Probiotics in the treatment of periodontitis: a systematic review and network meta-analysis

Carlota Duarte de Mendonça.[1,2], António Mata[1,2,3], Luís Azevedo[4,5], Joana Faria Marques[1,2,3], João Silveira[1,2,3], Duarte Marques[1,2,3]

1. Biology and Oral Biochemistry Group, Faculty of Dental Medicine, University of Lisbon, 1649-003, Lisbon, Portugal.
2. Center for Evidence-Based Dental Medicine, Faculty of Dental Medicine, University of Lisbon, 1649-003, Lisbon, Portugal.
3. LIBPhys-FCT UID/FIS/04559/2013, Faculty of Dental Medicine, University of Lisbon, 1649-003, Lisbon, Portugal.
4. Faculty of Medicine, University of Porto – Department of Community Medicine, Information and Decision in Health (MEDCIDS@FMUP), 4200-450 Porto, Portugal.
5. Center for Health Technology and Services Research & Associate Laboratory – Health Research Network (CINTESIS@RISE), 4200-450 Porto, Portugal.

Appendix 1: PRISMA checklist

PRISMA NMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.*	3
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly*	3

		describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	5
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	5
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	5
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6

Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	6
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	19
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	7
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	7
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests,	8

		or summary of inconsistency estimates from different parts of the treatment network.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	7
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	8
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	12

PICOS = population, intervention, comparators, outcomes, study design.
* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.
† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Appendix 2: Search strategy

Algorithm MEDLINE (via PubMed)

1 (“gingivitis” [MeSH Terms] OR “periodontal disease” [MeSH Terms] OR “periodontitis” [MeSH Terms] OR “alveolar bone loss” [MeSH Terms] OR “chronic periodontitis” [MeSH Terms])

2 (“oral conditions” [Text Word] OR “dental plaque” [MeSH Terms] OR “oral hygiene” [Text Word] OR “tooth diseases” [All fields])

3 (#1) OR (#2)

4 ("probiotic*” [MeSH Terms] OR “probiotic*” [All Fields])) OR “prebiotic*” [All Fields OR “symbiotic*” [All Fields]

5 “Bifidobacterium"[All Fields] OR "Lactobacillus" [All Fields] OR “Streptococcus” [All Fields] OR “Bacillus” [All Fields]

6 (#4) OR (#5)

7 (#3) AND (#6)

Appendix 3: Table of excluded studies

Table 2 - Table of excluded studies.

Author (year)	Reason for exclusion
Szkaradkiewicz et al. (2014)	7
Mani et al. (2017)	7
Shimauchi et al. (2008)	7
Dhawan et al. (2013)	4
Grusovin et al. (2020)	4
Kuru et al. (2017)	4
Khoramian et al. (2020)	4
Alanzi et al. (2018)	4
Deshmukh et al. 2017	4
Jung et al. (2014)	5
Shah et al. 2013	4
Boia et al. 2019	5
Nagarajappa et al. (2015)	4
Carvalho et al. (2005)	5
Tobita et al. (2018)	4
Harper et al. (1990)	4
Tyagi et al. (2011)	5
Flemmig et al. (2011)	5
Hirota et al. (2011)	4
Fujiwara et al. (2019)	4
Mayanagi et al. (2009)	4
Botelho et al. (2009)	4
Bae et al. (2006)	4
Iwasaki et al. (2016)	4
Marttinen et al. (2012)	4
Ten Bruggencate et al. (2014)	4
Pedrazzoli et al. (1992)	5
Okuda et al. (1992)	5
Feres et al. (1999)	5
Thomas et al. (1998)	5
Fonseca et al. (2015)	5
Twetman et al. (2009)	4
Kang et al. (2020)	4
Grudianov et al. (2002)	2
Imran et al. (2015)	2
Pozharitskaia et al. (1994)	2
Nędzi-Góra et al. (2020)	4
Matsuoka et al. (2005)	2
Kerdar et al. (2019)	2
Laleman et al. (2019)	4
Keller et al. (2017)	4
Jain I et al. (2016)	6
Schaeken et al. (1996)	4
Fine et al. (2000)	4
Stomatologiia et al. (2002)	2
Koll-Klais et al. (2005)	2
Ishikawa et al. (2003)	2
Baca-Castanõn et al. (2015)	2
Maekawa et a. (2014)	2
Matsuoka et al. (2006)	2
Montalto et al. (2004)	4
Mousques et al. (1980)	1
Oh et al. (2017)	5
Zahradnik et al. (2009)	4
Schlagenhauf et al. (2020)	4
Vohra et al. (2020)	3
Patyna et al. (2021)	2
Godowski et al. (1995)	5
Bhavana et al. (2017)	5
Riccia et al. (2007)	2
Yuki O, et al. (2019)	3
Sajedinejad et al. (2017)	2
Sinulingga et al. (2019)	2
Ann et al. (2017)	5
Monaca et al. (2023)	1

(1) studies lacking essential data required for a meta-analysis; (2) non-randomized clinical studies, cohort studies, and case series; (3) studies involving patients with systemic diseases (HIV/AIDS or diabetes) or intellectual disabilities; (4) studies focused on forms of periodontal disease other than chronic periodontitis, patients in periodontal supportive therapy, or healthy volunteers; (5) studies examining therapies other than probiotics; (6) studies targeting children, adolescents, or the elderly population; (7) studies failing to meet the transitivity assumption.

