin 1.2%	2 mg	6 months	10/13
Panjak et al (2018) ⁶²	CP	90	1.2% rosuvastatin gel	1.2mg	1 year	12/13
Sharma et al (2023) ⁶³	CP	30	1.2% rosuvastatin gel +simvastatin 1.2%	1.2mg	6 months	9/13
Surve et al (2015) ⁶⁴	Moderate to severe chronic periodontitis	45	1.2% rosuvastatin gel +simvastatin 1.2%	1.2mg	6 months	11/13
Martande et al (2017) ⁶⁵	CP	88	1.2% simvastatin gel	10 µL	9 months	11/13
Ranjan et al (2017) ⁶⁶	Generalized chronic periodontitis	40	1.2% simvastatin gel	1.2mg	9 months	11/13
Priyanka et al (2017) ⁶⁷	Aggressive periodontitis	21	1.2% simvastatin gel	1.2mg	6 months	11/13
Rahman et al (2020) ⁶⁸	Grade A and Stage II periodontitis	15	1.2% simvastatin gel	1.2mg	3 months	10/13
Soni et al ⁶⁹	Chronic periodontitis	20	1.2% rosuvastatin gel + SRP	1.2 mg/0.1 mL	One-time + Coe-Pak	11/13
Shetty et al ⁷⁰	Chronic periodontitis with intrabony defects	18	1.2% simvastatin gel + SRP	1.2 mg/site	Single dose	12/13
Rao et al ⁷¹	Smokers with chronic periodontitis	35	1.2% simvastatin + SRP	1.2 mg/site	One-time at baseline	11/13
Pradeep et al ⁷²	Chronic periodontitis with intrabony defects	90	1.2% rosuvastatin gel + SRP	1.2 mg/0.1 ml	Single dose + Redose at 6months	10/13
Pradeep et al ⁵⁹	Chronic periodontitis	65	1.2% rosuvastatin gel + SRP	1.2 mg/0.1 ml	Single dose	11/13
Pawar et al ⁷³	Patients with generalized chronic periodontitis	30	1.2% rosuvastatin hydrogel + SRP	1.2% RSV hydrogel	Single application, 3-month follow-up	11/13
Killeen et al ⁷⁴	Periodontal maintenance patients with 6–9 mm residual pockets	50	1.2% simvastatin gel in methylcellulose (SIM/MCL) + mini-flap + SRP	2.2 mg (1.2 mg retained)	12-month follow-up	11/13
Vemanaradhya et al ⁴¹	Chronic periodontitis	46	1.2% simvastatin gel + SRP	1.2 mg/0.1 ml	Single dose (Day 0)	11/13
Garg et al ⁷⁵	CP patients with mandibular Class II furcation defects	90	1.2% rosuvastatin gel + SRP	1.2 mg/0.1 ml	Single dose + Redose at 6 months	10/13
Christiansen et al ⁷⁶	Chronic periodontitis with residual inflamed pocket (6-9 mm) under periodontal maintenance	50	2.2 mg simvastatin in methylcellulose (SIM/MCL) + mini-flap + SRP	2.2 mg, ~1.2 mg retained	Single application, follow-up at 12 months	9/13
Bashir et al ⁷⁷	Chronic periodontitis patients with ≥5 mm PPD	48	1.2% simvastatin gel + SRP	1.2 mg/0.1 ml	Single dose, 6-month follow-up	11/13
Gaewad et al. ⁷⁸	CP	20	1.2% simvastatin gel	1.2mg	6 months	11/13
Rath et al. ⁷⁹	CP	60	1.2% simvastatin gel	1.2mg	6 months	10/13
Halan et al. ⁸⁰	Stage II periodontitis	10	1.2% SMV gel vs Placebo gel as adjunct to SRP	1.2mg	3 months	12/13
Devi et al. ⁸¹	Moderate-to-severe periodontitis with bilateral interproximal intraosseous defects	15 (30 sites)	PRF alone vs PRF plus simvastatin	1.2mg	6 months	11/13
Ali et al. ⁸²	Chronic periodontitis	24	Simvastatin microsponges + debridement	6 mg/session	Weekly for 3 months	9/13
Rahman et al. ⁸³	Stage II Grade A periodontitis	11	1.2% simvastatin gel + SRP	1.2 mg/0.1 ml	Single dose	12/13
Meghana Devi et al. ⁸⁴	Moderate-to-severe periodontitis with bilateral intrabony defects	15	1.2% simvastatin gel + PRF	1.2 mg/0.1 ml	Single surgical placement, 6-mo. follow-up	12/13
Kanoriya et al. ⁸⁵	Smokers with chronic periodontitis	60	1.2% rosuvastatin gel + SRP	1.2 mg/0.1ml	One-time dose	10/13
Hasan et al. ⁸⁶	Gingivitis & periodontitis	10	1% simvastatin gel + SRP	1% gel	Weekly x4	11/13

