Table 1. Technical Expert Advisory Group for the Evidence Report on Effectiveness of Adjuncts to Scaling and Root Planing Therapy for Periodontitis

Name	Affiliation
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Table 2. Strategy and Results of Original and Follow-up MEDLINE Searches

Step	Search Terms and Strategy	Number of Articles
1	Explode periodontitis	10,670
2	Limit 1 to randomized controlled trial	417
3	Explode single-blind method/ or explode double-blind method/or explode random allocation/ or explode epidemiologic study characteristics/ or explode comparative study	164,891
4	1 and 3	3,120
5	2 and 4	3,189
6	Limit 5 to human	2,987
7	Explode dental scaling/ or dental scaling.mp	1,757
8	Explode root planing/ or root planing.mp	1,087
9	7 or 8	2,047
10	Limit 9 to randomized controlled trial	260
11	9 and 3	841
12	10 or 11	896
13	Limit 12 to human	836
14	6 and 13	517
15	Explode metronidazole	7,150
16	Explode chlorhexidine	3,106
17	Explode doxycycline	3,270
18	Explode tetracycline	12,460
19	Explode minocycline	1,644
20	Explode amoxicillin	5,034
21	Explode amoxicillin-potassium clavulanate combination/ or augmentin.mp	1,067
22	Povidone iodine	1,359
23	15 or 16 or 17 or 18 or 19 or 10 or 21 or 22	31,725
24	Explode antibiotics	347,992
25	23 or 24	356,095
26	14 and 25	203
27	From 26 keep 1-200	200
28	From 26 keep 201-203	3
29	November 2002 rerun of the above search for new (unduplicated) articles	41
30	December 2002 search beginning with periodontal disease and steps 2-29	2

Table 3. Strategy and Results of EMBASE Search

Step	Search Terms and Strategy	Number of Articles
1	Periodontitis	2,099
2	Randomized controlled trial	69,265
3	Single blind procedure	3,883
4	Double blind procedure	45,593
5	Randomization	5,018
6	Comparative study	38,078
7	2 or 3 or 4 or 5 or 6	129,259
8	1 and 7*	68

*68 records yielded 36 new (unduplicated with MEDLINE) records (articles).

Table 4. Inclusion/Exclusion Criteria For Studies of Added Effectiveness of Periodontitis Therapies Adjunctive to Scaling and Root Planing

Include studies if:	Exclude studies if:
They compare scaling and root planing (SRP) to SRP with some (single/combination agent) adjunctive therapy (chemical and antimicrobial).	Either they have no comparison/control group or the comparison/control group is historical.
They use concurrent comparison/control and experimental/test groups.	They compare therapies but do not include SRP alone (or with placebo).
They compare multiple adjunctive therapies to SRP alone (or with placebo) but report outcomes separately for each therapy.	They do not perform SRP in the experimental/test group in addition to the adjunctive therapy.
They measure outcomes at one or more specified intervals.	They use bundled adjunctive therapies.
	They do not report therapy outcomes separately for each therapy.
	They do not specify time intervals for outcomes reported or do not report outcomes separately for each interval.
They are published in English.	Periodontitis treated is not chronic or adult type (i.e. is aggressive, juvenile, early onset, refractory, etc.).
They involve a human population.	The population under study has a behavioral factor or comorbidity that complicates the therapy or alters prognosis (smokers, HIV/AIDS, diabetes, etc.).