Appendix 4: Data items

4.1. Main variables of the included studies

Table 3 – Main variables of the included studies

studlab	study design	population/diagnostic criteria	intervention	comparison	outcomes	*smoking habits*	*follow-up period*
Abuazab2021(Abuazab, El-Shinnawi, & El-Daker, 2021)	clinical study	PPD ≥ 4 mm and CAL 3-4mm.	Group I: SRP + probiotic	Group II: SRP + CHX gel Group III: SRP only	CAL, PPD, PI, CFU	All non-smokers	6 weeks
Alshareef2020(Alshareef et al., 2020)	RCT	Moderate to severe chronic periodontitis (CAL ≥ 3 mm)	SRP + probiotic	SRP alone	CAL, PPD, PI, BOP	NR	30 days
Butera2020(Butera et al., 2020)	RCT, parallel	Presence of periodontal disease (stage II–III)	SRP + Probiotic toothpaste SRP + Probiotic toothpaste+chewing gum	SRP + Curasept CHX toothpaste	CAL, PPD, PI, BOP, CFU	NR	6 months
Chandra2016(Chandra et al., 2016)	RCT	At least two periodontal pockets ≥ 5 mm with at least one pocket in each quadrant were included in the study.	SRP + probiotic	SRP	CAL, PPD, PI	All non-smokers	6 months
Costacurta2018(Costacurta, Sicuro, Margiotta, Ingrasciotta, & Docimo, 2018)	RCT, parallell	Chronic periodontitis, show for each quadrant at least two elements with PPD ≥4 mm and positive BOP.	SRP + probiotic	SRP alone	CAL, PPD, BOP	NR	4 weeks
deOliveira2022(de Oliveira, Lourenco, & Colombo, 2022)	RCT, parallell, double-blind, placebo-controlled	Stage I–III periodontitis Inclusion criteria were: aged≥18 years;≥12 teeth; non-smokers; and untreated periodontitis with≥1 site with PPD)≥6mmand≥2 sites with PPD≥5mmin different teeth.	SRP + probiotic	SRP + placebo	CAL, PPD, BOP	All non-smokers	2 months
Dhaliwal2017(Dhaliwal, Grover, Malhotra, & Kapoor, 2017)	RCT	Patients having moderate to severe chronic generalized periodontitis (≥ 3 mm clinical attachment loss involving > 30% of sites)	SRP + probiotic	SRP alone	CAL, PPD, PI, CFU	NR	3 months
El-bagoory2021(El-Bagoory, El-Guindy, Shoukheba, & El-Zamarany, 2021)	RCT; prospective; single-blind	Moderate chronic periodontitis according to Armitage criteria; having at minimum two teeth with one proximal site with ([CAL]) of 3–4 mm, and ([PPD]) of 5–6 mm; horizontal bone erosion by panoramic radiography.	SRP + probiotic	SRP alone	CAL, PPD, CFU	All non-smokers	6 months
Ghasemi2020(Ghasemi, Babaloo, Mohammadi, & Esmailzadeh, 2020)	RCT	Definitive diagnosis of chronic periodontitis, at least 4 teeth with a PPD of ≥5 mm, and a CAL of ≥4 mm.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	All non-smokers	3 months

Grover(Grover)	[thesis file]	Patients suffering from moderate to severe chronic generalized periodontitis (≥3mm clinical attachment loss involving >30% of sites).	SRP + probiotic	SRP alone	CAL, PPD, PI, CFU	NR	3 months
Ikram2019(Ikram et al., 2019)	RCT, double-blind, placebo-controlled	Subjects from both genders, age ≥ 30 years, who were systemically healthy with clinically diagnosed CP, having pocket depth of ≥ 4mm were included in the study.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	All non-smokers	84 dias
Ince2015(Ince et al., 2015)	RCT, parallell, double-blind, placebo-controlled	Chronic periodontitis23 patients with radiographically detected horizontal bone loss, the presence of at least 2 teeth with na approximal site each with a PD of 5-7 mm and a GI of ≥2 in each quadrant.	SRP + probiotic	SRP + placebo	PPD, PI, BOP	All non-smokers	1 year
Invernici2018(Invernici et al., 2018)	RCT, parallell, double-blind, placebo-controlled	30% or more of the sites with PPD ≥ 4 mm and CAL ≥ 4 mm, (4) presence of bleeding on probing (BOP) and a minimum of five teeth with at least one site with CAL and PPD ≥ 5 mm. All patients had to be in good general health.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	All non-smokers	90 days
Invernici2020(Invernici et al., 2020)	RCT, parallell, double-blind, placebo-controlled	30% or more of the sites with PPD ≥ 4 mm and CAL ≥ 4 mm, (4) presence of bleeding on probing (BOP) and a minimum of five teeth with at least one site with CAL and PPD ≥ 5 mm. All patients had to be in good general health.	SRP + probiotic	SRP + placebo	PI, BOP	All non-smokers	90 days
Jebin2021(Jebin, Nisha, & Padmanabhan, 2021)	RCT, parallell, double-blind	Patients with Stage II/Stage III and Grade A/Grade B periodontitis according to the American Academy of Periodontology 2018 classification with CAL 3–6 mm in at least 2 quadrants, presence of at least 16 remaining teeth with a minimum of four teeth in each quadrant, presence of at least single tooth with PPD 5–7 mm in minimum 2 quadrants.	SRP + probiotic	SRP alone	CAL, PPD, PI, CFU	All non-smokers	3 months
Kanagaraj2019(Kanagaraj, Elavarasu, Thangavelu, Subaramoniam, & Dutta, 2019)	Single-blind, RCT, prospective	Moderate chronic periodontitis, as defined by probing depth ≥ 4 mm to ≤ 7mm and generalized interproximal attachment loss were considered in the study.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP, CFU	All non-smokers	6 weeks
Kumar2021(Kumar et al., 2021)	RCT, parallell, double-blind, placebo-controlled	Generalized CP with a minimum of 3 natural teeth in each quadrant (excluding third molars), with at least 1 site having a mean PPD ≥5 mm, a CAL ≥4 mm, and presence of BOP	SRP+single application of probiotic (G2); SRP+incremental application of probiotic (G3)	SRP+placebo (G1)	CAL PPD, PI, BOP	All non-smokers	24 weeks
Laleman2015(Laleman et al., 2015)	RCT, parallell, double-blind,	Previously untreated moderate to severe generalized adult periodontitis (Van der Velden 2005). - ≥ 14 teeth; ≥ 36 years; moderate = bone loss > 1/3 and ≤ 1⁄2 of the root length or attachment loss 4–5 mm;	SRP + probiotic	SRP + placebo	CAL, PPD, BOP	NR	24 weeks