ized controlled trial design; (2) involved human participants diagnosed with chronic periodontitis; (3) investigated local delivery of simvastatin or rosuvastatin; and (4) reported clinically relevant treatment outcomes. Exclusion criteria encompassed: (1) non-original studies such as reviews, meta-analyses, letters, or conference abstracts; (2) animal experiments; (3) irrelevant drug delivery routes; (4) reports without pertinent clinical data; (5) lack of full-text availability; and (6) duplicate or overlapping publications. All stages of study selection were independently conducted by two reviewers, with any inconsistencies addressed through mutual discussion.

Data synthesis and methodological appraisal - Information from the selected studies was independently collated by two reviewers, who organized the extracted content into four principal domains: (1) study characteristics; such as authorship, geographical setting, publication date, and type of study; (2) demographic attributes of the participants, including age and gender; (3) study design; including sample size, drug agent, dosage, and duration; and (4) clinical outcome measures;

gingival index (GI), plaque index (PI), modified sulcus bleeding index (MSBI), probing pocket depth (PD), clinical attachment level (CAL), and relative attachment level (RAL). To evaluate the internal validity and methodological rigor of the included randomized controlled trials, the same reviewers applied standardized critical appraisal tools developed by the Joanna Briggs Institute (JBI), which are publicly available at <https://jbi.global/critical-appraisal-tools>. Any disagreements were resolved through consultation with a third reviewer to ensure methodological alignment.

Statistical analysis - Pooled weighted mean differences (WMDs) were reported along with their corresponding variances and 95% confidence intervals. Incidence data from individual studies were combined using a weighted average, where study weights were inversely proportional to their variances. Heterogeneity among studies was assessed using the I² statistic and the Q test, with significance set at the 10% level. To stabilize variance, the Freeman-Tukey Double Arcsine Transformation was applied. Studies were considered heterogeneous if the I² value exceeded 50%. A random-effects model

was implemented using STATA^a software version 13.1. The Meta-prop command was employed to manage extreme proportions approaching 0 or 1, ensuring more reliable statistical interpretation. Finally, funnel plot symmetry and Eggers' regression test were used to evaluate the presence of potential publication bias.

Results

Study selection - A total of 205 articles through database searches: (PubMed/Medline = 74, Scopus = 80, Google Scholar = 27, and ClinicalTrials.gov = 24) were included. After software-assisted removal of 43 duplicates using Endnote, 21,162 records remained for title and abstract screening. Out of these, 84 were excluded for not meeting the inclusion criteria. Then, 78 full-text articles were reviewed for eligibility parameters and 48 articles were excluded due to having irrelevant outcomes. Finally, 30 studies were selected for inclusion in the systematic review and meta-analysis. The selection process is shown in the PRISMA 2020 flow diagram (Fig. 1).

Study characteristics - This study included 30 RCT studies involving 1,211 participants, spanning from 2012 to 2024. Except one in Pakistan, two in the USA and one in Egypt, all other studies were conducted in India and all published in the English language. The research focused on patients afflicted with periodontitis who administered 10 µg to 2 mg of rosuvastatin or simvastatin gel 1.2%. The follow-up period ranged from 3 months to 1 year (Table 2).

