ADA CE Program ARTICLE 2

Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts

Christopher J. Smiley, DDS; Sharon L. Tracy, PhD; Elliot Abt, DDS, MSc, MS; Bryan S. Michalowicz, DDS; Mike T. John, Dr med dent, PhD, MPH; John Gunsolley, DDS, MS; Charles M. Cobb, DDS, PhD; Jeffrey Rossmann, DDS, MS; Stephen K. Harrel, DDS; Jane L. Forrest, EdD; Philippe P. Hujoel, DDS, MSD, MS, PhD; Kirk W. Noraian, DDS, MS, MBA; Henry Greenwell, DMD, MSD; Julie Frantsve-Hawley, PhD; Cameron Estrich, MPH; Nicholas Hanson, MPH

ABSTRACT

Background. Conduct a systematic review and meta-analysis on nonsurgical treatment of patients with chronic periodontitis by means of scaling and root planing (SRP) with or without adjuncts.

Methods. A panel of experts convened by the American Dental Association Council on Scientific Affairs conducted a search of PubMed (MEDLINE) and Embase for randomized controlled trials of SRP with or without the use of adjuncts with clinical attachment level (CAL) outcomes in trials at least 6 months in duration and published in English through July 2014. The authors assessed individual study bias by using the Cochrane Risk of Bias Tool and conducted meta-analyses to obtain the summary effect estimates and their precision and to assess heterogeneity. The authors used funnel plots and Egger tests to assess publication bias when there were more than 10 studies. The authors used a modified version of the US Preventive Services Task Force methods to assess the overall level of certainty in the evidence.

Results. The panel included 72 articles on the effectiveness of SRP with or without the following: systemic antimicrobials, a systemic host modulator (subantimicrobial-dose doxycycline), locally delivered antimicrobials (chlorhexidine chips, doxycycline hyclate gel, and minocycline microspheres), and a variety of nonsurgical lasers (photodynamic therapy with a diode laser, a diode laser, neodymium:yttrium-aluminum-garnet lasers, and erbium lasers).

Conclusions and Practical Implications. With a moderate level of certainty, the panel found approximately a 0.5-millimeter average improvement in CAL with SRP. Combinations of SRP with assorted adjuncts resulted in a range of average CAL improvements between 0.2 and 0.6 mm over SRP alone. The panel judged the following 4 adjunctive therapies as beneficial with a moderate level of certainty: systemic subantimicrobial-dose doxycycline, systemic antimicrobials, chlorhexidine chips, and photodynamic therapy with a diode laser. There was a low level of certainty in the benefits of the other included adjunctive therapies. The panel provides clinical recommendations in the associated clinical practice guideline.

Key Words. Antibiotics; chlorhexidine; evidence-based dentistry; lasers; MEDLINE; minocycline; periodontitis; root planing.

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Chronic periodontitis is a prevalent condition, affecting 47.2% of the adult US population aged 30 years or older.[1] Chronic periodontitis results in the loss of tooth-supporting connective tissue and alveolar bone and, if untreated, is a major cause of tooth loss in adults.[2] According to the Centers for Disease Control and Prevention and American Academy of Periodontology case definitions,[3] the prevalences of moderate and severe periodontitis are estimated as 30.0% and 8.5%, respectively, among US adults.[4]

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Clinicians are challenged daily with managing patients with periodontitis of varying extent and severity. Treatment options range from scaling and root planing (SRP) to SRP with adjunctive treatments to surgical interventions. In 2011, the Council on Scientific Affairs of the American Dental Association (ADA) resolved to develop a clinical practice guideline for the nonsurgical treatment of chronic periodontitis with SRP with or without adjuncts on the basis of a systematic review of the literature. This report summarizes the systematic review results and is intended to aid the clinician in making evidence-based treatment decisions regarding the nonsurgical management of chronic periodontitis and provides the evidence base for the companion clinical practice guideline.[5] An unabridged version of this systematic review is available online.[6]

We evaluated the effect of SRP alone and in combination with adjuncts. Clinical attachment level (CAL) was the sole outcome on which we compared the various treatments. We evaluated the following professionally applied or prescribed medical adjuncts: locally applied antimicrobials (chlorhexidine chips, doxycycline hyclate [DH] gel, and minocycline microspheres), nonsurgical use of lasers (diode, both photodynamic therapy [PDT] and non-PDT; neodymium:yttrium-aluminum-garnet [Nd:YAG]; and erbium), systemic antimicrobials, and systemic subantimicrobial-dose doxycycline (SDD). We considered systemic antimicrobials and systemic SDD separately because the latter appears to inhibit mammalian collagenase activity (matrix metalloproteinase 8) and not function as an antibiotic.[7,8] We did not consider experimental adjuncts, adjuncts not currently available in the United States, nonprescription (over-the-counter) adjuncts, or surgical treatments.

We addressed the following clinical questions, formatted in the Patient-Intervention-Comparator-Outcome style:

- Question 1: In patients with chronic periodontitis, does SRP (hand or ultrasonic), when compared with no treatment, supragingival scaling and polish (prophylaxis), or debridement, result in greater improvement of CAL?
- Question 2: In patients with chronic periodontitis, does the use of local antibiotics or antimicrobials, systemic antibiotics, combinations of local and systemic antibiotics, agents for biomodification or host modulation, or nonsurgical lasers as adjuncts to SRP, compared with SRP alone, result in greater improvement of CAL?

METHODS

Our group of authors, consisting of a multidisciplinary panel of subject matter experts and ADA staff methodologists convened by the ADA Council on Scientific Affairs, followed modified US Preventive Services Task Force methods to conduct this systematic review.[9] Details regarding methods specific to this review, including the full search strategy and inclusion and exclusion criteria, are presented elsewhere.[6] We searched 2 electronic databases (PubMed and Embase) and reviewed the references of selected systematic reviews to identify missed references. The search was first conducted in October 2012 and updated in July 2014.

We developed study inclusion and exclusion criteria through consensus. Briefly, we included randomized controlled trials if they were published after 1960, written in English, and reported changes in CAL at least 6 months after randomization. We chose CAL as a primary outcome because probing depth changes fail to capture the effect of nonsurgical treatment.[10-14] We included both parallel-arm and split-mouth studies. We excluded studies of aggressive periodontitis, as well as studies in which the adjunct was administered more than 1 week after SRP or was reapplied to progressing (worsening) tooth sites. We screened all citations and full-text articles independently and in duplicate (S.L.T., J.F.H., C.E., and N.H.). In cases of discrepancies, we made decisions via discussion with the rest of the panel.

Definitions. We defined SRP according to the Code on Dental Procedures and Nomenclature[15]:

- D4341, Periodontal scaling and root planing: "Root planing is the definitive procedure designed for the removal of cementum and dentin that is rough and/or permeated by calculus or contaminated with toxins or microorganisms."

SRP should be differentiated from supra- or subgingival debridement, again as defined in the Code on Dental Procedures and Nomenclature:

- D4355, Full mouth debridement: "The gross removal of calculus that interferes with the ability of the dentist to perform a comprehensive oral evaluation. This preliminary procedure does not preclude the need for additional procedures."

We excluded studies on debridement as the experimental treatment as well as studies using the terms *instrumentation*, *ultrasonic instrumentation*, *ultrasonic scaling*, or *subgingival scaling* to mean *debridement*.

Data extraction and critical appraisal of individual studies. In groups of 2 (1 ADA staff member and 1 panelist for each paper), the authors independently reviewed and extracted the relevant data from included studies and appraised each study with the Cochrane Risk of Bias Tool.[16] Details on the tool and summaries of the extracted data and critical appraisals are presented elsewhere.[6] In short, 6 domains are assessed and judged as

ABBREVIATION KEY. **ADA:** American Dental Association. **CAL:** Clinical attachment level. **CHX:** Chlorhexidine. **DH:** Doxycycline hyclate. **MM:** Minocycline microspheres. **Nd:YAG:** Neodymium:yttrium-aluminum-garnet. **Non-PDT:** Nonphotodynamic therapy. **PDT:** Photodynamic therapy. **RCT:** Randomized controlled trial. **SDD:** Subantimicrobial-dose doxycycline. **SRP:** Scaling and root planing.

TABLE 1

Level of certainty in the body of evidence included within the systematic review.*

LEVEL OF CERTAINTY IN EFFECT ESTIMATE	DESCRIPTION
High	**The body of evidence usually includes consistent results from well-designed, well-conducted studies in representative populations. This conclusion is unlikely to be affected strongly by the results of future studies.** This statement is established strongly by the best available evidence.
Moderate	**As more information becomes available, the magnitude or direction of the observed effect could change, and this change could be large enough to alter the conclusion.** This statement is based on preliminary determinations from the current best available evidence, but confidence in the estimate is constrained by 1 or more factors, such as the following: - Limited number or size of studies - Plausible bias that raises some doubt about the results - Inconsistency of findings across individual studies - Imprecision in the summary estimate - Limited applicability because of the populations of interest - Evidence of publication bias - Lack of coherence in the chain of evidence
Low	**More information could allow a reliable estimation of effects on health outcomes.** The available evidence is insufficient to support the statement, or the statement is based on extrapolation from the best available evidence. The evidence is judged to be insufficient, or the reliability of estimated effects is limited by factors such as the following: - Limited number or size of studies - Plausible bias that seriously weakens confidence in the results - Inconsistency of findings across individual studies - Imprecision in the summary estimate - Gaps in the chain of evidence - Findings not applicable to the populations of interest - Evidence of publication bias - Lack of information on important health outcomes

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low, unclear, or high risk of bias. Furthermore, a summary assessment risk of bias of the outcome across domains and across studies was conducted according to the Cochrane Handbook.[17] We extracted information concerning adverse effects, which are described fully in the clinical practice guideline[5] associated with this systematic review and in the unabridged version.[6]

Data synthesis and meta-analysis: evaluating the effect of the intervention. We decided to use CAL as the primary outcome to compare the effectiveness of various periodontal therapies. We chose to subgroup results on the basis of trial design. We chose not to stratify the studies according to levels of disease at baseline. In assessing the effectiveness of SRP alone (question 1), we compared mean change in CAL between SRP and controls. To assess adjuncts (question 2), we compared mean changes between groups receiving SRP and those receiving SRP plus an adjunct. We conducted meta-analyses by using the random effects model.

We noted inconsistency among studies regarding the number of tooth sites and teeth assessed. Investigators in some studies reported data for periodontal sites, whereas others reported data at the tooth level and whole-mouth averages. Whole-mouth measurements may lead to underestimation of the treatment effect by including healthy sites in the computation of teeth or mouth averages or of changes over time. The estimates in the meta-analyses include studies in which the investigators reported at these different levels of assessment.

Determining the level of certainty in the evidence. We reviewed overall results for each treatment or adjunct and assessed the level of certainty in the evidence as *high*, *moderate*, or *low* (Table 1).[9]

RESULTS

Literature search and screening. The initial search yielded 1,681 unique records after duplicates were removed. After the updated search, we screened 1,944 records by title and abstract and 483 by full text. We included 72 studies in the final analyses. We found no additional citations through reviewing references of relevant systematic reviews. Characteristics of included and excluded studies, including reasons for exclusion, are available elsewhere.[6] Figure 1 shows the study flow diagram.