	placebo-controlled	severe = bone loss > 1/2 of the root length or attachment loss ≥ 6 mm					
Meenakshi2020(Meenakshi & Varghese, 2018)	NR	Patients with moderate periodontitis with a pocket depth <6 mm.	SRP + probiotic	SRP alone	CAL, PPD, PI, CFU	All non-smokers	1 month
Minic2020(Minic, Pejcic, & Bradic-Vasic, 2022)	RCT, prospective study	Have periodontal pockets depth ≥5 mm (at least two sites per tooth: mesial and mesiobuccal on maxillary and mandible part).	SRP + probiotic	SRP alone	PPD, PI, BOP	NR	30 days
Morales2016(Morales et al., 2016)	RCT, parallell, double-blind, placebo-controlled	Chronic periodontitis was defined as having at least five teeth with periodontal sites with pocket probing depth (PPD) ≥ 5mm and CAL ≥ 3 mm, 20% BOP and extensive radiographically determined bone loss.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	NR	12 months
Oliveira2021(Oliveira, Lourenço, & Colombo, 2021)	RCT, double-blind, placebo-controlled prospective	Inclusion criteria were: ≥18 years of age; ≥12 teeth; non-smokers; and untreated periodontitis with ≥ 1 site with PPD ≥ 6 mm and ≥ 2 sites with PPD ≥ 5 mm in different teeth.	SRP + probiotic	SRP + placebo	CAL, PPD, PI, BOP, CFU	NR	2 months
Özener2023(Ozener, Kuru, Kadir, & Kuru, 2023)	RCT, double-blind, placebo-controlled	30 chronic periodontitis patients that are considered under stage III grade B; the presence of at least 2 teeth with one approximal site having a PPD of 4–6 mm and a GI of ≥2 in each quadrant	SRP + probiotic	SRP + placebo	PPD, PI, GI, CAL, BOP, CFU	All non-smokers	3 months
Paul2019(Paul, Gandhimadhi, & Babu, 2019)	RCT, double-blind, placebo-controlled	Mild-to-moderate chronic periodontitis, as defined by PPD 5–7 mm in >30% of the probing sites, having a minimum of 16 remaining natural teeth (minimum of at least four teeth per quadrant) were included.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP, CFU	All non-smokers	12 weeks
Pelekos2020(Pelekos et al., 2020)	RCT, parallell, double-blind, placebo-controlled	Stage III and IV of periodontitis (presence of at least 2 probing sites in PPD ≥ 5mm and radiographically determined bone loss)	SRP + probiotic	SRP + placebo	CAL, PPD, BOP	All non-smokers	180 days
Penala2016(Penala et al., 2016)	RCT, parallell, double-blind, placebo-controlled	Chronic periodontitis clinically evident with at least 4 teeth showing PPD ≥5 mm, CAL ≥4 mm, and with clinically perceptible halitosis were included.	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	All non-smokers	3 months
Pudgar2021(Pudgar et al., 2021)	RCT, parallell, double-blind,	Advanced periodontitis with a PPD of ≥ 5 mm on at least four teeth in four different quadrants (stage III or IV according to the AAP/EFP classification of 2018), has stable occlusion and with the presence of at least 16 teeth of which at least 12 were scorable (excluding third molars).	SRP + probiotic	SRP + placebo	CAL PPD, PI, BOP	Smokers and non-smokers	3 months

	placebo-controlled						
Ranjith2021(Ranjith, Nazimudeen, & Baiju, 2022)	RCT, triple-blind, parallell	Inclusion criteria: Systemically healthy patients of age >30 years; Generalized Stage II periodontitis; Bleeding on probing in at least 30% sites; Non-smokers or who stopped smoking for at least 6 months CAL 3 to 4mm; Radiographic bone loss coronal third (15% to 33%); No tooth loss due to periodontitis; Maximum probingdepth ≤5mm. Mostly horizontalbone loss.	SRP + probiotic	SRP + placebo	CAL PPD, PI	All non-smokers	90 days
Tekce2015(Tekce et al., 2015)	RCT, parallell, double-blind, placebo-controlled	Chronic periodontitis patients with radiographically detected horizontal bone loss (Armitage 1999), the presence of at least 2 teeth with one approximal site with a PD of 5–7 mm and a GI of ≥2 in each quadrant.	SRP + probiotic	SRP + placebo	PPD, PI, BOP, CFU	All non-smokers	360 days
Teughels2013(Teughels et al., 2013)	RCT, parallell, double-blind, placebo-controlled	Previously untreated moderate to severe generalized adult periodontitis (Van der Velden 2005). - ≥ 14 teeth; ≥ 36 years; moderate = bone loss > 1/3 and ≤ 1⁄2 of the root length or attachment loss 4–5 mm; severe = bone loss > 1/2 of the root length or attachment loss ≥ 6 mm	SRP + probiotic	SRP + placebo	CAL, PPD, PI, BOP, CFU	All non-smokers	12 weeks
Theodoro2019(Theodoro et al., 2019)	RCT, parallell, placebo-controlled	Diagnosis of severe generalised chronic periodontitis, with at least 6 teeth presenting at least 1 site each with PPD and CAL ≥5 mm, and at least 30% of sites with PD and CAL ≥4 mm and BOP (Armitage, 1999), being heavy smokers (more than 10 cigarettes per day for more than 5 years) (Ammenheuser et al., 1997), and at least 15 teeth in the mouth, excluding third molars.	SRP + probiotic	SRP + placebo	CAL, PPD, BOP	All smokers	90 days
Tsubura2009(Tsubura et al., 2009)	RCT	Chronic periodontitis (They also had at least 20 natural teeth, including at least eight sites with PPD>4 mm on molar teeth)	SRP + probiotic (Extraction 300E (containing Bacillus subtilis: E-300)	SRP + control (NG - Neosteline Green (NG), containing benzethonium chloride 0.2 g/100 ml)	PPD, BOP	All non-smokers	30 days
Vicario2013(Vicario, Santos, Violant, Nart, & Giner, 2013)	RCT, double-blind, placebo-controlled	Chronic periodontitis according to the criteria at the 1999 International Classification by Armitage, good general health, stated availability throughout the entire study period and willingness and capacity to comply with the protocol. (Armitage) Chronic Periodontitis (slight: 1-2 mm CAL; moderate: 3-4 mm CAL; severe: > 5 mm CAL) A. Localized B. Generalized (> 30% of sites are involved)	SRP + probiotic	SRP + placebo	PPD, PI, BOP	All non-smokers	30 days

AL: attachment loss; BOP: bleeding on probing; CAL: clinical attachment level; CFU: colony forming units; CHX: chlorhexidine; CP: chronic periodontitis; GI: gingival index; NR: not reported; PI: plaque index; PPD: periodontal probing depth; RCT: randomized controlled trial; SRP: scaling and root planning.

4.2. Data according to group and outcome

Table 4

– Data according to group and outcome.