Simvastatin impact - According to the current meta-analysis, locally delivered 1.2% simvastatin significantly improved all clinical outcomes compared to the control group. It reduced CAL [WMD = -1.20, 95% CI (-1.41, -0.99)], PD [WMD = -0.83, 95% CI (-1.03, -0.63)], RAL [WMD = -0.54, 95% CI (-0.75, -0.33)], GI [WMD = -0.60, 95% CI (-0.76, -0.45)], mSBI [WMD = -0.61, 95% CI (-0.74, -0.48)], and PI [WMD = -0.38, 95% CI (-0.55, -0.20)]. All these results were statistically significant ($P < 0.001$). However, a high level of heterogeneity was observed across the included studies ($I^2 > 85\%$) (Fig. 2). Funnel plots were visually inspected to assess publication bias (Fig. 3). The plots were roughly symmetrical for most outcomes, especially for

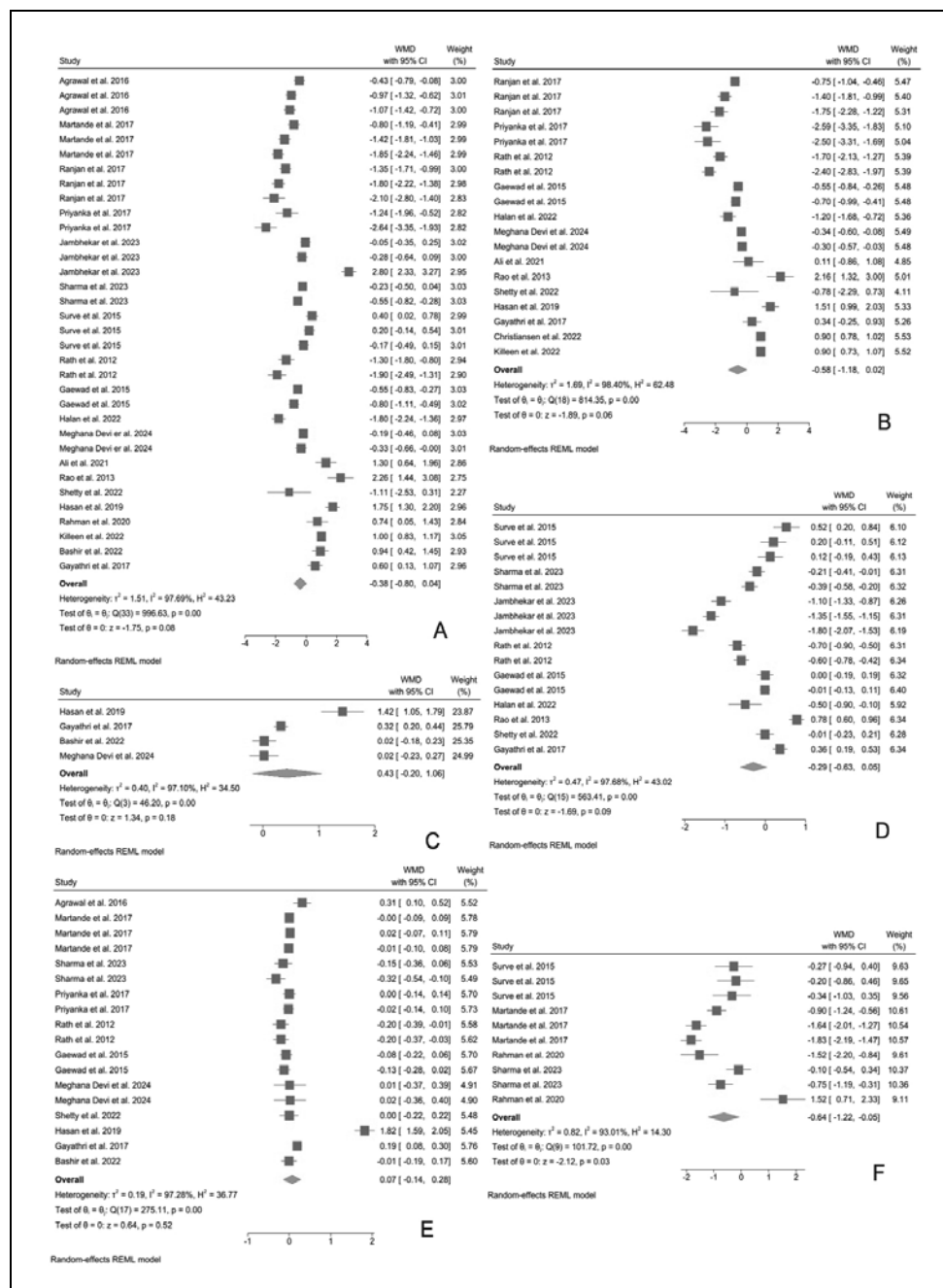


Fig. 2. Simvastatin mean effects on Periodontitis: A) PD: (WMD = -0.38, 95%CI = [-0.80, 0.04]), B) CAL: (WMD = -0.58, 95%CI = [-1.18, 0.02]), C) GI: (WMD = 0.43, 95%CI = [-0.20, 1.46]), D) MSBI: (WMD = -0.29, 95%CI = [-0.63, 0.05]), E) PI: WMD = 0.07, 95%CI = [-0.14, 0.28], F) RAL: (WMD = -0.64, 95%CI = [-1.22, -0.05]).

those with a higher number of studies. This suggests that there was no serious indication of publication bias.

Rosuvastatin impact - Similarly, the 1.2% rosuvastatin was significantly associated with decreased PD [WMD = -1.31, 95% CI = (-2.05, -0.58)], RAL [WMD = -0.89, 95% CI = (-1.59, -0.20)], GI [WMD = -1.42, 95% CI = (-2.36, -0.47)], MSBI [WMD = -0.36, 95% CI = (-0.47, -0.25)], and CAL [WMD = -1.59, 95% CI = (-2.73, -0.45)] ($P < 0.001$). In fact, the results show rosuvastatin significantly improved all clinical parameters except PI [WMD = -0.20, 95% CI = (-0.50, 0.10)], which showed a non-significant reduction. The heterogeneity varied from 42.5% to 99.1% (Fig. 4). Additionally, an Egger's