Table 5. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Tetracycline

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Listgarten et al., 1978[43]	R NP NR	25 weeks	N: 12 subjects T: 6 subjects C: 6 subjects	250 mg tetracycline 4xday, days 0 to 14 and days 42 to 56	+0.20, NS	Data NR, NR
Lindhe et al., 1983[44]	R PL DB	50 weeks	N: 14 subjects T: 7 subjects C: 7 subjects	250 mg tetracycline 4xday, days 0 to 14 and 250 mg 1xday days 15 to 350	+0.8, NR	+0.3, NR
Al-Joburi et al., 1989[45]	R PL DB	24 weeks	N: 51 subjects T: 27 subjects C 24 subjects	250 mg tetracycline 4xday, days 0 to 14	Initial PD = 3 mm: +0.12, NS Initial PD 4-6 mm: -0.05, NS Initial PD = 7 mm: +0.19, NS	Initial PD = 3 mm: +0.49, NS Initial PD 4-6 mm: +0.04, NS Initial PD = 7 mm: +0.45, NS
Haffajee et al., 1995[46]	R PL DB	43 weeks (10 months)	N: 24 subjects T: 13 subjects C: 11 subjects	250 mg tetracycline 3xday, days 0 to 30, plus 0.12% chlorhexidine rinse for same 30 days	+0.29, NS	Data NR, NS
Ramberg et al., 2001[47]	Non-R NP NR	52 weeks	N: 89 subjects T: 28 subjects C: 61 subjects	250 mg tetracycline 4xday, days 0 to 21 and 0.2% chlorhexidine rinse 2xday	+0.3, NS	+0.31, $P < 0.001$

R, randomized; Non-R, nonrandomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 6. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Tetracycline

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Goodson et al., 1985[48]	R NP SB	52 weeks	N: 10 subjects T: 9 teeth C: 9 teeth	25% tetracycline fibers for 10 days	Data NR, NR	Initial PD > 3 mm: +0.34, NS Initial PD > 6 mm: +0.33, NS
MacAlpine et al., 1985[31]	Non-R PL NR	24 weeks	N: 11 subjects T: 16 sites C: 16 sites	50 mg/ml tetracycline irrigation every 2 weeks for 22 weeks	+0.4, NR	+0.3, NS
Nylund and Egelberg, 1990[51]	Non-R PL NR	52 weeks	N: 20 subjects T: 20 subjects C: 20 subjects	50 mg/ml tetracycline irrigation once every 2 weeks for 3 months	Data NR, NS	Data NR, NS
Minabe et al., 1991[52]	R NP NR	8 weeks	N: 16 subjects T: 10 sites C: 8 sites	Tetracycline immobilized collagen film, 4 consecutive weekly administrations	+0.7, NS	Data NR, NS
Unsal et al., 1994[59]	R NP NR	12 weeks	N: 15 subjects T: 7 subjects C: 8 subjects	40% tetracycline in white petroleum, single application	-0.43, NS	-0.23, NS
Jeong et al., 1994[33]	R NP NR	12 weeks	N: 16 subjects T1: 16 subjects T2: 16 subjects C: 16 subjects	T1: 5% tetracycline in gel, 1 application T2: 5% tetracycline with citric acid in gel, 1 application	T1: +0.27, NS T2: +0.93, $P < 0.05$	T1: +0.14, NS T2: +0.73, NS
Newman et al., 1994[57]	R NP SB	26 weeks (6 months)	N: 105 subjects T: 105 subjects C: 105 subjects	12.1 cm of tetracycline fiber for 10 days	+0.73, $P < 0.01$	+0.48, $P < 0.05$
Shiloah and Patters 1994[54]	R PL SB	4 weeks	N: 7 subjects T: 12 sites C: 12 sites	5% aqueous tetracycline, 1 application	Data NR, NS	Data NR, NS

Table 6. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Tetracycline (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Drisko et al., 1995[49]	R NP SB	52 weeks	N: 116 subjects T: 116 subjects C: 116 subjects	17 mg tetracycline fibers for 10 days	Data NR, NS	Data NR, NS
Darhous et al., 1995[50]	Non-R NP NR	8 weeks	N: 7 subjects T: 7 subjects C: 7 subjects	100 mg/ml tetracycline irrigation, 5 minutes, 1 application	+1.04, NR	+1.8, NR
Trombelli et al., 1996[55]	R NP SB	8 weeks (60 days)	N: 12 subjects T1: 20 sites T2: 24 sites C: 19 sites	T1: 100 mg/ml tetracycline irrigation, 4 minutes, 1 application T2: 25% tetracycline fibers for 10 days	T1: +0.4, *P* = 0.011 T2: +0.5, *P* = 0.011	T1: -0.2, NS T2: +0.4, NS
Lie et al., 1998[34]	R NP DB	26 weeks	N: 18 subjects T: 18 subjects C: 18 subjects	3% tetracycline ointment after each SRP session, 1 week apart	Defect sites:* +0.6, NS Nondefect sites:* -0.3, NS	Defect sites:* +1.0, NS Nondefect sites:* +0.2, NS
Tonetti et al., 1998[35]	R NP SB	26 weeks	N: 123 subjects T: 63 subjects C: 60 subjects	25% tetracycline fibers for 10±3 days	+0.4, NS	-0.1, NS
Yalcin et al., 1999[56]	R NP SB	7 weeks	N: 17 subjects T: 221 sites C: 191 sites	Slow-release tetracycline fibers for 10 days	+0.41, *P* = 0.047	+0.20, NS