studlab	sample size	Age ± SD	gender (M/F)	probiotic strain and concentration	form of administration	duration of probiotic therapy	CAL (mm)	PPD (mm)	PI (%)	BOP (%)	CFU	adverse effects	notes
Abuazab2021(Abuazab et al., 2021)	30 (SRP:10; SRP+CHX:10 SRP+Prob:10)	30-50	12 males; 18 females	Bifidobacterium bifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12, isolated from intestine of adults and supplied as actively growing cultures.	Gel	6w	(SRP) Day 0: 2.78 ± 0.31; 6w: 2.25 ± 0.35; (SRP+CHX) Day 0: 2.57 ± 0.34; 6w: 1.96 ± 0.41; (SRP+prob) Day 0: 2.79 ± 0.34; 6w: 1.87 ± 0.41.	(SRP) Day 0: 3.28 ± 0.39; 6w: 1.92 ± 0.23; (SRP+CHX) Day 0: 3.06 ± 0.45; 6w: 1.97 ± 0.32; (SRP+prob) Day 0: 3.29 ± 0.39; 6w: 2.02 ± 0.42.	(SRP) Day 0: 2.33 ± 0.21; 6w: 0.826 ± 0.109; (SRP+CHX) Day 0: 2.49 ± 0.245; 6w: 0.889 ± 0.138; (SRP+prob) Day 0: 2.34 ± 0.24; 6w: 0.766 ± 0.096.	Not reported	(Pg) (SRP) Day 0: 29.0 ± 10.15; 6w: 17.0 ± 1.9; (SRP+CHX) Day 0: 28.0 ± 17.52; 6w: 9.0 ± 2.0; (SRP+prob) Day 0: 30.0 ± 14.43; 6w: 7.0 ± 1.4; (Pi) (SRP) Day 0: 32.0 ± 8.93; 6w: 19.0 ± 3.1; (SRP+CHX) Day 0: 33.0 ± 18.7; 6w: 12.0 ± 1.5; (SRP+prob) Day 0: 35.0 ± 11.28; 6w: 11.0 ± 2.5; (Total load) (SRP) Day 0: 965.0 ± 166.02; 6w: 612.0 ± 146.35; (SRP+CHX) Day 0: 884.0 ± 187.39; 6w: 581.0 ± 177.60; (SRP+prob) Day 0: 928.50 ± 183.88; 6w: 505 ± 174.42.	None	Also report data related to GI and total count of bacteria Data from PI are presented in % but the method is not explained
Alshareef2020(Alshareef et al., 2020)	25 (SRP: 10; SRP+prob: 15)	29 ± 96	Not reported	Each probiotic lozenge contains five bifid bacteria including Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, Lactobacillus rhamnosus, and Lactobacillus salivarius.	Lozenges	not reported	(SRP) Day 0: 3.4930 ± 0.66101; 30d: 3.1490 ± 0.65514; . (SRP+prob) Day 0: 3.5740 ± 0.58024; 30d: 3.1487 ± 0.59010.	(SRP) Day 0: 2.6130 ± 0.41508; 30d: 2.3380 ± 0.43235; . (SRP+prob) Day 0: 2.5533 ± 0.23654; 30d: 2.1973 ± 0.27830.	(SRP) Day 0: 47.3250 ± 15.38717; 30d: 37.3160 ± 12.29990; . (SRP+prob) Day 0: 44.0127 ± 10.06966; 30d: 35.7433 ± 15.18255.	(SRP) Day 0: 49.7550 ± 13.93193; 30d: 40.8200 ± 13.21242; . (SRP+prob) Day 0: 40.7533 ± 9.58256; 30d: 32.1533 ± 8.50200.	Not reported	Not reported	Also reported Unpaired t-test statistical comparisons of clinical parameters for both examined groups
Butera2020 (Butera et al., 2020)	60 (SRP+CHX: 20; SRP+probToothpaste:20; SRP+probToothpaste&gum: 20)	SRP+CHX: 55 SRP+probToothpaste: 49 SRP+probToothpaste &gum: 55	SRP+CHX: 9/11 SRP+probToothpaste: 13/7 SRP+probToothpaste&gum: 10/10	Toothpaste: Bifidobacterium *, Lactobacillus * Chewing gum: L. reuteri (SGL 01), L. salivarius (SGL 03), L. plantarum (SGL 07)	Toothpaste and chewing gum	6m	(CHXtoothpaste) Day 0: 5.83 ± 1.87; 6m: 5.57 ± 1.72; (ProbToothpaste) Day 0: 5.64 ± 2.27; 6m: 4.44 ± 2.14; (ProbToothpaste+gum) Day 0: 5.36 ± 1.46; 6m: 3.46 ± 0.94.	(CHXtoothpaste) Day 0: 5.88 ± 1.26; 6m: 5.80 ± 1.08; (ProbToothpaste) Day 0: 5.67 ± 0.74; 6m: 4.46 ± 0.84; (ProbToothpaste+gum) Day 0: 5.57 ± 0.85; 6m: 3.52 ± 0.53.	(CHXtoothpaste) Day 0: 70.00 ± 26.56; 6m: 67.00 ± 22.33; (ProbToothpaste) Day 0: 68,50 ± 22.48; 6m: 34.15 ± 14.08; (ProbToothpaste+gum) Day 0: 70.50 ± 20.38; 6m: 28.50 ± 17.85.	(CHXtoothpaste) Day 0: 66.25 ± 17.23; 6m: 64.00 ± 14.01; (ProbToothpaste) Day 0: 67.00 ± 24.94; 6m: 33.00 ± 20.39; (ProbToothpaste+gum) Day 0: 66.15 ± 34.89; 6m: 21.50 ± 17.55.	*(Aa)* (CHXtoothpaste) Day 0: 1247.48 ± 1238.52; 6m: 1030.08 ± 1202.40; (ProbToothpaste) Day 0: 528 ± 1121.42; 6m: 734.5 ± 2076.09; (ProbToothpaste+gum) Day 0: 650.25 ± 1114.43; 6m: 406.2 ± 919.53; *(Pg)* (CHXtoothpaste) Day 0: 10530.55 ± 18424.41; 6m: 8479 ± 3974.44; (ProbToothpaste) Day 0: 9107.65 ± 21882.53; 6m: 7625.75 ± 22714.00; (ProbToothpaste+gum) Day 0: 11644.1 ± 23306.05; 6m: 7553.641 ± 15781.77; *(Tf)* (CHXtoothpaste) Day 0: 34012.51 ± 54134.03; 6m: 40990 ± 19938.19; (ProbToothpaste) Day 0: 57690.4 ± 90873,28;	Not reported	Also reported data relative to Bleeding Score, Sulcus Bleeding Index, Approximal Plaque Index, Adherent Gingiva (distance between the mucogingival junction and the projection on the external surface of the bottom of the gingival sulcus), Gingival Recession and Pathological Sites.).