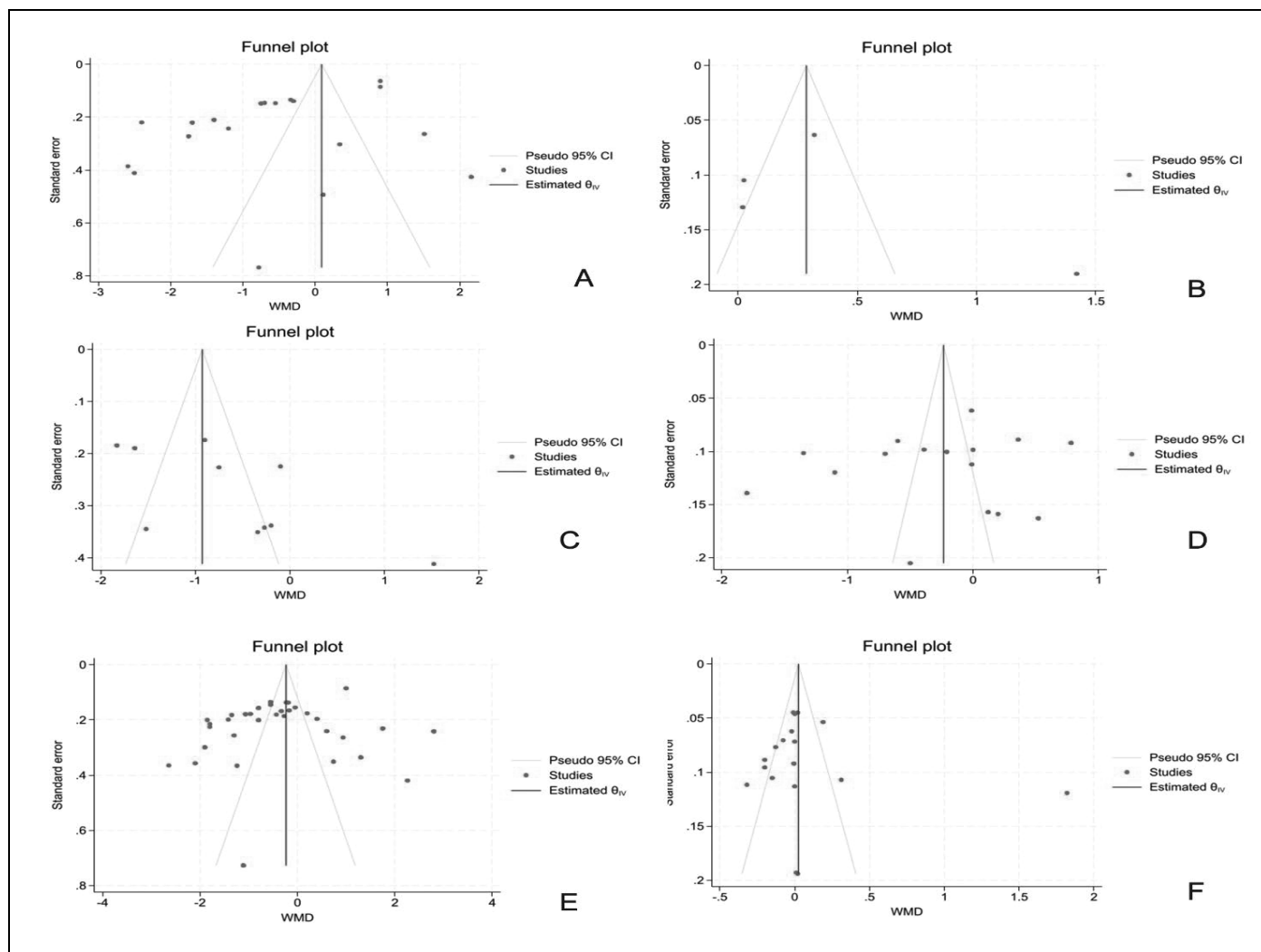


Fig. 3. Simvastatin mean and confidence level of its effects on Periodontitis. A) CAL B) GI C) RAL D) mSBI E) PD F) PI.

test and funnel plot analysis were used to identify any publication bias. Results from Fig. 5 demonstrate the funnel plot, which is symmetrical, indicating no evidence of publication bias.

Discussion

The present systematic review and meta-analysis evaluated locally delivered statins (simvastatin and rosuvastatin) in non-surgical treatment of chronic periodontitis. Based on the evaluation of 30 RCTs involving 1,211 subjects in total, statins topically applied locally in PD do significantly improve the main clinical outcomes in terms of PD, CAL, GI, and MSBI. There was no significant alteration in plaque index (PI) after treatment in either the simvastatin or the rosuvastatin groups. In other words, while they can be very helpful in treatment, those drugs cannot take the place of physically eliminating plaque.

Chronic periodontitis is a multifactorial inflammation of the tissue that begins with a bacterial infection, which initiates an immune response and ultimately causes damage to the tissues supporting the teeth and bone resorption.^{37,38} Conventional therapy of scaling and root planing (SRP) remains a primary treatment in periodontal therapy;³⁷ but its effectiveness could be limited, especially in pocket depth, furcation and hard-to-reach