Table 6. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Tetracycline (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Kinane and Radvar, 1999[53]	R NP SB	26 weeks (6 months)	N: 39 subjects T: 19 subjects C: 20 subjects	25% tetracycline fibers for 10 days	+0.67, $P = 0.008$	+0.15, $P < 0.05$
Friesen et al., 2002[58]	R NP SB	26 weeks (6 months)	N: 24 subjects T1: 24 subjects T2: 24 subjects C: 24 subjects	13.5 mg tetracycline strips for 7 to 10 days T1: single strip T2: multiple strips	T1: +0.43, NR T2: +0.87, NR	T1: +0.44, NS T2: +0.48, NS

R, randomized; Non-R, nonrandomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NB, not blinded; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

*Defect and nondefect sites refer to, respectively, the mean of measurements from the buccal and lingual side versus measurements for all remaining parts of the tooth.

Table 7. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Minocycline

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Ciancio et al., 1982[61]	R PL DB	10 weeks	N: 26 subjects T: 13 subjects C: 13 subjects	200 mg minocycline per day for 7 days	Data NR, NS	N/A
Atilla et al., 1996[62]	Non-R NP NR	6 weeks	N: 21 subjects T1: 5 (PD 4-5 mm) C1: 6 (PD 4-5 mm) T2: 5 (PD = 6 mm) C2: 5 (PD = 6 mm)	100 mg minocycline per day for 14 days	Initial PD 4-5 mm: -0.06, NS Initial PD = 6 mm: +0.49, NS	N/A

R, randomized; Non-R, nonrandomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 8. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Minocycline

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
van Steenberghe et al., 1993[63]	R PL DB	12 weeks	N: 81 subjects T: 42 subjects C: 39 subjects	2% minocycline ointment applied at baseline and weeks 2, 4, and 6	Initial PD = 5 mm: +0.3, *P* = 0.0018 Initial PD = 7 mm: +1.0, *P* = 0.0001	Initial PD = 5 mm: 0.0, NS Initial PD =7 mm: +0.40, NS
Jones, et al., 1994[64]	R PL DB	26 weeks (6 months)	N: 17 subjects T: 11 subjects C: 6 subjects	1 mg microencapsulated minocycline injected into =5 mm pockets, single application	Data NR, NS	Data NR, NR
Graca et al., 1997[32]	R PL DB	12 weeks	N: 26 subjects T: 13 subjects C: 13 subjects	2% minocycline gel applied at baseline and weeks 2 and 4	+0.34, NS	+0.39, *P* < 0.05
Kinane and Radvar, 1999[53]	R NP DB	26 weeks (6 months)	N: 39 subjects T: 20 subjects C: 19 subjects	2% minocycline gel applied at baseline and weeks 2 and 4	+0.39, NS	+0.36, NS
van Steenberghe et al., 1999[65]	R PL DB	65 weeks (15 months)	N: 93 subjects T: 46 subjects C: 47 subjects	2% minocycline ointment applied at baseline week 2, and months 1, 3, 6, 9, and 12	Initial PD = 5 mm: +0.77, *P* < 0.0001 Initial PD =7 mm: +1.10, *P* < 0.0001	Initial PD =5 mm: +0.49, *P* < 0.0001 Initial PD =7 mm: +0.43, *P* < 0.0001
Williams et al., 2001[66]	R PL DB	39 weeks (9 months)	N: 467 subjects T: 237 subjects C: 230 subjects	2% minocycline microspheres in polymer gel applied at baseline and months 3 and 6	+0.32, *P* < 0.001	Data NR, NR