												6m: 25656.4 ± 48302.74; (ProbToothpaste+gum) Day 0: 35091.9 ± 40463.06; 6m: 3929080 ± 66828.91; *(Td)* (CHXtoothpaste) Day 0: 7339.82 ± 19922.95; 6m: 4651 ± 2158.87; (ProbToothpaste) Day 0: 5318 ± 10086.63; 6m: 10244.63 ± 15860.15; (ProbToothpaste+gum) Day 0: 5521.75 ± 18720.46; 6m: 6065.13 ± 19738.92; *(Pi)* (CHXtoothpaste) Day 0: 11018 ± 10208.32; 6m: 8830 ± 5617.44; (ProbToothpaste) Day 0: 9720.1 ± 2405.66; 6m: 3536 ± 5931.72; (ProbToothpaste+gum) Day 0: 7476.55 ± 4787.82; 6m: 2520.5 ± 2435.87; *(Fn)* (CHXtoothpaste) Day 0: 17607.3 ± 25342.18; 6m: 16298.82 ± 17212.96; (ProbToothpaste) Day 0: 19381.2 ± 10360.37; 6m: 7843.6 ± 5509.43; (ProbToothpaste+gum) Day 0: 18053 ± 10931.75; 6m: 7211.78 ± 5971.25; *(Total Bacteria Count)* (CHXtoothpaste) Day 0: 1648650 ± 2571189.00; 6m: 561150 ± 349477.80; (ProbToothpaste) Day 0: 1150665 ± 2270115.00; 6m: 535470 ± 306466.90; (ProbToothpaste+gum) Day 0: 808115 ± 1619913.00; 6m: 2097731 ± 5655579.00;		
Chandra2016(Chandra et al., 2016)	30 (SRP: 27; SRP+prob:30)	25-50	Not reported	(250 mg; Florafi x®, Unique Biotech, Hyderabad, India) + The probiotic was mixed with a prebiotic (fructooligosaccharide, FOS; Mitushi Pharma, Ahmedabad, India), in the ratio of 4:1 to induce growth and activity in S boulardii. Briefl y, 30 preparations of 1 g S boulardii-FOS mixture were made by stirring 200 mg of FOS and 800 mg of probiotic with a spatula. containing approximately 5 billion colony forming units (CFU) of the yeast Saccharomyces boulardii.	Powder	Single application	(SRP) Day 0: 3.52 ± 0.74; 6m: 1.80 ± 0.92; (SRP+prob) Day 0: 3.57 ± 0.74; 6m: 0.61 ± 0.58.	(SRP) Day 0: 5.52 ± 0.74; 6m: 3.61 ± 0.97; (SRP+prob) Day 0: 5.66 ± 0.73; 6m: 2.19 ± 0.51.	(SRP) Day 0: 1.79 ± 0.36; 6m: 0.92 ± 0.27; (SRP+prob) Day 0: 1.58 ± 0.34; 6m: 0.64 ± 0.28.	Not reported	Not reported	Not reported	Also analyse Viability of S. boulardii in the gingival sulcus *in vitro*
Costacurta2018(Costacurta et al., 2018)	40 (SRP: 20; SRP+prob: 20)	SRP: 51.8±14.94 SRP+prob: 41.3±11.85	SRP: F:60%, M:40% SRP+prob: F:40%, M:60%	probiotic containing 10 8 CFU of Lactobacillus reuteri DSM 17938 and 10 8 CFU of Lactobacillus reuteri ATCC PTA 5289	Tablets	4w	(SRP) Day 0: 4.95 ± 0.56; 4w: 4.3 ± 0.52; (SRP+prob) Day 0: 4.56 ± 0.94; 4w: 3.94 ± 0.85.	(SRP) Day 0: 4.51 ± 0.54; 4w: 3.91 ± 0.50; (SRP+prob) Day 0: 4.12 ± 0.89; 4w: 3.47 ± 0.65.	Not reported	(SRP) Day 0: 88.45 ± 9.63; 4w: 58.15±10.38; (SRP+prob) Day 0: 87.5±14.75; 4w: 31.45±15.97.	Not reported	Not reported	-
deOliveira2022(de Oliveira et al., 2022)	48 (SRP+plac: 23; SRP+prob: 19)	Not reported	Not reported	Dive strains of Lactobacillus spp. and three of Bifidobacterium spp.	Capsule	1capsule/day (2m)	(SRP+plac) Day 0: 3.18 ± 0.785; 2m: 2.89 ± 0.711; (SRP+prob) Day 0: 3.31 ± 0.830; 2m: 2.74 ± 0.844.	(SRP+plac) Day 0: 2.82 ± 0.460; 2m: 2.24 ± 0.207; (SRP+prob) Day 0: 3.00 ± 0.363; 2m: 2.36 ± 0.319.	Not reported	(SRP+plac) Day 0: 45.10 ± 16.333; 2m: 24.70 ± 14.740; (SRP+prob) Day 0: 53.30 ± 24.148; 2m: 32.20 ± 17.111. (%)	Not reported	Most patients reported feeling well during treat-ments; however, gastrointestinal symptoms	-