Evidence summary. Tables 2 and 3 present evidence profile summaries from the 72 included studies of 10 nonsurgical treatments. Further detailed information regarding the critical appraisals and extracted study information is available elsewhere.[6]

SRP. ***General description of studies.*** Eleven studies met the inclusion criteria for reporting the effect of SRP compared with no treatment, supragingival scaling, or debridement on chronic periodontitis.[18-28] Six were split-mouth studies,[18-23] and 5 were parallel-group studies.[24-28] All studies were small (from 7 to 43 per group). The studies were published between 1983 and 2014. One study[24] included only participants with type 2 diabetes, and another[28] only participants with chronic obstructive pulmonary disease.

Critical appraisal. Figure 2 depicts the judgments of bias according to domain. We judged the overall risk of bias from this body of evidence as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with no treatment,

SRP treatment resulted in a 0.49-millimeter gain in CAL (95% confidence interval [CI], 0.36-0.62 mm) (Figure 3).[18-28] Two of the observations were outliers, with 1 study[20] having a large benefit and 1 study[25] having a small standard error; however, when we removed these 2 studies, the result remained statistically significant (0.43; 95% CI, 0.19-0.67). We judged the overall level of certainty in the evidence to be *moderate* on the basis of the evidence profile in Table 2.

Systemic SDD and SRP. ***General description of studies.*** SDD (Periostat, CollaGenex Pharmaceuticals) is considered a host-modulating agent. Specifically, it inhibits host collagen-degrading enzymes.[29,30] Eleven studies[31-42] in 12 publications met the inclusion criteria for reporting the effect of SRP plus SDD versus SRP alone. All were parallel-group trials. Sample sizes ranged from 7 to 133 per treatment group. The studies were published between 2000 and 2011. With respect to participants, investigators in 1 study included only institutionalized geriatric patients,[40] and investigators in 2 included adults with diabetes.[31,33]

Critical appraisal. eFigure 1 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias from this body of evidence as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus SDD resulted in a 0.35-mm mean gain in CAL (95% CI, 0.15-0.56) (Figure 4).[31-42] We judged the overall level of certainty in the evidence to be *moderate* on the basis of the evidence profile in Table 3.

Systemic antimicrobials and SRP. ***General description of studies.*** Twenty-four studies[18,20,22,39,43-62] met the inclusion criteria for reporting the effect of SRP plus a systemic antimicrobial versus SRP alone. All were parallel-group trials. The sample sizes were relatively small, ranging from 7 to 46 per treatment group. The studies were published between 1983 and 2014. Investigators in 2 studies included only patients with diabetes,[60,62] and investigators in 1 study[52] reported results subgrouped according to smoking status.

We decided to combine all antimicrobials into 1 treatment class for an overall analysis and 1 evidence profile. The study investigators reported on 6 major groups of antimicrobials: amoxicillin and metronidazole combination therapy,[18,44,45,47,50,55,60] metronidazole,[39,52,61] erythromycin analogues (azithromycin[39,46,49,51,56-59] and clarithromycin[53]), moxifloxacin[48] (a fourth-generation fluoroquinolone antibacterial agent), and others (for example, tetracycline[20,43,54] and doxycycline[22,48,62] as the antimicrobial dose of doxycycline, not to be confused with SDD, which is covered in a separate section). The variety of dosing regimens used for each systemic antimicrobial drug is described elsewhere.[6]

Critical appraisal. eFigure 2 (available online at the end of this article) depicts the judgments of bias

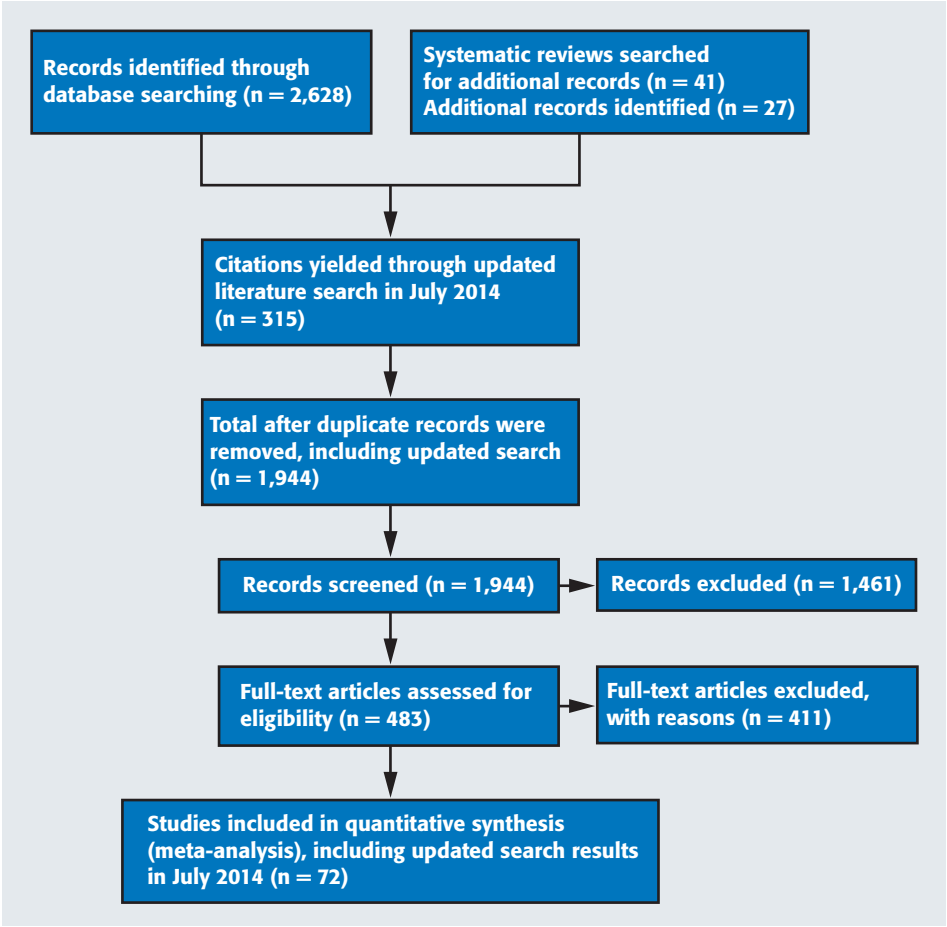

Figure 1. Flow diagram of literature search and screening process.

TABLE 2

Evidence profile summary: scaling and root planing versus no treatment, supragingival scaling, or debridement.

THERAPY	LEVEL OF CERTAINTY ASSESSMENT CRITERIA							LEVEL OF CERTAINTY	BENEFIT,‡ MILLIMETERS
	Quantity of Evidence		Risk of Bias	Consistency	Applicability†	Precision	Publication Bias		
	No. of RCTs*	No. of participants							
Scaling and Root Planing Versus No Treatment, Supragingival Scaling, or Debridement	11	331	Unclear	Consistent	Yes	No serious imprecision	None detected ($P = .707$)§	Moderate	0.49 (0.36-0.62)

* RCT: Randomized controlled trial.
† Applicability refers to whether the study results are applicable to populations of interest in real-world circumstances.
‡ Benefit is mean difference (95% confidence interval) in clinical attachment level.
§ When there were 10 or more studies for a treatment, the authors undertook an assessment of publication bias by means of visual inspection and an Egger test for funnel plot asymmetry. See the complete article for further details.

according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus systemic antimicrobials resulted in a 0.35-mm mean gain in CAL (95% CI, 0.20-0.51) (Figure 5).[18,20,22,39,43-62] We judged the overall level of certainty in the evidence to be *moderate* on the basis of the evidence profile in Table 3.

Locally delivered antimicrobials and SRP. ***Chlorhexidine chips and SRP.*** *General description of studies.* Investigators in 6 studies compared the effects of SRP plus the local delivery of chlorhexidine chips with SRP alone on chronic periodontitis.[63-68] Four were split-mouth studies,[63,65-67] and 2 were parallel-group studies.[64,68] All but 2 trials[66,67] had small sample sizes (ranging from 12 to 25 participants per group); the larger studies included between 82 and 116 participants per treatment arm. The studies were conducted from 2001 through 2011.

Critical appraisal. eFigure 3 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus chlorhexidine chips resulted in a 0.40-mm mean gain in CAL (95% CI, 0.24-0.56) (Figure 6).[63-68] We judged the overall level of certainty in the evidence to be *moderate* on the basis of the evidence profile in Table 3.

DH gel and SRP. *General description of studies.* Three small studies met the inclusion criteria for reporting the effect of SRP plus the local delivery of DH gel compared with SRP alone.[69-71] Two were split-mouth studies,[69,71] and 1 study[70] was a parallel-group trial. The sample sizes ranged from 10 to 22 participants per group. The studies were conducted between 2004 and 2006. All participants in the study by Martorelli de Lima and colleagues[71] had type 1 diabetes mellitus.

Critical appraisal. eFigure 4 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus DH gel resulted in a 0.64-mm mean gain in CAL (95% CI, 0.00-1.28) (Figure 7).[69-71] We judged the overall level of certainty in the evidence to be *low* on the basis of the evidence profile in Table 3.

Minocycline microspheres and SRP. *General description of studies.* Three small[27,72,73] and 2 relatively large and unpublished new drug application studies (Study 103A and Study 103B available in 1 document[74]) met the inclusion criteria for reporting the effect of SRP plus the local delivery of minocycline microspheres compared with SRP alone. The sample sizes in the small studies ranged from 10 to 15 participants per group, whereas the unpublished study sample sizes ranged from 121 to 128 per group. One study had a split-mouth design,[72] whereas the others were parallel-group studies. The studies were conducted between 2000 and 2004. All participants in the study by Skaleric and colleagues[73] had type 1 diabetes.

Critical appraisal. eFigure 5 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus minocycline microspheres resulted in a 0.24-mm mean gain in CAL (95% CI, −0.06 to 0.55) in Figure 8.[27,72-74] We judged the overall level of certainty

TABLE 3

Evidence profile summary: scaling and root planing with adjuncts versus scaling and root planing alone.

THERAPY	LEVEL OF CERTAINTY ASSESSMENT CRITERIA							LEVEL OF CERTAINTY	BENEFIT,‡ MILLIMETERS
	Quantity of Evidence		Risk of Bias	Consistency	Applicability†	Precision	Publication Bias		
	No. of RCTs*	No. of participants							
SRP§ and Systemic Subantimicrobial-Dose Doxycycline	11	813	Unclear	Moderate inconsistency	Yes	No serious imprecision	None detected ($P = .121$)¶	Moderate	0.35 (0.15-0.56)
SRP and Systemic Antimicrobials	24	1,086	Unclear	Substantial inconsistency	Yes	No serious imprecision	None detected ($P = .803$)¶	Moderate	0.35 (0.20-0.51)
SRP and Chlorhexidine Chips	6	316	Unclear	Consistent	Yes	No serious imprecision	Too few studies to assess	Moderate	0.40 (0.24-0.56)
SRP and Doxycycline Hyclate Gel	3	64	Unclear	Moderate inconsistency	Yes	Serious imprecision	Too few studies to assess	Low	0.64 (0.00-1.28)
SRP and Minocycline Microspheres	5	572	Unclear	Moderate inconsistency	Yes	Serious imprecision	Too few studies to assess	Low	0.24 (−0.06 to 0.55)
SRP and Diode Laser (PDT#)	10	306	Low	Inconsistent	Yes	Serious imprecision	None detected ($P = 0.679$)¶	Moderate	0.53 (0.06-1.00)
SRP and Diode Laser (non-PDT)	4	98	Unclear	Substantial inconsistency	Yes	Serious imprecision	Too few studies to assess	Low	0.21 (−0.23 to 0.64)
SRP and Nd:YAG** Laser	3	82	Unclear	Moderate inconsistency	Yes	Serious imprecision	Too few studies to assess	Low	0.41 (−0.12 to 0.94)
SRP and Erbium Laser	3	82	Low	Inconsistent	Yes	Serious imprecision	Too few studies to assess	Low	0.18 (−0.63 to 0.98)

* RCT: Randomized controlled trial.
† Applicability refers to whether the study results are applicable to populations of interest in real-world circumstances.
‡ Benefit is mean difference (95% confidence interval) in clinical attachment level.
§ SRP: Scaling and root planing.
¶ When there were 10 or more studies for a treatment, the authors undertook an assessment of publication bias by means of visual inspection and an Egger test for funnel plot asymmetry. See the complete article for further details.
# PDT: Photodynamic therapy.
** Nd:YAG: Neodymium:yttrium-aluminum-garnet.

in the evidence to be *low* on the basis of the evidence profile in Table 3.