Table 8. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Minocycline (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Henderson et al., 2002[67]	R NP SB	26 weeks (6 months)	N: 15 subjects T: 15 subjects C: 15 subjects	1 mg microencapsulated minocycline, single application	+0.7, *P* = 0.05	+0.8, *P* = 0.04
Van Dyke et al., 2002[68]	R NP DB	26 weeks (6 months)	N: 22 subjects T: 12 subjects C: 10 subjects	1 mg microencapsulated minocycline, single application	+0.28, NS	+0.48, NS

R, randomized; Non-R, nonrandomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 9. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Metronidazole

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Loesche et al., 1984[69]	R PL DB	30 weeks	N: 14 subjects T: 7 subjects C: 7 subjects	250 mg metronidazole 3xday for 7 days	Initial PD 4-6 mm: +0.14, NS Initial PD = 7 mm: +1.64, $P < 0.03$	Initial PD 4-6 mm: +0.10, NS Initial PD = 7 mm: +1.19, $P = 0.05$
Joyston-Bechal et al., 1986[71]	R PL DB	156 weeks (3 years)	N: 28 subjects T: 15 subjects C: 13 subjects	1% chlorhexidine gel for first 10 weeks, then 200 mg metronidazole: 1 at evening of 3rd visit + 3xday for 5 days; repeated 4 weeks later	+0.41, NS	N/A
Soder et al., 1990[72]	R PL DB	26 weeks (6 months)	N: 92 subjects T: 46 subjects C: 46 subjects	400 mg metronidazole 3xday for 7 days	+0.05, NR	N/A
Loesche et al., 1991[73]	R PL DB	52 weeks	N: 39 subjects T: 18 subjects C: 21subjects	250 mg metronidazole 3xday for 7 days	Initial PD = 3 mm: -0.07, NS Initial PD 4-6 mm: -0.06, NS Initial PD = 7 mm: +0.41, NS	Initial PD = 3 mm: +0.10, NS Initial PD 4-6 mm: +0.13, NS Initial PD = 7 mm: +0.32, NS

Table 9. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Metronidazole (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Loesche et al., 1992[74]	R PL DB	104 weeks (2 years)	N: 33 subjects T: 15 subjects C: 18 subjects	250 mg metronidazole 3xday for 7 days	Initial PD = 3 mm: -0.15, P = 0.08 Initial PD 4-6 mm: +0.47, *P* < 0.01 Initial PD ≥ 7 mm: +1.05, *P* < 0.01	Initial PD = 3 mm: +0.37, P = 0.07 Initial PD 4-6 mm: +0.47, *P* < 0.01 Initial PD ≥ 7 mm: +0.66, NS
Noyan et al., 1997[75]	R NP NR	6 weeks	N: 10 subjects T: 5 subjects C: 5 subjects	250 mg metronidazole 3xday for 7 days, then SRP again	+0.60, NR	+0.41, NR
Palmer et al., 1998[76]	R NP SB	24 weeks	N: 58 subjects T: 31 subjects C: 27 subjects	200 mg metronidazole 3xday for 7 days	-0.06, NS	+0.16, NS
Rooney et al., 2002[70]	R PL DB	26 weeks	N: 31 subjects T: 16 subjects C: 15 subjects	200 mg metronidazole plus placebo 3xday for 7 days; plus 0.2% chlorhexidine irrigation	Initial PD = 6 mm: Data NR, *P* < 0.05	Initial PD = 6 mm: Data NR, NS

R, randomized; ; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 10. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Metronidazole