											were morefrequently reported in the probiotic than placebo group,in particular the occurrence of soft stools	
Dhaliwal2017(Dhaliwal et al., 2017)	27 (SRP: 13; SRP+prob: 14)	SRP: 31 ± 8.07 SRP+prob: 33.46 ± 6.63	20 males (74.07%) and 7 females (25.93%)	Bifi lac lozenges (Tablets India Private Limited, Chennai).It is a commercially available probiotic preparation combined with prebiotics to enhance its action. Each tablet contains Streptococcus faecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bacillus mesentericus TO-A JPC-1million CFU and Lactobacillus sporogenes IHS-50 million CFU.	Lozenges	3m	(SRP) Day 0: 9.17 ± 0.75; 3m: 8.21 ± 1.08; (SRP+prob) Day 0: 9.45 ± 1.14; 3m: 8.16 ± 1.55.	(SRP) Day 0: 4.97 ± 0.61; 3m: 4.15 ± 0.73; (SRP+prob) Day 0: 5.54 ± 1.08; 3m: 4.62 ± 1.32.	(SRP) Day 0: 1.51 ± 0.40; 3m: 1.11 ± 0.15; (SRP+prob) Day 0: 1.59 ± 0.34; 3m: 1.20 ± 0.20.	Not reported	(Aa) (SRP) Day 0: 10.57 ± 16.15; 3m:11.07 ± 24.03; (SRP+prob) Day 0: 5.82 ± 10.60; 3m: 0.00 ± 0.00; (Pg) (SRP) Day 0: 28.29± 30.68; 3m: 14.36 ± 21.68; (SRP+prob) Day 0: 21.38 ± 22.51; 3m: 0.00 ± 0.00; (Pi) (SRP) Day 0: 0.71 ± 1.86; 3m: 2.57 ± 8.05; (SRP+prob) Day 0: 2.00 ± 5.54; 3m: 7.69 ± 27.74;	None	Also report data relative to GI
El-bagoory2021(El-Bagoory et al., 2021)	12 (SRP: 6; SRP+prob:6)	SRP: 39.33 ± 3.20 SRP+prob: 39.33 ± 3.20	SRP:1/5 SRP+prob: 2/4	L. reuteri DSM 17938 [1 × 108 CFU]	Drops	4w	(SRP) Day 0: 3.30 ± 0.48; 6m: 2.30 ± 0.67; (SRP+prob) Day 0: 3.10 ± 0.32; 6m: 1.30 ± 0.48.	(SRP) Day 0: 5.30 ± 0.48; 6m: 4.30 ± 0.67; (SRP+prob) Day 0: 5.10 ± 0.32; 6m: 3.30 ± 0.48.	Not reported	Not reported	(Pg) (SRP) Day 0: 31.01 ± 5.43; 6m: 36.10 ± 2.81; (SRP+prob) Day 0: 34.41 ± 1.13; 6m: 24.34 ± 3.30.	None	Loss of attachment
Ghasemi2020(Ghasemi et al., 2020)	36 (SRP+plac:18; SRP+prob:18)	SRP+plac: 44.35 SRP+prob: 44.81	SRP+plac: 60%/40%; SRP+prob: 55%/45%	Prokid capsule (15×10 9 probiotic units per capsule), which contained a combination of bacterial strains, i.e., Bifidobacteriumlactis, Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus rhamnosus, which were purchased from Gostaresh Milad Pharmed Co	Mouth wash	20d	(SRP+plac) Day 0: 5.33±0.69; 3m: 4.69±0.69; (SRP+prob) Day 0: 5.31±0.58; 3m: 4.25±0.76.	(SRP+plac) Day 0: 5.78±0.57; 3m: 4.97±0.68; (SRP+prob) Day 0: 5.65±0.57; 3m: 4.29±0.71.	(SRP+plac) Day 0: 48.72±7.71; 3m: 20.11±7.54; (SRP+prob) Day 0: 50.76±7.87; 3m: 19.59±10.79.	(SRP+plac) Day 0: 47.55±8.14; 3m: 23.45±9.17; (SRP+prob) Day 0: 48.95±7.73; 3m: 19.46±10.97.	Not reported	Not reported	-
Grover(Grover)	30 (SRP: 15; SRP+prob: 15)	SRP: 31 ± 8.07 (A) SRP+prob: 33.46 ± 6.63 (B)	population: 20/7	Bifilac lozenges (Streptococcus faecalis T-110 JPC -30 millionCFU; Clostridium butyricum TO-A IHS-2 million CFU; Bacillus mesentericus TO-A JPC-1million CFU;Lactobacillus sporogenes IHS-50 million CFU)	Lozenges	21d	(SRP) Day 0: 9.17 ± 0.75; 3m: 8.21 ± 1.08; (SRP+prob) Day 0: 9.45 ± 1.14; 3m: 8.16 ± 1.55.	(SRP) Day 0: 4.97 ± 0.61; 3m: 4.15 ± 0.73; (SRP+prob) Day 0: 5.54 ± 1.08; 3m: 4.62 ± 1.32.	(SRP) Day 0: 1.51 ± 0.40; 3m: 1.11 ± 0.15; (SRP+prob) Day 0: 1.59 ± 0.34; 3m: 1.20 ± 0.20.	Not reported	(Aa) (SRP) Day 0: 10.57 ± 16.15; 3m: 11.07 ± 24.03; (SRP+prob) Day 0: 5.82 ± 10.60; 3m: 0 ± 0; (Pg) (SRP) Day 0: 28.29 ± 30.68; 3m: 14.36 ± 21.68; (SRP+prob) Day 0: 21.38 ± 22.51; 3m: 0 ± 0; (Pi) (SRP Day 0: 0.71 ± 1.86; 3m: 2.57 ± 8.05; (SRP+prob) Day 0: 2.00 ± 5.54; 3m: 7.69 ± 27.74	None	Relative attachment loss Also report data related to GI
Ikram2019b(Ikram et al., 2019)	67 (SRP+plac: 14; SRP+prob: 14)	SRP+plac: 40.14 ± 2.64; SRP+prob: 41.78 ± 3.58;	SRP+plac: 8/6 SRP+prob: 9/5	L. reuteri (doesn't mention dosage), but protocol has L. reuteri 1.2 billion CFU/g	Sachet	12wk	(SRP+plac) Day 0: 4.12 ± 0.74; 84d: 3.86 ± 0.59; (SRP+prob) Day 0: 4.08 ± 0.66; 84d: 3.24 ± 0.47.	(SRP+plac) Day 0: 4.25 ± 1.12; 84d: 3.95 ± 0.78; (SRP+prob) Day 0: 4.32 ±0.91; 84d: 2.54 ± 0.52.	(SRP+plac) Day 0: 84.58 ± 8.06; 84d: 33.67 ± 9.47; (SRP+prob) Day 0: 85.23 ± 8.23; 84d: 26.28 ± 4.12.	(SRP+plac) Day 0: 71.94 ± 23.13; 84d: 46.24 ± 11.40; (SRP+prob) Day 0: 70.47 ± 11.8; 84d: 13.89 ± 3.25.	Not reported	Not reported	-
Ince2015(Ince et al., 2015)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 42.20 ± 2.78 SRP+prob: 41 ± 3.17	SRP+plac: 8/7 SRP+prob: 9/6	L. reuteri DSM17938 and L. reuteri ATCC PTA5289 with 10^8 CFU for each strain (Prodentis, Biogaia, Sweden).	Lozenges	3wk	Not reported	(SRP+plac) Day 0: 5.57 ± 0.39; 360d: 5.01 ± 0.40; (SRP+prob) Day 0: 5.85 ± 0.54; 360d: 4.15 ± 0.44.	(SRP+plac) Day 0: 2.23 ± 0.24; 360d: 1.43 ± 0.26; (SRP+prob) Day 0: 2.25 ± 0.25; 360d: 0.76 ± 0.24.	(SRP+plac) Day 0: 88.65 ±4 .11; 360d: 19.00 ± 5.42; (SRP+prob) Day 0: 88.90 ± 7.66; 360d: 11.60 ± 4.35.	Not reported	None	Also report data relative to GI, GCF volum, MMP-8, TIMP-1