areas, especially in patients with systemic comorbidities such as diabetes or tobacco consumption. Scaling and root planing may not be effective in deep gum pockets, furcation areas, and hard-to-reach spots, especially if there are health issues such as having diabetes or using tobacco.³⁸ Furthermore, the beneficial effects of SRP tend to decrease within 8-12 weeks after treatment as the bacteria come back, and it reverses the improvement of the treatment.³⁹ Additional drug therapy with antibiotics has been suggested to solve these issues. Oral antibiotics can be effective, but they can also have serious side effects, including allergies, stomach problems, harmful effects to the body, or an increased risk of antibiotic resistance.^{40,41} Local drug delivery systems (LDDs) are a better option as they place the medicine in the gum pockets themselves. In the context of local drug delivery systems, statins have been highly sought after because of their pleiotropic effects. In addition to reducing lipids by inhibiting HMG-CoA reductase, statins also have anti-inflammatory, antioxidant, anti-thrombotic, immunomodulatory, antimicrobial, angiogenic, and bone-anabolic effects that contribute to how they work in treatment.⁴²⁻⁴⁴ These attributes render statins a useful alter-native for use in combination with other treatments in periodontal therapy. Delivering statins directly to the gums enhanced

healing, diminishes side effects throughout the body and simplifies medications for patients.