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Aziz-Gandour and Newman 1986[77]	R PL DB	12 weeks	N: 16 subjects T: 210 surfaces C: 118 surfaces	0.05% metronidazole irrigation for 28 days	Data NR; $P < 0.01$	N/A
Moran et al., 1990[37]	R NP DB	12 weeks	N: 33 pockets T: 15 pockets C: 18 pockets	Acrylic strips impregnated with metronidazole	+0.9, NS	+0.3, NS
Noyan et al., 1997[75]	R NP NR	6 weeks	N: 10 subjects T: 5 subjects C: 5 subjects	25% metronidazole gel applied on days 0 and 7	+0.78, NS	+0.66, $P < 0.01$
Awartani and Zulqarnain 1998[28]	R NP SB	14 weeks	N: 12 subjects T: 360 sites C: 378 sites	25% metronidazole gel applied on days 0 and 7	-0.12, NS	N/A
Lie et al., 1998[34]	R NP DB	26 weeks (6 months)	N: 18 subjects T: 18 subjects C: 18 subjects	25% sustained release metronidazole gel after SRP sessions on days 0 and 7	Defect sites:* +0.5, NS Nondefect sites:* -0.1, NS	Defect sites:* +0.7, NS Nondefect sites:* 0.0, NS
Palmer et al, 1998[76]	R NP SB	24 weeks	N: 53 subjects T: 26 subjects C: 27 subjects	25% metronidazole gel subgingival application on days 0 and 7	Data NR, NS	-0.04, NS
Kinane and Radvar, 1999[53]	R NP SB	26 weeks (6 months)	N: 36 subjects T: 19 subjects C: 20 subjects	25% metronidazole gel 2xday applied on day 0 and 7	+0.22, NS	+0.004, NS
Riep et al., 1999[78]	R NP SB	13 weeks (3 months)	N: 29 subjects T: 29 subjects C: 29 subjects	25% metronidazole gel applied 5 times over 10 days	0.0, NS	+0.17, NS

Table 10. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Metronidazole

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Al Mubarak et al., 2000[80]	R NP SB	13 weeks (90 days)	N: 14 subjects T: 14 subjects C: 14 subjects	25% metronidazole gel applied on days 0 and 7	+0.8, $P < 0.03$	N/A
Griffiths et al., 2000[79]	R NP SB	39 weeks (9 months)	N: 88 subjects T: 1,770 sites C: 1,780 sites	25% metronidazole gel 1xweek for 3 weeks	+0.5, $P < 0.001$	+0.4, $P < 0.001$
Stelzel and Flores-de-Jacoby, 2000[36]	R NP SB	37 weeks (9 months)	N: 59 subjects T: 59 subjects C: 59 subjects	25% metronidazole gel applied 2xday on days 0 and 7	+0.18, $P < 0.05$	+0.07, NS

R, randomized; ; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

*Defect and nondefect sites refer to, respectively, the mean of measurements from the buccal and lingual side versus measurements for all remaining parts of the tooth.

Table 11. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Metronidazole plus Amoxicillin

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Berglundh et al., 1998[81]	R PL NR	104 weeks	N: 16 subjects T: 8 subjects C: 8 subjects	250 mg metronidazole 3xday plus 375 mg amoxicillin 2xday for 2 weeks	+0.5, NR	+0.3, NR
Flemmig, Milian, et al., 1998[82]	R NP SB	52 weeks	N: 38 subjects T: 18 subjects C: 20 subjects	250 mg metronidazole plus 375 mg amoxicillin 3xday plus 0.06% chlorhexidine irrigation 1xday for 8 days	Data NR, NS	Data NR, NS
Winkel et al., 2001[83]	R PL DB	24 weeks	N: 49 subjects T: 23 subjects C: 26 subjects	250 mg metronidazole plus 375 mg amoxicillin 3xday for 7 days	+0.7, P < 0.05	+0.4, NS
Rooney et al., 2002[70]	R PL DB	26 weeks	N: 30 subjects T: 15 subjects C: 15 subjects	200 mg metronidazole plus 250 mg amoxicillin 3xday for 7 days; plus 0.2% chlorhexidine irrigation	Initial PD = 6 mm: Data NR, *P* < 0.001	Initial PD = 6 mm: Data NR, *P* < 0.05

R, randomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 12. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Chlorhexidine