Nonsurgical use of lasers and SRP. We analyzed all studies that met the inclusion criteria of nonsurgical application of a laser (pocket disinfection), and we did not consider studies in which the investigators used lasers for alternative surgical therapy. Several types of lasers are used nonsurgically as adjunctive treatments with SRP. The lasers are categorized primarily by the wavelength of the emitted light. Five categories of lasers are included and described here. One laser type was not available in the United States (potassium titanyl phosphate),[75] and we did not include that laser. There are no standard operating protocols (such as power intensity and density, power, spot size, energy, repetition rate, tip size, pulsing versus continuous mode, mean energy loss, or time of application) for the lasers.

PDT diode laser and SRP. *General description of studies.* Ten studies[75-84] published between 2008 and 2014 met the inclusion criteria for reporting the effect of SRP plus a PDT diode laser (wavelength, 660-810 nanometers) versus SRP alone. Six studies[75,76,79-82] were split-mouth trials, and 4 studies[77,78,83,84] were parallel-group trials. The sample sizes were relatively small, ranging from 12 to 44 per treatment group.

Critical appraisal. eFigure 6 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *low*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus PDT diode laser resulted in a 0.53-mm mean gain in

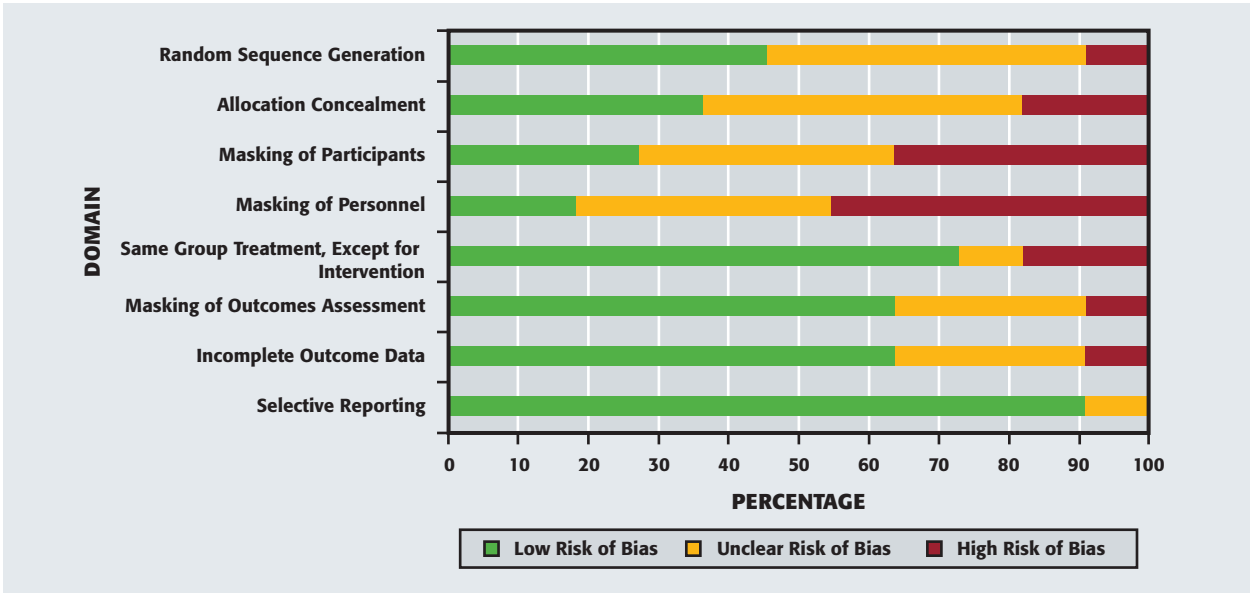

Figure 2. Risk of bias as a percentage of included studies for scaling and root planing according to domain.

Study or Subgroup	Mean Difference	SE	SRP Total	No Treatment Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Split mouth						
Lindhe and Colleagues,[20] 1983	1.8	0.63	7	7	1.1%	1.80 (0.57-3.03)
Neill and Mellonig,[21] 1997	0.8	0.59	10	10	1.3%	0.80 (−0.36 to 1.96)
Ng and Bissada,[22] 1998	0.5	0.29	8	8	5.2%	0.50 (−0.07 to 1.07)
Berglundh and Colleagues,[18] 1998	1	0.63	8	8	1.1%	1.00 (−0.23 to 2.23)
Kahl and Colleagues,[19] 2007	0.65	0.39	20	20	2.9%	0.65 (−0.11 to 1.41)
Rotundo and Colleagues,[23] 2010	0.3	0.51	26	26	1.7%	0.30 (−0.70 to 1.30)
Subtotal (95% CI)			79	79	13.3%	0.69 (0.33-1.04)
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 4.41$, $df = 5$, $P = .49$; $I^2 = 0\%$						
Test for overall effect: $z = 3.77$ ($P = .0002$)						
1.1.2 Parallel group						
Jones and Colleagues,[25] 1994	0.5	0.08	6	10	68.8%	0.50 (0.34-0.66)
Van Dyke and Colleagues,[27] 2002	0.3	0.3	12	13	4.9%	0.30 (−0.29 to 0.89)
Ribeiro and Colleagues,[26] 2008	−0.15	0.45	13	12	2.2%	−0.15 (−1.03 to 0.73)
Chen and Colleagues,[24] 2012 (versus debridement)	0.41	0.34	42	20	3.8%	0.41 (−0.26 to 1.08)
Chen and Colleagues,[24] 2012 (versus polish)	0.44	0.32	43	21	4.3%	0.44 (−0.19 to 1.07)
Zhou and Colleagues,[28] 2014 (versus no treatment)	0.88	0.62	10	20	1.1%	0.88 (−0.34 to 2.10)
Zhou and Colleagues,[28] 2014 (versus scale)	0.08	0.54	10	20	1.5%	0.08 (−0.98 to 1.14)
Subtotal (95% CI)			136	116	86.7%	0.46 (0.32-0.60)
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.35$, $df = 6$, $P = .76$; $I^2 = 0\%$						
Test for overall effect: $z = 6.50$ ($P < .00001$)						
Total (95% CI)			215	195	100%	0.49 (0.36-0.62)
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 9.05$, $df = 12$, $P = .70$; $I^2 = 0\%$						
Test for overall effect: $z = 7.42$ ($P < .00001$)						
Test for subgroup differences: $\chi^2 = 1.30$, $df = 1$, $P = .25$; $I^2 = 23.0\%$						

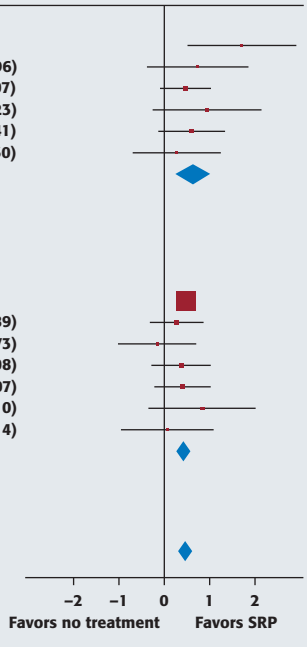

Figure 3. Meta-analysis of studies on scaling and root planing (SRP) grouped according to study design; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV, Inverse-variance; I. SE: Standard error.

CAL (95% CI, 0.06-1.00) (Figure 9).[75-84] We judged the overall level of certainty in the evidence to be *moderate* on the basis of the evidence profile in Table 3.

Non-PDT diode laser and SRP. *General description of studies.* Four studies[85-88] published between 2008 and 2014 met the inclusion criteria for reporting the effect

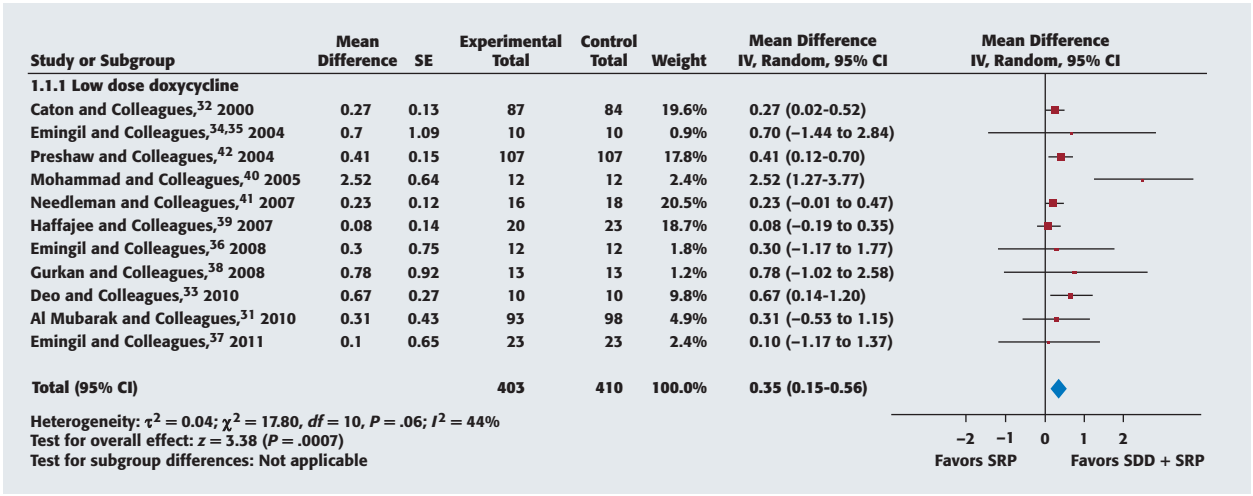

Figure 4. Meta-analysis of studies on scaling and root planing (SRP) plus subantimicrobial-dose doxycycline (SDD) versus SRP alone; mean difference in clinical attachment level is in millimeters. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

of SRP plus a non-PDT diode laser (wavelength, 808-980 nm). Three were split-mouth studies,[85,87,88] and 1 study[86] was a parallel-group study. Euzebio Alves and colleagues[85] tested only 1 site per mouth with each treatment. The sample sizes were relatively small, between 13 and 36.

Critical appraisal. eFigure 7 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus non-PDT diode laser resulted in a 0.21-mm mean gain in CAL (95% CI, −0.23 to 0.64) (Figure 10).[85-88] We judged the overall level of certainty in the evidence to be *low* on the basis of the evidence profile in Table 3.

Nd:YAG laser and SRP. *General description of studies.* Three studies[21,89,90] met the inclusion criteria for reporting the effect of SRP plus an Nd:YAG laser (wavelength, 1,064 nm). All were split-mouth studies with small sample sizes (10 to 26 participants). Investigators in 1 study[90] compared the effects of the addition of Nd:YAG lasers to SRP in smokers versus nonsmokers in 2 arms of the study.