As a lipophilic statin, simvastatin boosts osteoblast activity (bone-forming cells), raises the level of vascular endothelial growth factor (VEGF) in periodontal ligament cells, as well as increases the production of BMP-2. These processes enhance the formation of new bone and blood vessels (osteogenesis and angiogenesis), both vital to achieve healing and tissue regeneration in periodontal therapy.⁴⁵⁻⁴⁷ Also, unlike other statins, simvastatin seems to restrain the expression of pro-inflammatory mediators such as inducible nitric oxide synthase (iNOS), MMP-1, MMP-8, RANK, and RANKL in periodontal tissues.⁴⁶ All these actions work in tandem to slow the rate of bone loss and enhance tissue healing. In addition, being hydrophobic allows simvastatin to attack membranes of bacteria, leading to their death, especially key periodontal culprits such as *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis*.⁴⁸ A hydrophilic statin, rosuvastatin, has shown strong anti-inflammatory activity by reducing the expression of TLR4 on monocytes and the circulating levels of TNF- α .⁴⁹

This broad therapeutic potential for both cardiovascular and periodontal diseases can be seen with statins as well. These are known to improve endothelial function because of the added benefits of decreased oxidative stress and subendothelial LDL.^{49,50} On the other hand, isoprenoid synthesis blockade on the mevalonate pathway is what allows statins to reduce periodontal inflammatory processes. These isoprenoids, which include farnesyl pyrophosphate and geranylgeranyl pyrophosphate, serve vital functions in prenylation of small GTP binding proteins such as RHO and RAS, which are critical in controlling the inflammatory cytokine production, so their presence in the form of inactive oligomers enables the regulation. Through inhibiting the pathways, statins attenuate the synthesis of pro-inflammatory cytokines such as IL-1, IL-6, and IL-8, thus diminishing the inflammatory response in periodontal tissues.^{51,52} The present results corroborate previous findings where the use of 1.2% statin gels locally resulted in significant improvements in periodontal health. For instance, Pradeep et al⁵³ showed that simvastatin and rosuvastatin administered subgingivally led to an enhancement in clinical attachment levels (CAL) and a decrease in probing depth (PD) in patients suffering from chronic periodontitis. Studies,^{54,55} also showed that simvastatin was effective in alveolar bone regeneration and restoring the imbalance of bacteria within den-