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Braatz et al., 1985[30]	R PL NR	24 weeks	N: 14 subjects T: 54 sites C: 52 sites	Irrigation with 2% chlorhexidine solution daily for 24 weeks	+0.3, NS	+0.2, NS
MacAlpine 1985[31]	R PL NR	24 weeks	N: 11 subjects T: 16 sites C: 16 sites	Irrigation with 2% chlorhexidine solution every 2 weeks for 24 weeks	+1.0, NS	+0.9, NS
Aziz-Gandour and Newman, 1986[77]	R PL DB	12 weeks	N: 12 subjects T: 147 surfaces C: 118 surfaces	Irrigation with 0.02% chlorhexidine solution 1xday for 28 days	Data NR, NS	N/A
Watts and Newman, 1986[84]	R PL DB	12 weeks	N: 11 subjects T: 128 sites C: 134 sites	Irrigation with 0.02% chlorhexidine solution 1xday for 28 days	Data NR, NS	N/A
Wennstrom et al., 1987[85]	R PL SB	52 weeks	N: 10 subjects T: 28 subjects C: 24 subjects	Irrigation with 0.2% chlorhexidine solution 3xweek	+0.1, NR	-0.1, NS
Southard et al., 1989[86]	R NP DB	15 weeks	N: 8 subjects T: 8 subjects C: 8 subjects	Irrigation with 2% chlorhexidine solution at day 0 then 1xweek for 3 weeks	-0.1, NS	+0.1, NS
Taggart et al., 1990[87]	NR PL NR	10 weeks	N: 10 subjects T: 10 subjects C: 10 subjects	Irrigation with 0.02% chlorhexidine solution	+0.1, NS	+0.1, NS

Table 12. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Chlorhexidine (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Reynolds et al., 1992[88]	R PL DB	4 weeks (28 days)	N: 60 subjects T: 90 sites C: 90 sites	Irrigation with 0.12% chlorhexidine solution, 1 time	Data NR, NR	N/A
Shiloah and Patters, 1994[54]	R PL SB	4 weeks	N: 7 subjects T: 12 sites C: 12 sites	Irrigation with 0.12% chlorhexidine solution, 1 time	Data NR, NS	Data NR, NS
Oosterwaal et al., 1991[89]	R PL DB	36 weeks	N: 10 subjects T: 10 subjects C: 10 subjects	0.2% chlorhexidine gel applied 3x within 10 minutes after SRP	Data NR, NS	N/A
Unsal et al., 1994[59]	R NP NR	12 weeks	N: 15 subjects T: 7 subjects C: 8 subjects	1% chlorhexidine gel applied once	-0.25, NS	-0.34, NS
Soskolne et al., 1997[90]	R NP DB	26 weeks (6 months)	N: 94 subjects T: 94 subjects C: 94 subjects	2.5 mg chlorhexidine chip inserted into pockets 5-8 mm at day 0 and 3 months	-0.46, $P < 0.001$	+0.16, $P < 0.05$
Jeffcoat et al., 1998[91]	R PL DB	39 weeks (9 months)	N: 419 subjects T: 211 subjects C: 208 subjects	2.5 mg chlorhexidine chip inserted into pockets at baseline and months 3 and 6	+0.26, $P < 0.00056$	+0.20, $P < 0.012$
Heasman et al., 2001[92]	R NP SB	26 weeks (6 months)	N: 24 subjects T: 24 subjects C: 24 subjects	2.5 mg controlled release chlorhexidine chip	+0.33, $P = 0.05$	+0.28, $P = 0.048$
Azmak et al., 2002[93]	R NP SB	26 weeks (6 months)	N: 20 subjects T: 20 subjects C: 20 subjects	2.5 mg chlorhexidine chip in pockets	Data NR, NS	Data NR, NS

Table 12. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Chlorhexidine (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Grisi et al., 2002[94]	R NP SB	39 weeks (9 months)	N: 19 subjects T: 10 subjects C: 9 subjects	2.5 mg chlorhexidine chip at day 0, 3 and 6 months	-0.2, NS	-0.4, NS
Quirynen et al., 2000[95]	Non-R NP NR	35 weeks (8 months)	N: 24 subjects T: 12 subjects C: 12 subjects	Combination of 1% chlorhexidine gel for brushing and subgingival irrigation + 0.2% chlorhexidine rinse + spray within 24 hours, then 0.2% rinse and spray 2xday for 60 days	Single-root: -0.1, NS Multi-root: -0.5, NS	Initial PD =7 mm: Single-root: -0.3, NS Multi-root: -0.3, NS Initial PD < 7 mm Data NR, NR