Critical appraisal. eFigure 8 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *unclear*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus Nd:YAG laser resulted in a 0.41-mm mean gain in CAL (95% CI, −0.12 to 0.94) (Figure 11).[21,89,90] We judged the overall level of certainty in the evidence to be *low* on the basis of the evidence profile in Table 3.

Erbium laser and SRP. *General description of studies.* Three studies[23,91,92] published in 2010 and 2011 met the inclusion criteria for reporting the effect of SRP plus an erbium laser (either erbium,chromium:yttrium-scandium-gallium-garnet[91] or erbium:yttrium-aluminum-garnet,[23,92] with wavelengths of 2.79 and 2.94 µm, respectively). All were split-mouth studies with small sample sizes (19 to 33 participants).

Critical appraisal. eFigure 9 (available online at the end of this article) depicts the judgments of bias according to domain. We judged the overall risk of bias as *low*.

Results of intervention and assessment of the level of certainty in the evidence. Compared with SRP alone, SRP plus erbium laser resulted in a 0.18-mm mean gain in CAL (95% CI, −0.63 to 0.98) (Figure 12).[23,91,92] We judged the overall level of certainty in the evidence to be *low* on the basis of the evidence profile in Table 3.

Summary statements on nonsurgical use of lasers. Unlike other instruments, lasers have no defined and accepted protocols for standard usage. Because every operator determines his or her own protocol on the basis of anecdotal rules or experiences, the potential for adverse events to the tooth and patient is higher than it is with other local delivery systems. Also, every laser wavelength is different and affects the hard and soft tissues differently, making comparisons between lasers unpredictable and often incorrect. Common protocols are needed for each laser used in nonsurgical therapy of chronic periodontitis to allow for repeatable results and comparisons among studies in the literature. The wide ranges found in the few studies considered for CAL gain or loss demonstrate the need for larger sample sizes and additional studies to evaluate properly the potential benefits of laser use as an adjunct to SRP. At this time, on the basis of the criteria set in this systematic review, there is insufficient evidence with any laser wavelength except PDT diode lasers to define accurately the benefits for adjunctive nonsurgical therapy of periodontitis with evidence-based literature.

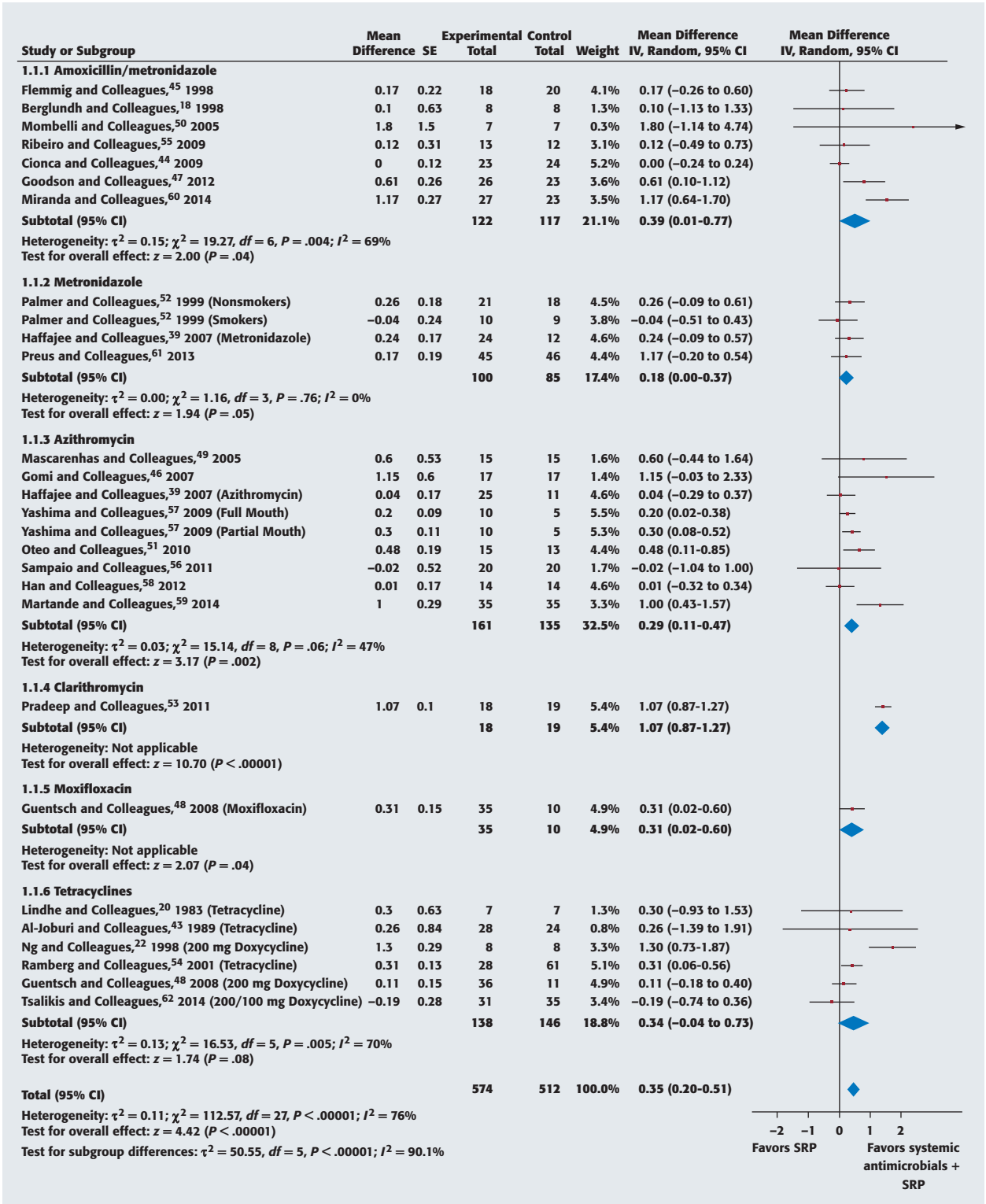

Figure 5. Meta-analysis of studies on scaling and root planing (SRP) plus systemic antimicrobials versus SRP alone, subgrouped according to antimicrobial type; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. mg: Milligrams. SE: Standard error.

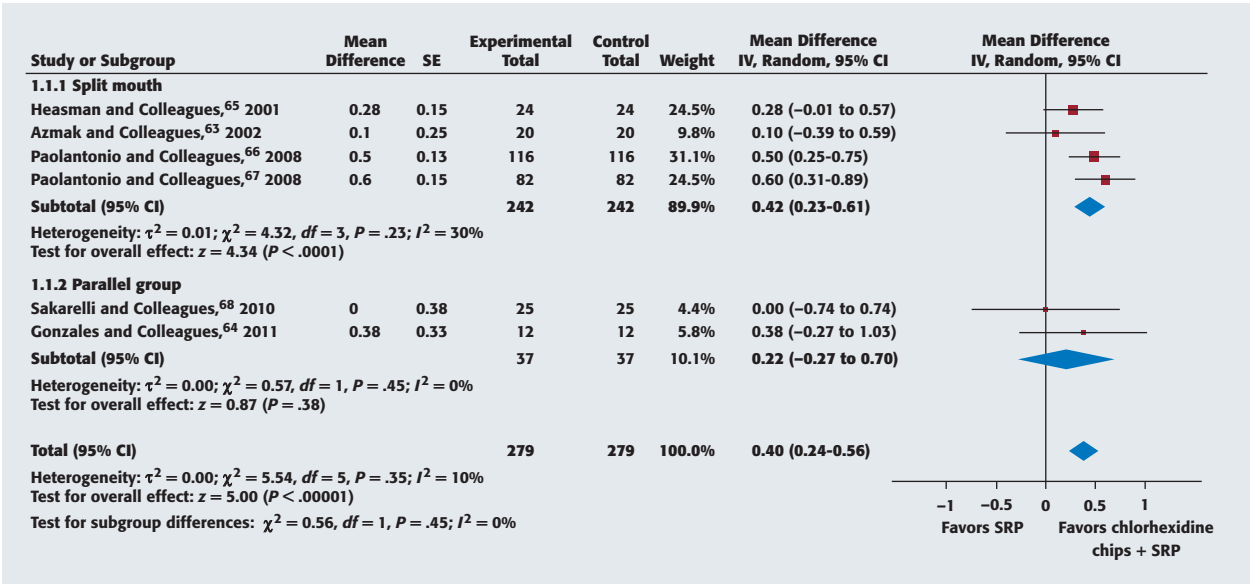

Figure 6. Meta-analysis of studies on scaling and root planing (SRP) plus chlorhexidine chips versus SRP alone, grouped according to study design; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

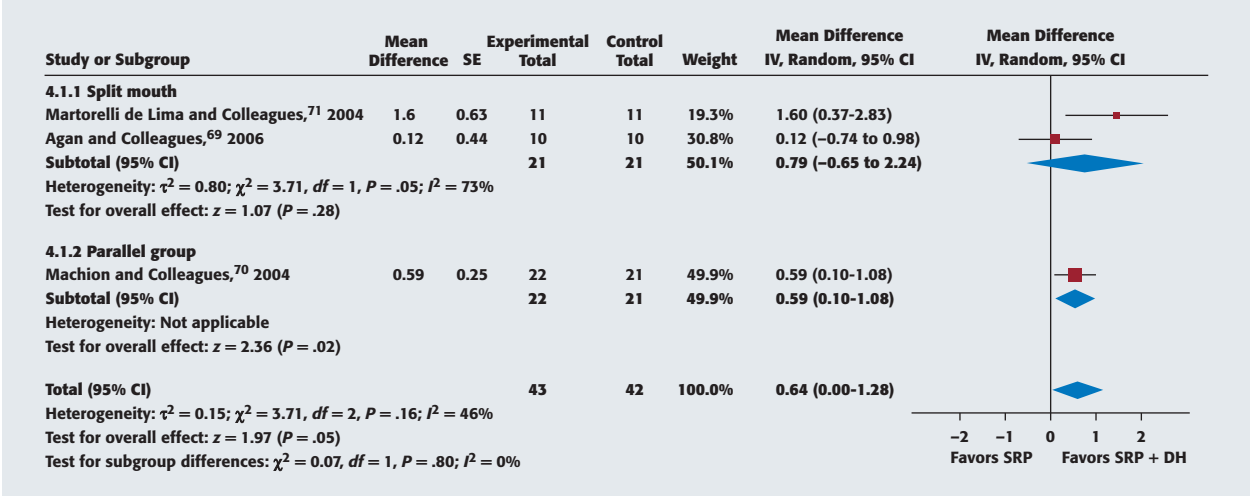

Figure 7. Meta-analysis of studies on scaling and root planing (SRP) plus doxycycline hyclate (DH) gel versus SRP alone, subgrouped according to study design; mean difference in clinical attachment level is in millimeters. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

DISCUSSION

As an expert panel, we critically appraised 72 randomized controlled trials and summarized the information for 10 nonsurgical treatments for chronic periodontitis. On average, SRP compared with no treatment resulted in a 0.5-mm improvement in CAL; we reached this conclusion with a moderate level of certainty because there were few trials.

We also assessed a variety of adjunctive therapies in addition to SRP treatment. Adjuncts comprised both systemic and locally applied modalities. The average improvements in CAL with adjunctive use (over SRP as a sole treatment) averaged between 0.2 and 0.6 mm. The level of certainty in the evidence for all adjuncts was either moderate or low.