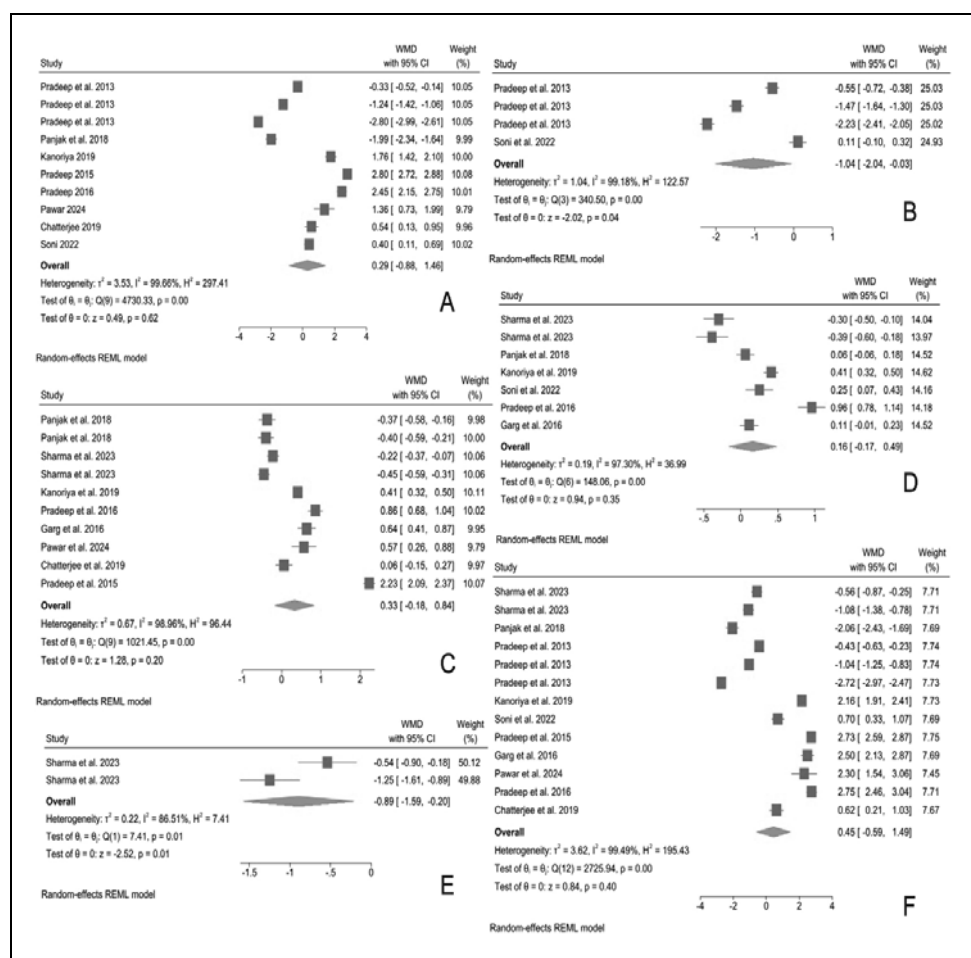


Fig. 4. Rosuvastatin mean effects on Periodontitis; A) CAL: WMD = 0.29, 95%CI = [-0.88, 1.46], B) GI: WMD = -0.55, 95%CI = [-1.04, -0.03], C) MSBI: WMD = 0.33, 95%CI = [-0.18, 0.84], D) PI: WMD = 0.16, 95%CI = [-0.17, 0.49], E) RAL: WMD = -0.89, 95%CI = [-1.59, -0.20], F) PD: WMD = 0.45, 95%CI = [-0.59, 1.49].

tal plaque biofilms.^{54,55}

Both statins had a minimal impact on plaque index (PI), which is quite interesting. That implies they aid in improving the body's response and healing, but do not reduce plaque formation directly. This demonstrates the need to combine these medications with proper cleaning and oral hygiene. In a clinical context, the findings of this review suggest that statins may augment the non-surgical periodontal treatment significantly with other systemic risk factors, or when mechanical debridement is the only option. In terms of controlling inflammation and bone regeneration, rosuvastatin may deliver better results due to its pharmacokinetic and pharmacodynamic characteristics, claim other researchers. Also, more recent research indicates statins might aid in modulating the body's defenses. For instance, Bradley et al⁶⁵ demonstrated that simvastatin uses locally mitigated inflammation and bone resorption around the teeth.

Studies^{53,56,57} also showed that simvastatin supported bone repair and controls inflammation by influencing specific genes. In conclusion, our meta-analysis shows strong evidence that using simvastatin and rosuvastatin alongside regular treatment can help manage chronic periodontitis. These drugs have many helpful effects, such as reducing inflammation, promoting bone growth, regulating the immune system, and fighting bacteria,