R, randomized; Non-R, nonrandomized; PL, placebo-controlled; NP, no placebo; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 13. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Systemic Antibiotics

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Chin Quee et al., 1987[96]	R PL DB	26 weeks (6 months)	N: 50 subjects T: 26 subjects C: 24 subjects	3 tablets (750,000 IU of spiramycin and 125 mg of metronidazole), 2xday for 14 days	Data NR, NS	Data NR, *P* < 0.05
Al-Joburi et al., 1989[45]	R PL DB	24 weeks	N: 52 subjects T: 28 subjects C: 24 subjects	500 mg spiramycin 2xday for 14 days	Initial PD = 3 mm: +0.42, NS Initial PD 4-6 mm: -0.40, NS Initial PD = 7 mm: -0.28, NS	Initial PD = 3 mm: +0.92, NS Initial PD 4-6 mm: -0.22, NS Initial PD = 7 mm: -0.08, NS
Bain et al., 1994[97]	R PL DB	24 weeks	N: 189 subjects T: 93 subjects C: 96 subjects	1,500,000 IU of spiramycin “500” capsules, 2xday for 14 days	+0.47, *P* < 0.0075	+0.29, NS
Haffajee et al., 1995[46]	R PL DB	43 weeks (10 months)	N: 21 subjects T: 10 subjects C: 11 subjects	250 mg amoxicillin with clavulanic acid 3xday for 30 days	+0.29, NS	Data NR, NS
Ng and Bissada, 1998[98]	R PL SB	24 weeks	N: 16 subjects T: 8 subjects C: 8 subjects	200 mg doxycycline on day 1 then 100 mg 1xday for 6 weeks	-0.6, NS	+1.3, *P* = 0.05

Table 13. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Systemic Antibiotics (continued)

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Rooney et al., 2002[70]	R PL DB	26 weeks (6 months)	N: 31 subjects T: 16 subjects C: 15 subjects	250 mg amoxicillin and placebo (calcium lactate tablets 3xday for 7 days, plus 0.2% chlorhexidine rinse	Initial PD = 6 mm: Data NR, *P* < 0.05	Initial PD = 6 mm: Data NR, NR
Smith et al., 2002[99]	R PL DB	22 weeks	N: 44 subjects T: 23 subjects C: 21 subjects	500 mg azithromycin 1xday for 3 days at week 2	Initial PD 1-3 mm: +0.14, NS Initial PD 4-5 mm: +0.52, *P* < 0.01 Initial PD = 6 mm: +0.87, *P* < 0.05	N/A

R, randomized; PL, placebo-controlled; DB, double-blind; SB, single blind; ; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 14. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Local Antibiotics

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Kimura et al., 1991[100]	R PL NR	4 weeks	N: 27 subjects T: 27 subjects C: 27 subjects	Controlled-release ofloxacin insert applied 1x week for 2 weeks, then SRP again and inserts applied 1xweek for next 3 weeks	N/A	N/A
Eickholz et al., 2002[101]	R PL DB	26 weeks (6 months)	N: 108 subjects T: 108 subjects C: 108 subjects	15% doxycycline gel, 1 subgingival application	+0.44, *P* = 0.0066	+0.37, *P* = 0.038

R, randomized; ; PL, placebo-controlled; ; DB, double-blind; NR, not reported; N/A, not applicable because not one of the clinical measures; NS, not significant