Invernici2018(Invernici et al., 2018)	41 (SRP+plac: 21; SRP+prob: 20)	Not reported	Not reported	Bifidobacterium animalis subsp. lactis (B. lactis) HN019 (HOWARU® Bifido LYO 40 DCUS, DuPont™ Danisco® Sweeteners Oy, Kantvik, Finland) (10^9 colony-forming units (CFUs))	Lozenges	30d	(SRP+plac) Day 0: 3.42 ± 0.54; 90d: 3.24 ± 0.51; (SRP+prob) Day 0: 3.26 ± 0.39; 90d: 2.77 ± 0.38.	(SRP+plac) Day 0: 3.10 ± 0.43; 90d: 2.85 ± 0.34; (SRP+prob) Day 0: 3.01 ± 0.27; 90d: 2.49 ± 0.27.	(SRP+plac) Day 0: 26.71 ± 16.60; 90d: 27.14 ± 18.64; (SRP+prob) Day 0: 23.85 ± 15.33; 90d: 21.65 ± 13.13.	(SRP+plac) Day 0: 35.00 ± 25.84; 90d: 30.71 ± 27.86; (SRP+prob) Day 0: 30.80 ± 22.07; 90d: 18.80 ± 16.14.	Not reported	None	Also report mean difference and data relative to moderate and deep pockets separately
Invernici2020(Invernici et al., 2020)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 47.67 ± 9.49 SRP+prob: 47.60 ± 9.97	SRP+plac: 8/7 SRP+prob: 5/10	10^9 colony-forming units (CFUs) of B. lactis HN019 (HOWARU1 Bifido LYO 40 DCU-S, DuPont™ Danisco1 Sweeteners Oy, Kantvik, Finland)	Lozenges	30d	Not reported	Not reported	(SRP+plac) Day 0: 22.50 ± 8.54; 90d: 22.66 ± 9.99; (SRP+prob) Day 0: 18.71 ± 12.14; 90d: 18.27 ± 17.11.	(SRP+plac) Day 0: 14.07 ± 7.99; 90d: 12.10 ± 8.19; (SRP+prob) Day 0: 9.17 ± 7.71; 90d: 5.92 ± 6.12.	Not reported	None	Also report data relative to immunocompetence of gingival tissues [expression of beta-defensin (BD)-3, toll-like receptor 4 (TLR4), cluster of differentiation (CD)-57 and CD-4], and on immunological properties of saliva (IgA levels)
Jebin2021(Jebin et al., 2021)	27 (SRP:13; SRP+prob:14)	SRP: 37.8 ± 7.90 SRP+prob: 37.5 ± 7.12	SRP: 10/3 SRP+prob:11/3	L. reuteri UBLRu-87, 0.5 billion CFU, Unique Biotech Ltd, Hyderabad, India	Chewable tablet	1m	(SRP) Day 0: 4.17 ± 0.20; 3m: 3.50 ± 0.21; (SRP+prob) Day 0: 3.99 ± 0.56; 3m: 2.97 ± 0.35.	(SRP) Day 0: 5.20 ± 0.40; 3m: 4.35 ± 0.38; (SRP+prob) Day 0: 5.27 ± 0.49; 3m: 3.6 ± 0.56.	(SRP) Day 0: 1.80 ± 0.32; 3m: 1.28 ± 0.23; (SRP+prob) Day 0: 1.69 ± 0.36; 3m: 0.95 ± 0.19.	Not reported	(SRP) Day 0: 6.43±0.64; 3m: 4.54±0.49; (SRP+prob) Day 0: 6.60±0.63; 3m: 3.94±0.33.	None	Also report data related to GI PI is reported according to mean of Silness & Loe index 1964
Kanagaraj2019(Kanagaraj et al., 2019)	60 (SRP+plac: 30; SRP+prob: 30)	25-50	Not reported	BIFILAC-lozenges) contains Lactobacillus sporogenes 100 million, Streptococcus faecalis T-110 JPC 60 million, Clostridium butyrium TO-A 4 million and Bacillus mesentericus TO-A JPC 2 million.	Lozenges	3w	(SRP+plac) Day 0: 3.09 ± 0.21; 6w: 1.27 ± 0.38; (SRP+prob) Day 0: 3.05 ± 0.13; 6w: 0.50 ± 0.47.	(SRP+plac) Day 0: 5.13 ± 0.10; 6w: 2.50 ± 0.54; (SRP+prob) Day 0: 5.19 ± 0.14; 6w: 1.69 ± 0.57.	(SRP+plac) Day 0: 2.12 ± 0.51; 6w: 1.92 ± 0.43; (SRP+prob) Day 0: 2.15 ± 0.48; 6w: 1.04 ± 0.51.	(SRP+plac) Day 0: 2.30 ± 0.47; 6w: 1.96 ± 0.43; (SRP+prob) Day 0:2 .24 ± 0.42; 6w: 1.13 ± 0.49.	In evaluating the presence of Porphyromonas gingivalis, more positive bands of P gingivalis was seen in both Group I and Group II at Day 0 and there was much reduction after 3 weeks in Group II after post therapy compared to Group I as shown in Fig. 3.	None	Sulcus bleeding index Also report data related to MMP 8 Levels in GCF Data from PI are presented in % but the method is not explained
Kumar2021 (Kumar et al., 2021)	48 (SRP+plac: 15; SRP+prob: 15; SRP+pprob: 15)	SRP+plac: 42.87 ± 3.42 SRP+prob: 41.79 ± 2.37 SRP+prob: 39.74 ± 2.97	SRP+plac: 7/8 SRP+prob: 6/9 SRP+pprob: 8/7	5.9 billion colony-forming units (CFU) of L. reuteri per gram and maltodextrin as a carrier (batch No. LR 12, Meteoric Lifesciences, Ahmedabad, India)	Free-flowing powder	4w	(SRP+plac) Day 0: 5.92 ± 0.65; 24w: 4.79 ± 0.90; (SRP+prob) Day 0: 6.27 ± 0.75; 24w: 4.82 ± 0.60; (SRP+pprob) Day 0: 6.44 ± 0.79; 24w: 4.88 ± 0.58.	(SRP+plac) Day 0: 6.72 ± 0.63; 24w: 5.08 ± 0.50; (SRP+prob) Day 0: 6.78 ± 0.72; 24w: 4.92 ± 0.58; (SRP+pprob) Day 0: 6.63 ± 0.75; 24w: 4.91 ± 0.73.	(SRP+plac) Day 0: 2.08 ± 0.18; 24w: 0.70 ± 0.40; (SRP+prob) Day 0: 2.10 ± 0.23; 24w: 0.73 ± 0.24; (SRP+pprob) Day 0: 2.20 ± 0.43; 24w: 0.46 ± 0.19.	(SRP+plac) Day 0: 81.67 ± 19.97; 24w: 43.33 ± 22.09; (SRP+prob) Day 0: 93.33 ± 11.44; 24w: 35.00 ± 22.76; (SRP+pprob) Day 0: 92.86 ±15.28; 24w: 31.21 ± 15.39.	Not reported	None	Also reported Intra-group comparisons of clinical outcomes at various time intervals for test teeth and Biochemical outcome measures with inter-group comparisons at various time intervals for the test teeth PI is reported according to mean of Silness & Loe index 1964
Laleman2015(Laleman et al., 2015)	48 (SRP+plac: 24; SRP+prob: 24)	SRP+plac: 46.0 ±- 5,0 SRP+prob: 47.0 ± 5.0	SRP+plac: 14/10 SRP+prob: 12/12	S. oralis KJ3, S. uberis KJ2 and S. rattus JH145 (Probiora3,;Oragenics, Alachua, FL, USA) were added (at least 108 CFU of each strain/tablet)	Tablet	12wk	(SRP+plac) Day 0: 5.36 ± 0.45; 24w: 4.60 ± 0.48; (SRP+prob) Day 0: 5.22 ± 0.41; 24w: 4.51 ± 0.41.	(SRP+plac) Day 0: 4.59 ± 0.52; 24w: 2.98 ± 0.47; (SRP+prob) Day 0: 4.50 ± 0.51; 24w: 2.99 ± 0.47.	Not reported	(SRP+plac) Day 0: 85.55 ± 7.29 24w: 30.11 ± 10.36; (SRP+prob) Day 0: 87.44 ± 6.03; 24w: 26.98 ± 9.34.	Not reported	None	Also report data relative to moderate and deep pockets separately
Meenakshi2020(Meenakshi & Varghese, 2018)	20 (SRP:10; SRP+prob:10)	Not reported	Not reported	Yakult containing *Lactobacillus casei* strain Shirota	Mouth wash	1m	(SRP) Day 0: 4.89±0.55; 1m: 4.54±0.53; (SRP+prob) Day 0: 4.95±0.40; 1m: 4.01±0.53.	(SRP) Day 0: 4.46±0.75; 1m: 4.14±0.66; (SRP+prob) Day 0: 4.57±0.51; 1m: 3.43±0.39.	(SRP) Day 0: 1.76±0.41; 1m: 1.40±0.35; (SRP+prob) Day 0: 1.93±0.40; 1m: 0.80±0.35.	Not reported	(SRP) Day 0: 163.9±37.6; 1m: 122.5±28.6; (SRP+prob) Day 0: 169.4±34.7; 1m: 98.9±16.2.	Not reported	Also report data relative to gingival index
Minic2020(Minic et al., 2022)	80 (SRP: 40; SRP+prob: 40)	35-55	Not reported	6.5 billion live Lactobacillus acidophilus, concentration of 107 CFU, at least 107 CFU Bifidobacterium infantis and at least 106 CFU Enterococcus faecium colony-forming units per capsule	Gel	5d	Not reported	(SRP) Day 0: 5.22 ± 0.56; 30d: 4.72 ± 0.36; (SRP+prob) Day 0: 5.30 ± 0.46; 30d: 4.08 ± 0.22.	(SRP) Day 0: 1.92 ± 0.53; 30d: 0.61 ± 0.03; (SRP+prob) Day 0: 2.00 ± 0.56; 30d: 0.10 ± 0.04.	(SRP) Day 0: 1.87 ± 0.38; 30d: 0.82 ± 0.13; (SRP+prob) Day 0: 1.80 ± 0.35; 30d: 0.18 ± 0.06.	Not reported	None	PI were recorded as follows: 0 = no plaque present; 1 = plaque covering not more than 1/3 of the tooth; 2 = plaque covering more than 1/3, but not more than 2/3 of exposed tooth surface; and 3 = plaque covering