We found 11 trials for SDD. With moderate certainty, SDD showed a small and statistically significant adjunctive benefit. We found 24 trials using a variety of systemic antimicrobials and regimens. With moderate certainty, we found a statistically significant but small

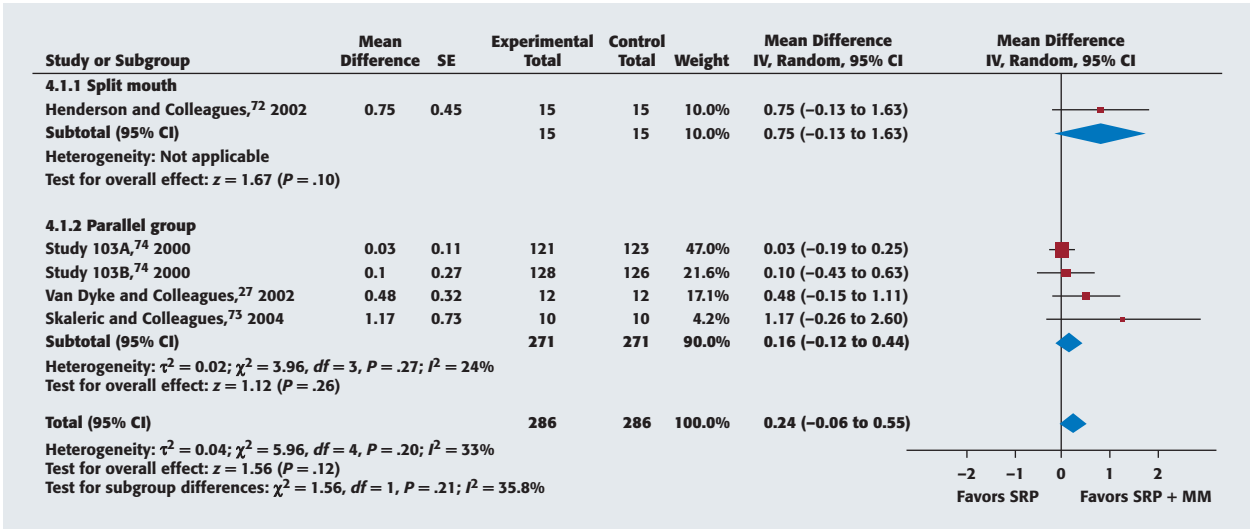

Figure 8. Meta-analysis of studies on scaling and root planing (SRP) plus minocycline microspheres (MM) versus SRP alone, subgrouped according to study design; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

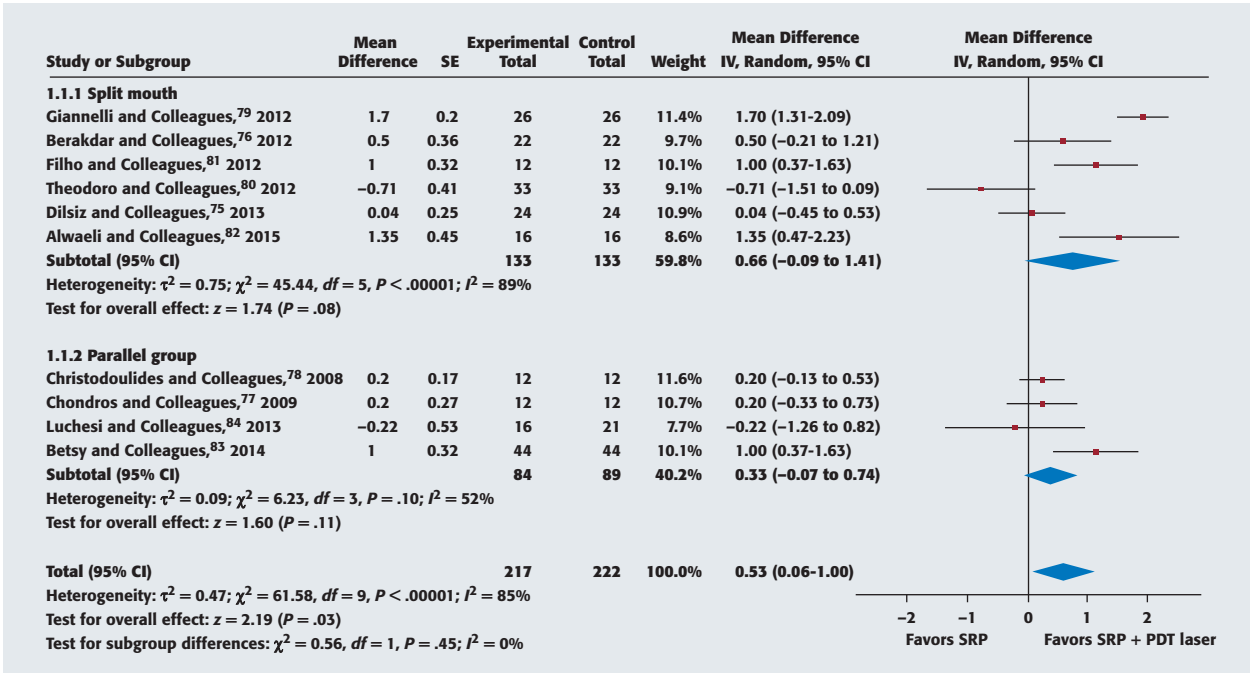

Figure 9. Meta-analysis of studies on scaling and root planing (SRP) plus photodynamic therapy (PDT) diode laser versus SRP alone, grouped according to study design; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

benefit from systemic antimicrobials in aggregate. With moderate certainty, we observed a statistically significant, moderate benefit with the adjunctive use of chlorhexidine chips.

Clinicians should bear in mind the ambiguity of the adjunctive benefits of DH gel and minocycline microspheres before recommending their use as part of the nonsurgical treatment of periodontitis. We found

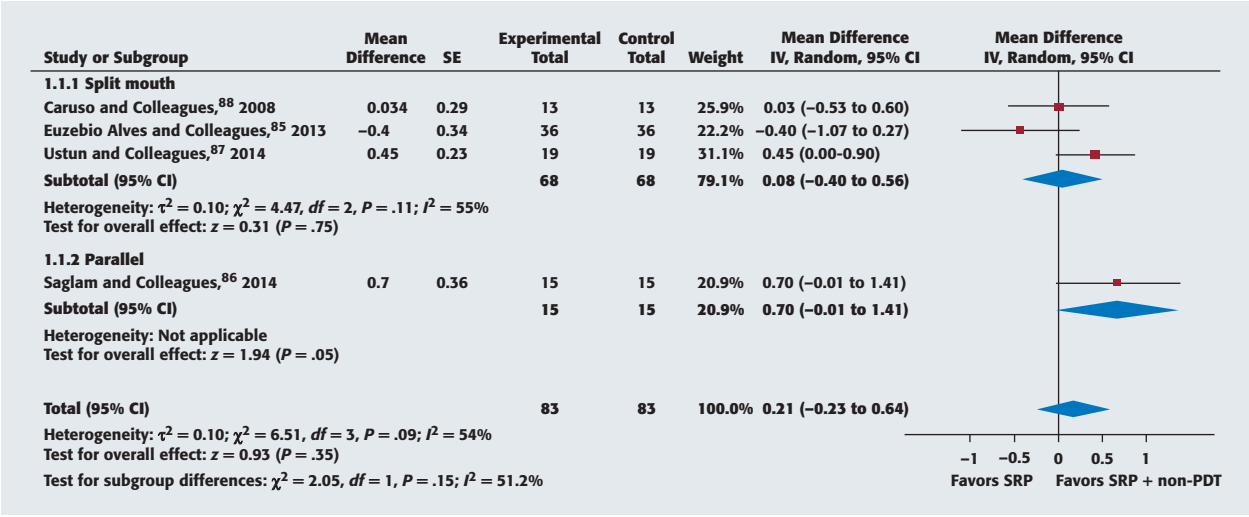

Figure 10. Meta-analysis of studies on scaling and root planing (SRP) plus nonphotodynamic therapy (non-PDT) laser versus SRP alone; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

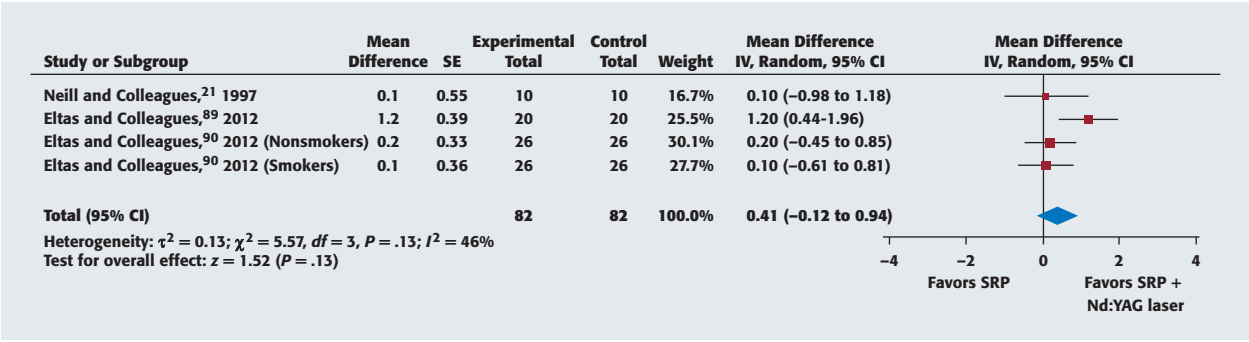

Figure 11. Meta-analysis of studies on scaling and root planing (SRP) plus neodymium:yttrium-aluminum-garnet (Nd:YAG) laser versus SRP alone; mean difference in clinical attachment level is in millimeters. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

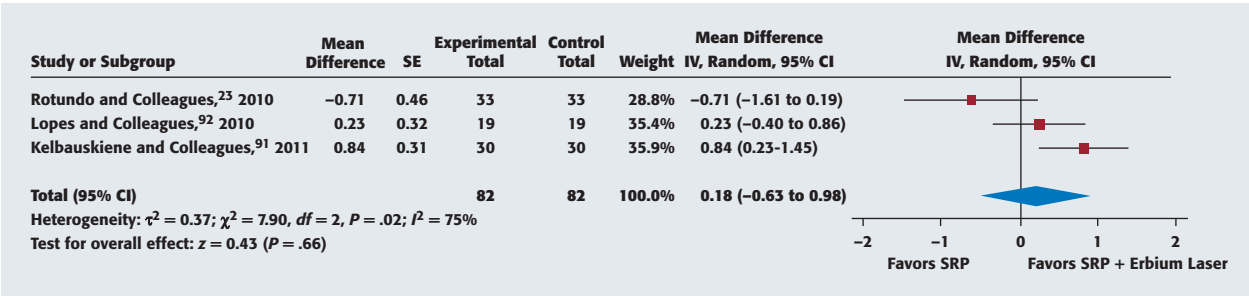

Figure 12. Meta-analysis of studies on scaling and root planing (SRP) plus erbium laser versus SRP alone; mean difference in clinical attachment level is in millimeters. Weighted percentages may not add up due to rounding and significant figures reported. CI: Confidence interval. df: Degrees of freedom. IV: Inverse-variance. SE: Standard error.

low certainty in the evidence for both of these treatments.

For DH gel, we observed a substantial adjunctive benefit; however, because of a wide CI around the estimated benefit, the data were also compatible with no benefit. DH gel was developed and approved by the US Food and Drug Administration as a stand-alone product (that is, used without SRP). We did not include use of

DH gel as a stand-alone product in this review. Garret and colleagues[93,94] did not find statistically significant differences between DH gel and SRP.