Table 15. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Antimicrobials

Author, Year	Randomization Placebo Blinded	Duration	Number Completing Treatment Control	Dosage and Mode	Treatment Group PD Reduction (mm) Level of Significance	Treatment Group CAL Gain (mm) Level of Significance
Wennstrom et al., 1987[85]	R PL SB	52 weeks	N: 10 subjects T: 10 subjects C: 10 subjects	3% hydrogen peroxide irrigation 3xweek for 2 weeks	+0.8, $P < 0.05$	+0.1, NS
Listgarten et al., 1989[103]	R PL DB	8 weeks	N: 40 subjects T: 20 subjects C: 20 subjects	7% tetrapotassium peroxydiphosphate irrigation 2xday for 8 weeks	+0.65, NS	+0.25, NS
Oosterwaal et al., 1991[89]	R PL DB	36 weeks	N: 10 subjects T: 10 subjects C: 10 subjects	T1:1.25% amine fluoride gel 3x within 10 minutes T2: 4% stannous fluoride gel 3x within 10 minutes	T1:Data NR, NS T2: Data NR, NS	T1: N/A T2: N/A
Furuichi et al., 1997[102]	R PL DB	2 weeks	N: 16 subjects T: 32 sites C: 32 sites	0.6% triclosan gel + 0.3% triclosan dentifrice 2xday for 2 weeks, repeated again after 1 week washout period	-0.1, NS	N/A
Rosling et al., 2001[104]	NR PL NR	676 weeks (13 years)	N: 150 subjects T: 58 subjects C: 92 subjects	0.1% povidone iodine solution	+0.6, NR	-0.59, NR

R, randomized; PL, placebo-controlled; DB, double-blind; SB, single blind; NR, not reported; N/A, not applicable because not one of the clinical measures used; NS, not significant.

Table 16. Summary of Qualitative and Quantitative Results for Probing Depth and Clinical Attachment Level

Adjunctive Therapy	Probing Depth Reductions		Clinical Attachment Level Gains	
	Number of Studies/ Number of Positive Studies*	Effect Sizes (in mm): Range and Meta-Analytic Estimate (95% CI) †	Number of Studies/ Number of Positive Studies	Effect Sizes (in mm): Range and Meta-Analytic Estimate (95% CI)
Tetracycline, systemic	5/0	Range: NA MA : 0.15 (-0.29 - 0.58)	5/1	Range: 0.31 MA: none done
Tetracycline, local	16/5	Range: 0.40-0.93 MA: 0.47 (0.22 - 0.72)	16/2	Range: 0.15 - 0.48 MA: 0.24 (0.07 - 0.42)
Minocycline, systemic	2/0	Range: NA MA: none done	0/0	Range: NA MA: none done
Minocycline, local	8/4	Range: 0.30‡ – 1.10' MA: 0.49 (0.40 - 0.58)	8/3	Range: 0.39 – 0.80 MA: 0.46 (0.32 - 0.60)
Metronidazole, systemic	8/3**	Range: 0.47¶ – 1.64¦ MA: none done	6/2	Range: 0.47¶ – 1.19# MA: none done
Metronidazole, local	11/4**	Range: 0.18 – 0.80 MA: 0.32 (0.20 - 0.44)	8/2	Range: 0.40 – 0.66 MA: 0.12 (0.01 – 0.24)
Metronidazole with amoxicillin, systemic	4/2**	Range: 0.7 MA: none done	4/1**	Range: NR MA: none done
Chlorhexidine, local	17/2	Range: 0.26 – 0.33 MA: 0.24 (0.13 - 0.35)	13/3	Range: 0.16 – 0.28 MA: 0.16 (0.04 – 0.28)
Other antibiotics, systemic	7/3**	Range: 0.47 – 0.87†† MA: none done	6/2**	Range: 1.30 MA: none done
Other antibiotics, local	1/1	Range: 0.44 MA: none done	1/1	Range: 0.37 MA: none done
Other antimicrobials, local	5/1	Range: 0.8 MA: none done	4/0	Range: NA MA: none done

*Positive studies are defined as those showing statistically significant effects in favor of the adjunctive therapy as contrasted with scaling and root planing alone. For details on studies, see the specific text tables in Chapter 3 or evidence tables in Chapter 7.
†CI, confidence interval; MA, meta-analysis; mm, millimeters NA, Not applicable; NR, not reported.
‡ 0.30 mm PD reduction for baseline probing depths of 5 mm or greater.
' 1.10 mm PD reduction for baseline probing depths of 7 mm or greater.
¶ 0.47 mm PD reduction and CAL gain for baseline probing depths of 4 mm to 6 mm.
¦ 1.64 mm PD reduction for baseline probing depths of more than 6 mm.
1.19 mm CAL gain for baseline probing depths of more than 6 mm.
** One of these studies did not report any specific data, only a significant difference.
†† 0.87 mm PD reduction for baseline probing depths of 6 mm or greater.