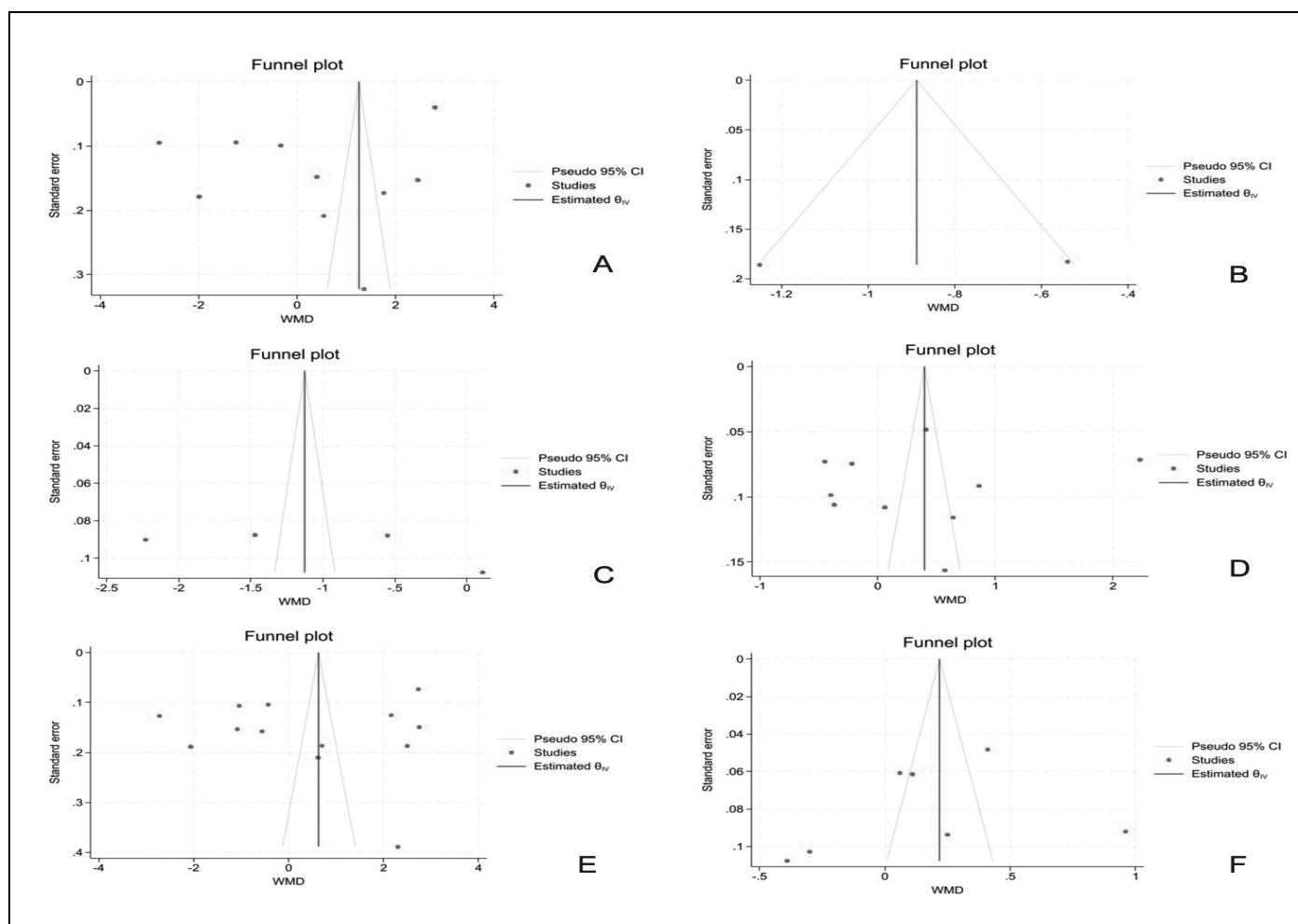


Fig. 5. Rosuvastatin mean and confidence level of its effects on Periodontitis. A) CAL B) RAL C) GI D) mSBI E) PD F) PI.

which leads to better clinical results when applied directly to the affected areas. Applying the drugs locally also has benefits like higher drug levels where needed, less breakdown by the body, and fewer side effects, which can help patients stick to their treatment. Although the current results are encouraging, more large and long-term studies are needed to find the best doses, delivery methods, and to confirm lasting benefits for more patients.⁵⁸ Simvastatin also aids bone repair and regulates inflammation by acting on certain genes.^{53,56,57} With that in mind, our meta-analysis clearly illustrates that the use of simvastatin and rosuvastatin in conjunction with standard treatment may prove beneficial for managing chronic periodontitis. The medications possess numerous beneficial properties, such as mitigating inflammation, enhancing osteogenesis, modulating immunity, and antibacterial action, which in turn lead to improved clinical outcomes when dosed directly into the lesions. Local administration also results in higher concentrations of the drug at the target site, reduced metabolic degradation by the body, fewer peripheral effects, and generally greater patient compliance. While these results are promising, there is a need for more extensive and prolonged research to determine the optimal therapeutic levels and administration routes and to establish durable benefits for a broader patient population.

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