For minocycline microspheres, we observed a small adjunctive benefit. On the basis of the width of the CI, the data for the microspheres also were compatible with no benefit. The US Food and Drug Administration approved minocycline microspheres on the basis of their beneficial effect on probing depth, not CAL.

Unlike other instruments, lasers have no defined and accepted protocols for standard usage. Many dental providers establish their own protocol on the basis of anecdotal rules or experiences. However, the potential for adverse events was considered to be higher than for other adjunctive treatment systems. Also, every laser type and wavelength is different and affects the hard and soft tissues differently, making comparisons between lasers virtually impossible. We concluded that there are no benefits for any laser type or wavelength except PDT diode lasers.

Diabetes is a risk factor for chronic periodontitis.[95] Five of the 72 studies included exclusively patients with diabetes. We included these studies on patients with diabetes with other studies of the same treatment. Investigators in 1 study[24] tested SRP alone versus no treatment and supragingival prophylaxis, investigators in 2 studies[31,33] tested SRP plus SDD versus SRP alone, investigators in 1 study[71] tested SRP plus DH gel versus SRP alone, and investigators in 1 study[73] tested SRP plus minocycline microspheres versus SRP alone. Because there are only 1 or 2 studies per treatment exclusively on patients with diabetes, we could not draw any conclusion regarding the effect of SRP and adjuncts on chronic periodontitis among patients with diabetes.

Smoking is a risk factor for chronic periodontitis.[96] Investigators in only 2 studies[52,90] compared the effect of treatment between smokers and nonsmokers: 1 study of systemic antibiotics and 1 study of using an Nd:YAG laser as adjunctive treatment. Investigators in 1 study performed post hoc analyses comparing smokers with nonsmokers; however, we rejected this study on the basis of methodological concerns. Investigators in no other studies compared results in smokers with those in nonsmokers. Therefore, we were unable to reach a general conclusion regarding the effect of SRP or any of the adjuncts in smokers versus nonsmokers.

LIMITATIONS

Of the evidence. There is an abundance of published studies on the nonsurgical treatment of chronic periodontitis. However, in this systematic review, we could use only a reduced number of studies because of the ambiguity in describing the tested treatment. For example, investigators in many studies did not specify clearly that root planing was performed or used terms such as *debridement*.

The literature is also inconsistent on what is a clinically relevant outcome. Investigators in some studies defined clinical relevance in attachment gain as low as 0.2 mm.

Another limiting factor was the lack of uniformity in assigning levels of severity to chronic periodontitis. This finding is a reflection on the lack of agreement and multiple changes in the last 30 years in cutoff points to categorize severity occurring. We strongly urge researchers to report the numerical cutoffs used to describe disease severity.

Investigators in many otherwise rigorous studies reported changes in probing depth and not CAL. Although probing depths are the routine clinical measure used in most day-to-day treatment of patients, probing depths do not distinguish the role of recession in the treatment of periodontal diseases. Impressive reductions in probing depth can be obtained through treatment-induced recession. With the use of CAL, the reader can gauge the magnitude of clinical improvement due to gain in soft-tissue attachment to the root surface. In contrast, probing depths can be reduced as a result of both soft-tissue reattachment and gingival recession.

Most of the included studies were small in terms of the number of participants. Small studies can have a problem with low statistical power. Investigators in several of the included studies tested only 1 site per patient per treatment, whereas others provided measures for the entire mouth.

A major concern in judging the reliability of the results is participant attrition. Many studies did not include data on retention of participants and whether there were differences in different treatment arms; this ambiguity in turn influenced our ability to judge the strength of the study's findings. Also, investigators often did not report issues regarding safety and adverse events.

Of the systematic review. For this systematic review, we selected articles only in the English language. These choices could lead to bias in the results and interpretations if important studies published in languages other than English exist because we did not capture them.

Although we captured the disease severity information during the data abstraction process, we did not assess the results across degrees of disease severity at baseline. Also, because we chose to rely on CAL, we did not review studies that provided results only in terms of probing depth.

The competitive environment in which clinical trials are financed and conducted, as well as the nonreporting of negative results by some investigators or publications, fosters publication bias.[97] As a rule of thumb, quantitative analysis of publication bias should only be conducted when there are 10 or more studies in the meta-analysis.[98] Only 3 treatments in this systematic review met this criterion; therefore, the presence of publication bias for the other treatments is unknown.

CONCLUSIONS

On average, treatment of chronic periodontitis with SRP was associated with a 0.5-mm improvement in CAL against no treatment at a moderate level of certainty. We found benefits in 4 adjunctive therapies as compared with SRP alone: systemic SDD, systemic antimicrobials, chlorhexidine chips, and PDT with a diode laser at a moderate level of certainty. We had a low level of certainty on the benefits of the other 5 adjunctive therapies. Combinations of SRP with these assorted adjuncts resulted in a range of average CAL improvements between 0.2 and 0.6 mm over SRP alone. We also assessed the balance between the benefits and potential for adverse events from each treatment. We make clinical recommendations in a companion clinical practice guideline.[5] ■

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at: http://dx.doi.org/10.1016/j.adaj.2015.01.028.

Dr. Smiley is a dentist in private practice in Grand Rapids, MI. He was the chair of the panel.

Dr. Tracy is the assistant director, Center for Evidence-Based Dentistry, Division of Science, American Dental Association, Chicago, IL, e-mail tracys@ada.org. Address correspondence to Dr. Tracy.

Dr. Abt is an attending staff member, Department of Dentistry, Advocate Illinois Masonic Medical Center, Chicago, IL.

Dr. Michalowicz is a professor and the Erwin Schaffer Chair in Periodontal Research, Division of Periodontology, Department of Developmental and Surgical Sciences, University of Minnesota, Minneapolis, MN.

Dr. John is an associate professor, Division of TMD and Orofacial Pain, Department of Diagnostic and Biological Sciences, University of Minnesota, Minneapolis, MN.

Dr. Gunsolley is a professor, Periodontics, Virginia Commonwealth University, Richmond, VA.

Dr. Cobb is the interim director, Advanced Program, and professor emeritus, Department of Periodontics, University of Missouri-Kansas City, Kansas City, MO. He represented the American Academy of Periodontology on the panel.

Dr. Rossmann is a professor and the chair, Department of Periodontics, Texas A&M University Baylor College of Dentistry, Dallas, TX.

Dr. Harrel is an adjunct professor, Periodontology, Texas A&M University Baylor College of Dentistry, Dallas, TX.

Dr. Forrest is the director, National Center for Dental Hygiene Research & Practice, Ostrow School of Dentistry, University of Southern California, Los Angeles, CA. She represented the American Dental Hygienists Association on the panel.

Dr. Hujoel is a professor, Periodontics, Department of Oral Health Sciences, School of Dentistry, and an adjunct professor, Epidemiology, Department of Epidemiology, School of Public Health, University of Washington, Seattle, WA.

Dr. Noraian is a periodontist in private practice, Bloomington, IL, and Urbana, IL.

Dr. Greenwell is a professor and the director, Graduate Periodontics, University of Louisville, Louisville, KY.

Dr. Frantsve-Hawley was the senior director, Center for Evidence-Based Dentistry, Division of Science, American Dental Association, Chicago, IL, when this article was written. She now is the executive director, American Association of Public Health Dentistry, Springfield, IL.

Ms. Estrich is a health science research analyst, Division of Science, American Dental Association, Chicago, IL.

Mr. Hanson was a health science research analyst, Division of Science, American Dental Association, Chicago, IL, when this article was written. He now is a research analyst, Incisent Labs, Chicago, IL.

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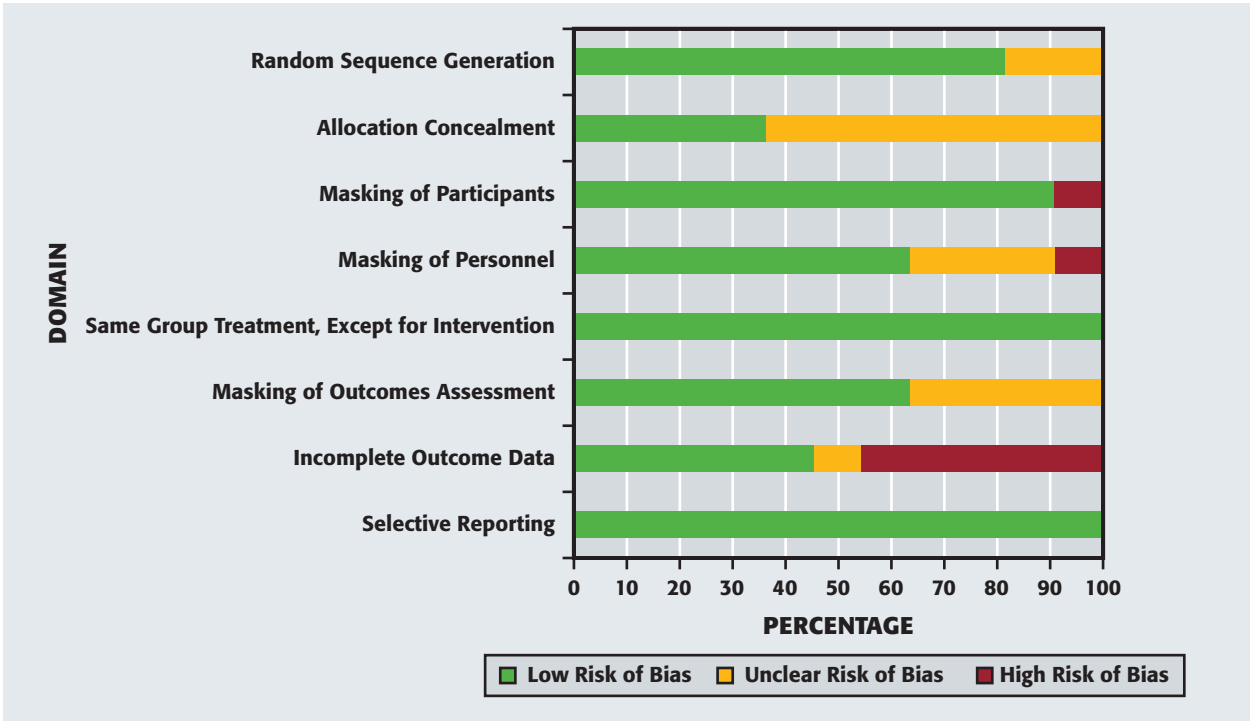
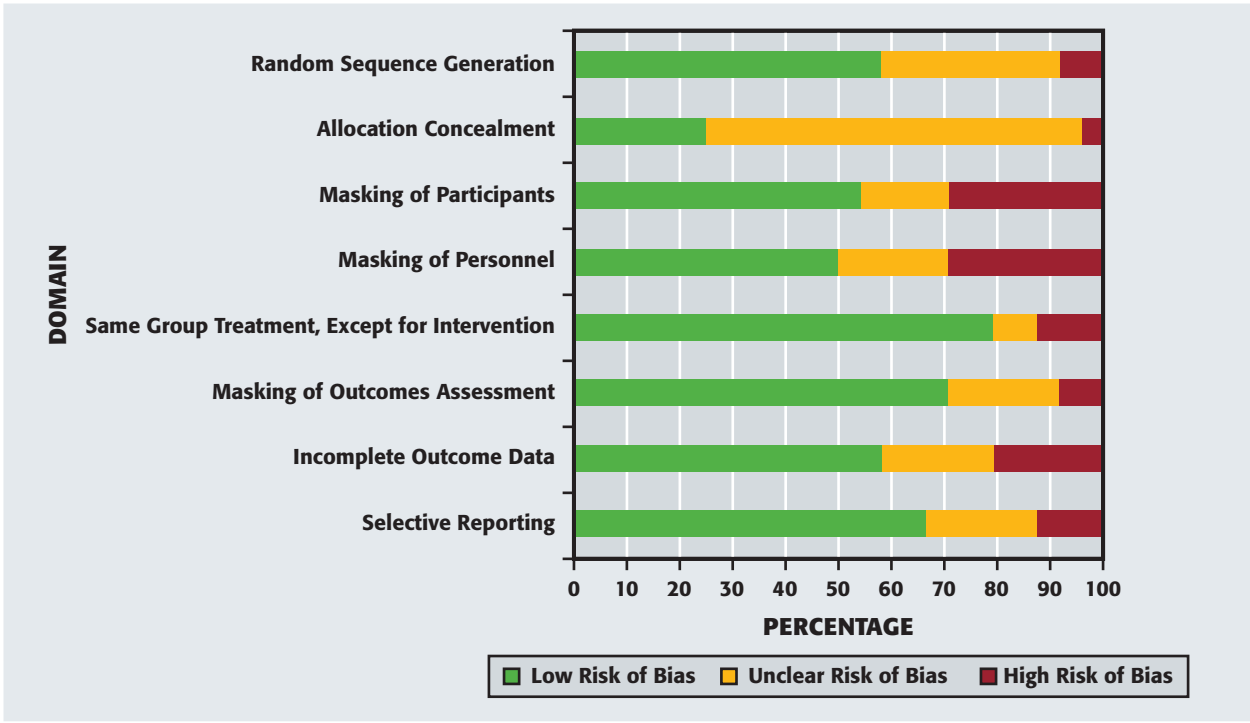
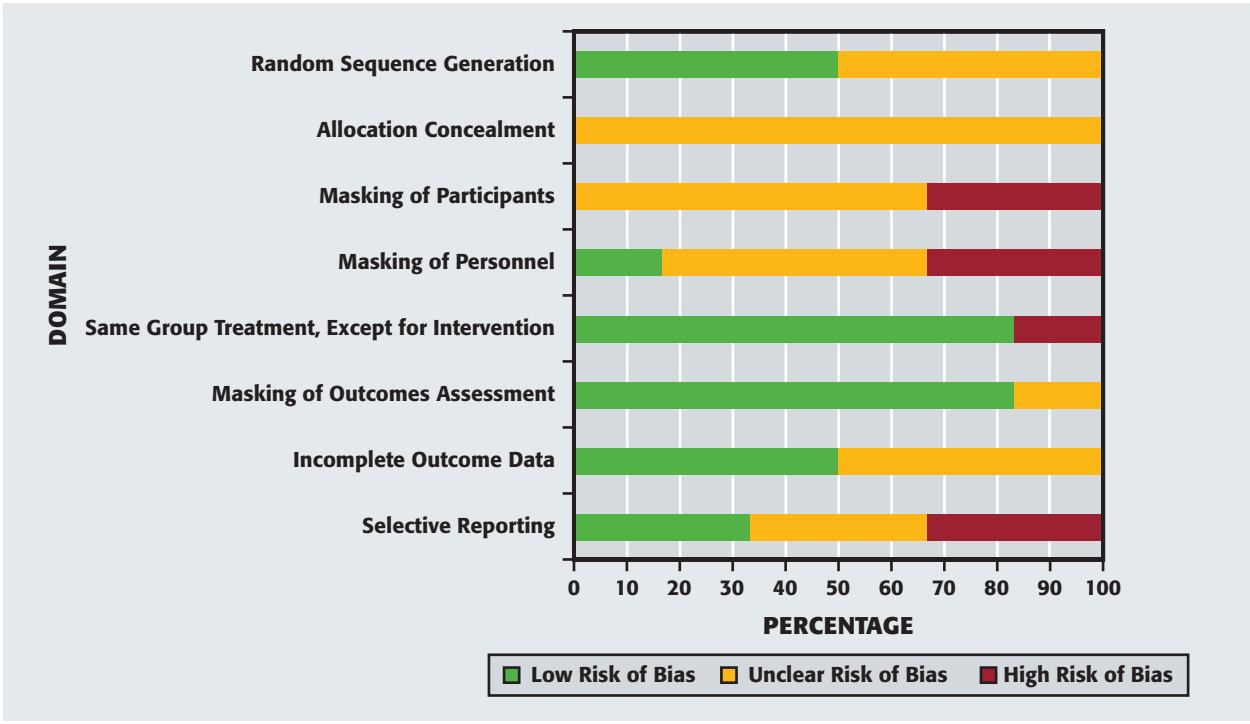


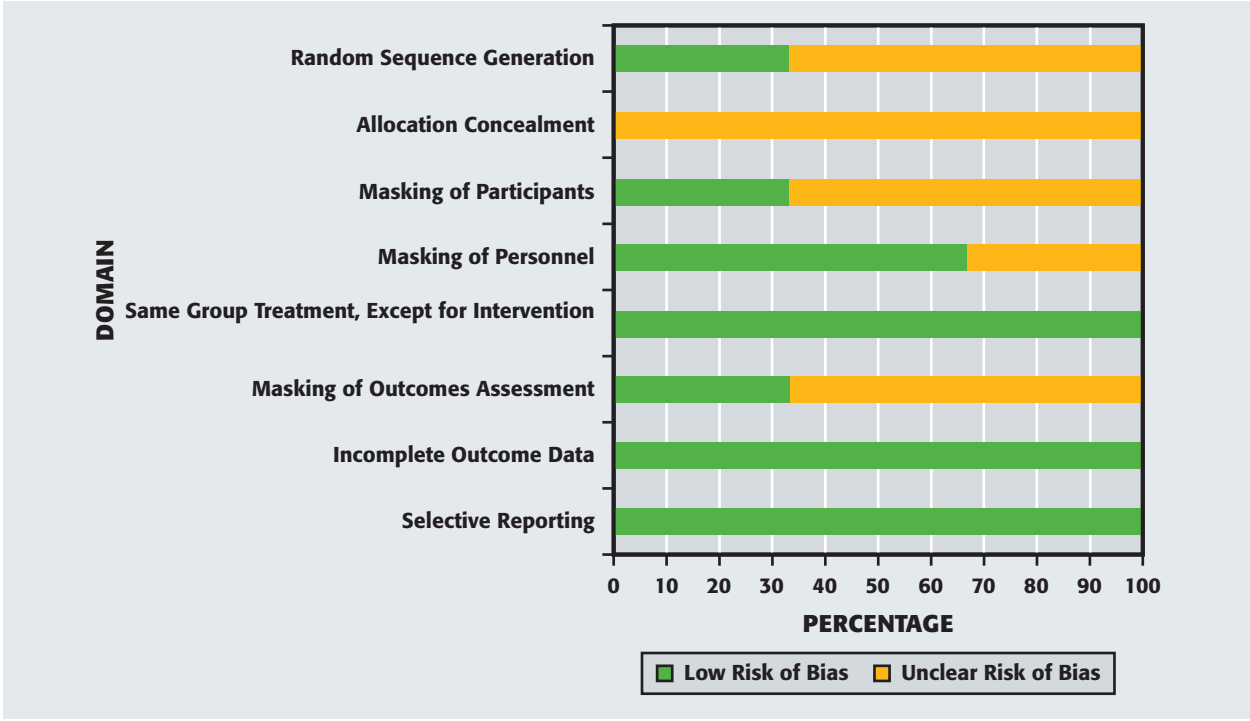
eFigure 1. Risk of bias as a percentage of included studies for scaling and root planing plus subantimicrobial-dose doxycycline, according to domain.



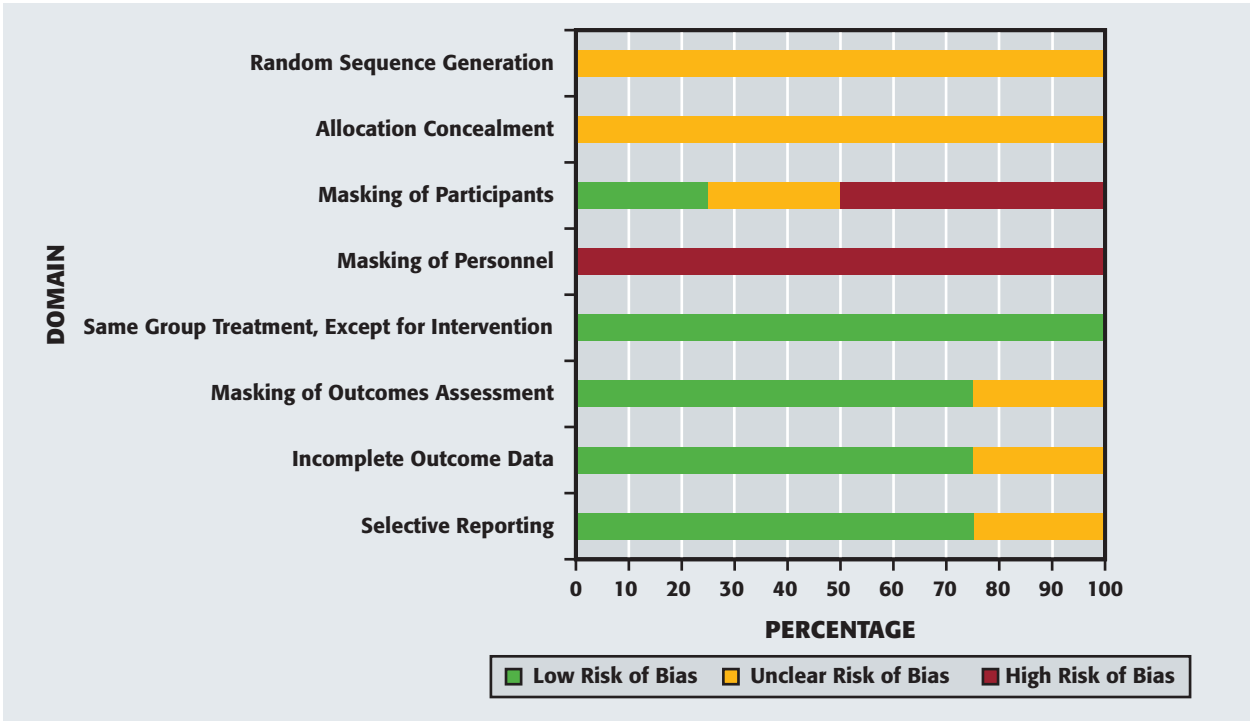
eFigure 2. Risk of bias as a percentage of included studies for scaling and root planing plus systemic antimicrobials, according to domain.



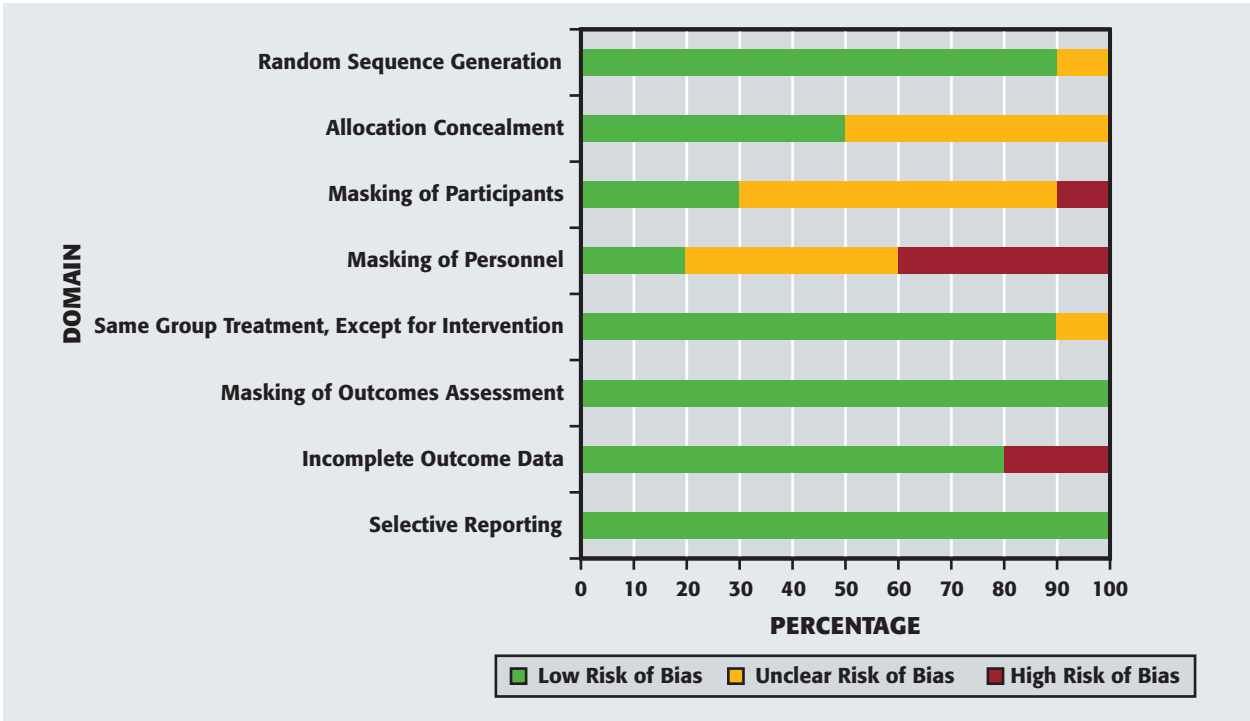
eFigure 3. Risk of bias as a percentage of included studies for scaling and root planing plus chlorhexidine chips, according to domain.



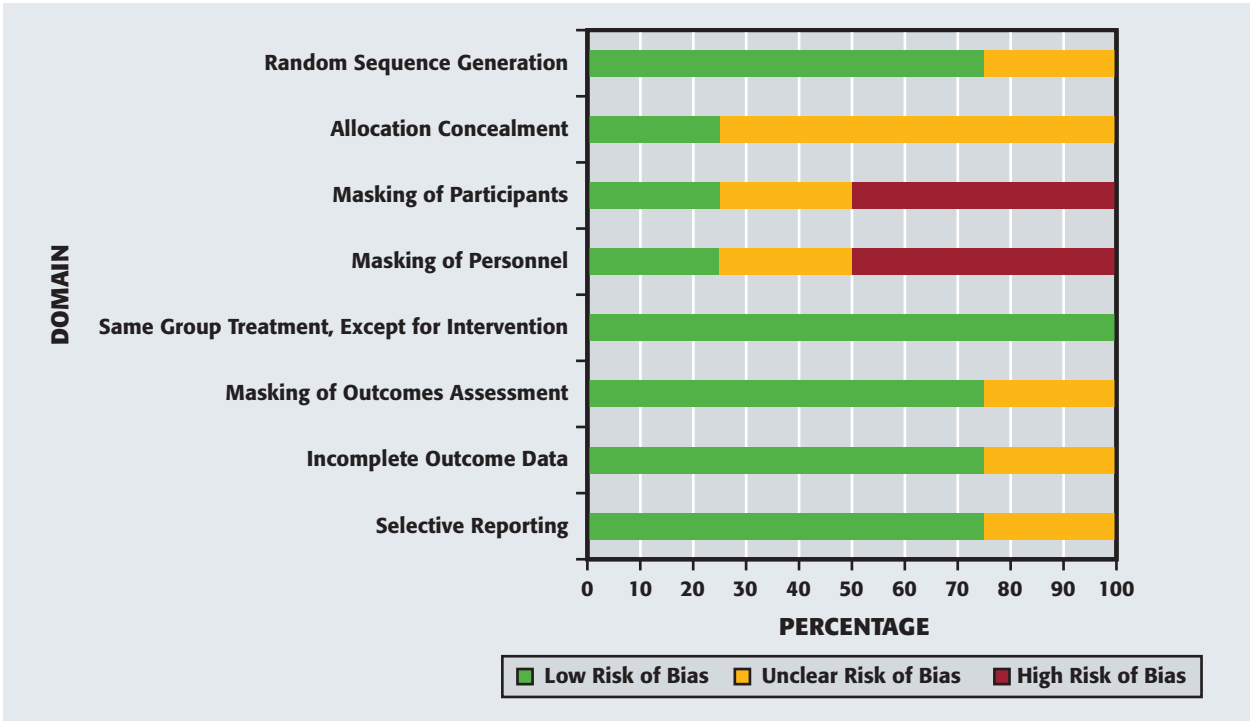
eFigure 4. Risk of bias as a percentage of included studies for scaling and root planing plus doxycycline hyclate gel, according to domain. There were 3 studies.



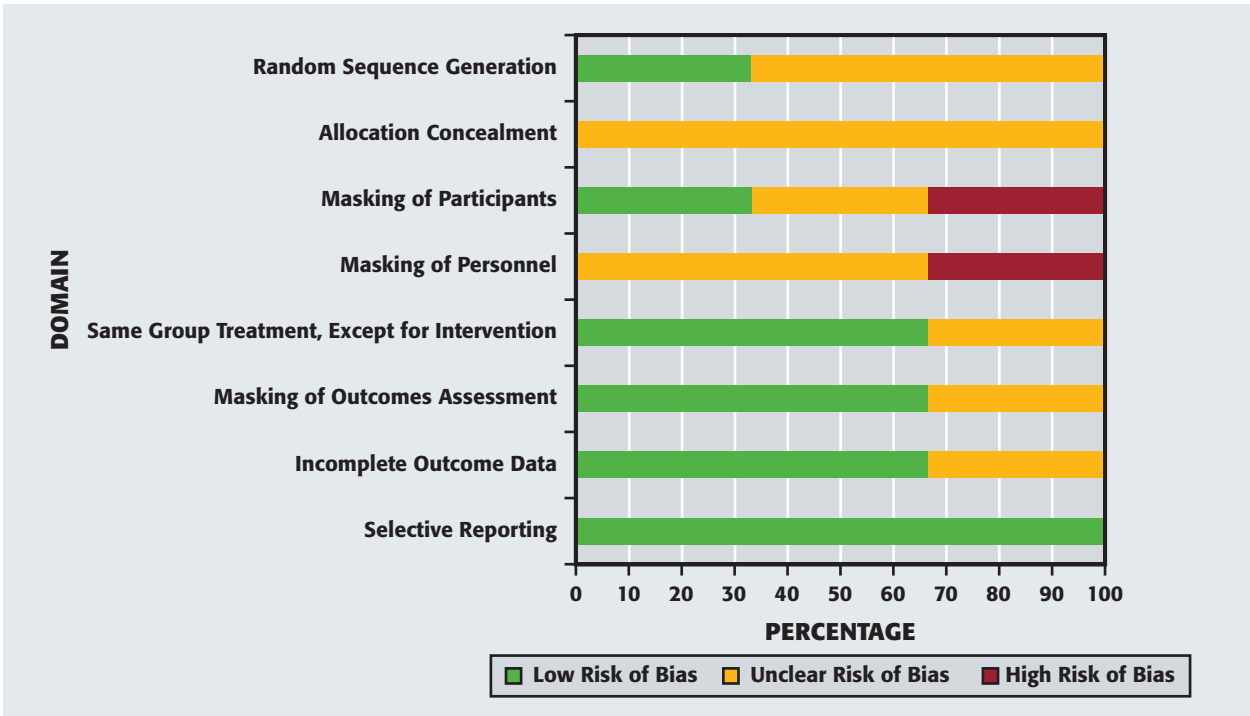
eFigure 5. Risk of bias as a percentage of 4 included studies for scaling and root planing plus minocycline microspheres, according to domain.



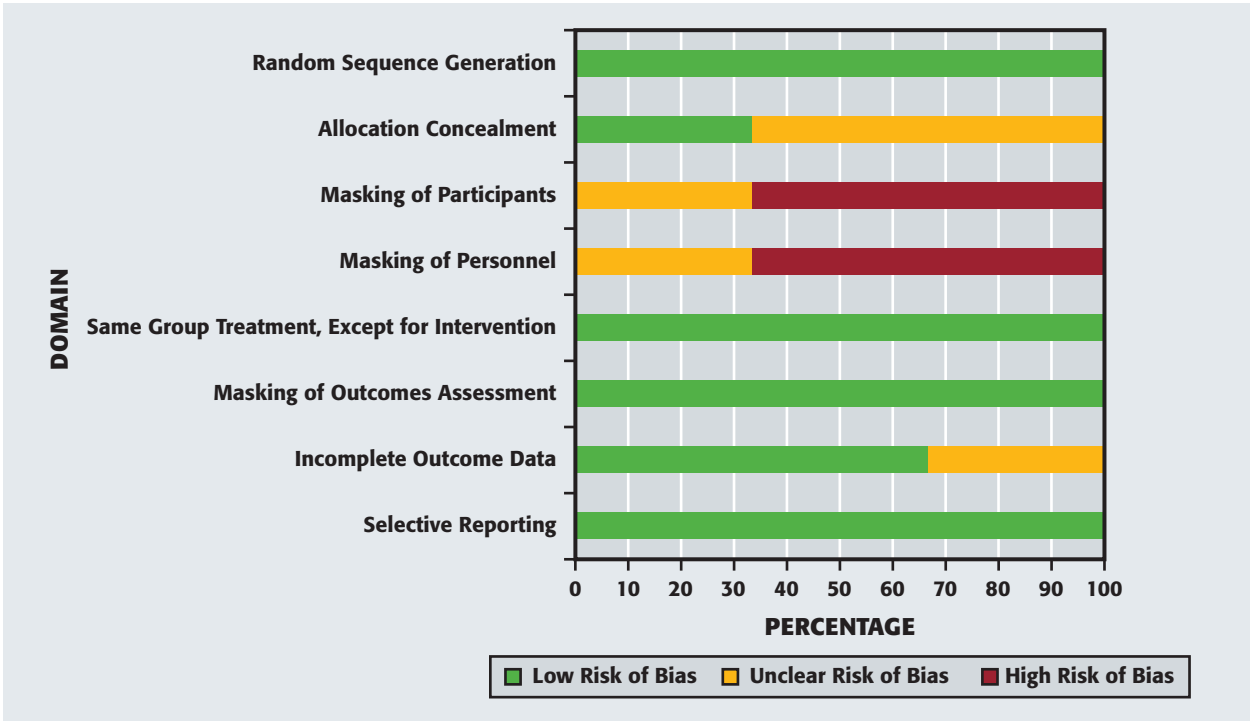
eFigure 6. Risk of bias as a percentage of included studies for scaling and root planing plus a photodynamic therapy diode laser, according to domain.



eFigure 7. Risk of bias as a percentage of included studies for scaling and root planing plus a non-photodynamic therapy diode laser, according to domain.



eFigure 8. Risk of bias as a percentage of included studies for scaling and root planing plus a neodymium:yttrium-aluminum-garnet laser, according to domain.



eFigure 9. Risk of bias as a percentage of included studies for scaling and root planing plus an erbium laser, according to domain.