														more than 2/3 of exposed tooth surface. BOP was evaluated using a scoring scheme, where 0 = no bleeding within 10 seconds after probing; 1 = bleeding within 10 seconds after probing; and 2 = bleeding on probing.
Morales2016(Morales et al., 2016)	28 (SRP+plac: 14; SRP+prob:14)	SRP+plac: 46.9 ±- 10.3 SRP+prob: 52.7 ± 7.3	SRP+plac: 7/7 SRP+prob: 7/7	L. rhamanosus SP1 (2 × 10^7 CFU/day) (Macrofood SA, Santiago, Chile)	Sachet	3m	(SRP+plac) Day 0: 4.9 ± 1.3; 12m: 4.8 ± 1.3; (SRP+prob) Day 0: 4.2 ± 0.9; 12m: 4.1 ± 1.0.	(SRP+plac) Day 0: 2.5 ± 0.3; 12m: 2.0 ± 0.2; (SRP+prob) Day 0: 2.7 ± 0.6; 12m: 2.1 ± 0.5.	(SRP+plac) Day 0: 52.1 ± 20.7; 12m: 35.5 ± 11.4; (SRP+prob) Day 0: 63.1 ± 18.59. 12m: 33.1 ± 21.3.	(SRP+plac) Day 0: 33.8 ± 16.1; 12m: 25.4 ± 10.3; (SRP+prob) Day 0: 41.1 ± 16.3; 12m: 29.3 ± 12.7.	Not reported	None	-
Oliveira2021(Oliveira et al., 2021)	48 (SRP+plac: 23; SRP+prob: 19)	SRP+plac: 53.0 (12.0) SRP+prob: 49.0 (10.0)	SRP+plac: 9/14 SRP+prob: 10/9	The probiotic selected * contained 5 strains of Lactobacillus spp. and 3 of Bifidobacterium spp.	Capsule	30d	(SRP+plac) Day 0: 3.18 (1.06); 2m: 2.89 (0.96); (SRP+prob) Day 0: 3.31 (1.12); 2m: 2.74 (1.14).	(SRP+plac) Day 0: 2.82 (0.62); 2m: 2.24 (0.28); (SRP+prob) Day 0: 3.00 (0.49); 2m: 2.36 (0.43).	(SRP+plac) Day 0: 62.10 (20); 2m: 44.90 (19.10); (SRP+prob) Day 0: 61.30 (22.10); 2m: 47.90 (22.40).	(SRP+plac) Day 0: 45.10 (22.05); 2m: 24.70 (19.90); (SRP+prob) Day 0: 53.30 (32.60); 2m: 32.20 (23.10).	Change in mean counts, 41 bacteria, but only in graphics Not reported on other way	The 42 individuals who finished the study reported full adherence to the prescribed products, but 3 did not fill the side effects form correctly. Most patients reported feeling well during treatments; however, gastrointestinal symptoms were more frequently reported in the probiotic than placebo group, in particular the occurrence of sooft stools. Median (IQR)	-
Özener2023 (Ozener et al., 2023)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 42.27± 8.8; SRP+prob: 41.40± 6.8	SRP+plac:7/8 SRP+prob:8/7	B. lactis DN-173010, $\geq 10^8$ CFU	Iogurt	28d	(SRP+plac) Day 0: 2.67±0.46; 3m: 2.16±0.43; (SRP+prob) Day 0: 2.93±0.37; 3m: 2.26±0.45.	(SRP+plac) Day 0: 2.59±0.43; 3m: 2.06±0.35c; (SRP+prob) Day 0: 2.76±0.38; 3m: 2.05±0.36.	(SRP+plac) Day 0: 1.79±0.36 ; 3m: 0.35±022 ; (SRP+prob) Day 0: 1.81±0.23; 3m: 0.18±0.08.	(SRP+plac) Day 0: 49.16±15.09; 3m: 22.34±5.23; (SRP+prob) Day 0: 52.70±21.98; 3m: 10.58±3.16.	(SRP+plac) Day 0: 75.64±42.72; 3m: 24.90±28.31; (SRP+prob) Day 0: 93.95±76.18; 3m: 31.95±39.62.	None	PI is reported according to mean of Silness & Loe index 1964; CFU was calculates for total viable count
Paul2019(Paul et al., 2019)	30 (SRP+plac: 13; SRP+prob:14)	38.1	13/17	Lactobacillus brevis (dosage not reported)	Lozenges	3w	(SRP+plac) Day 0: 3.584 ± 0.73; 12w: 2.776 ± 0.71; (SRP+prob) Day 0: 3.580 ± 1.00; 12w: 3.133 ± 1.15.	(SRP+plac) Day 0: 3.420 ± 0.77; 12w: 2.617 ± 0.97; (SRP+prob) Day 0: 3.280 ± 0.83; 12w: 2.57 3 ±0.60.	(SRP+plac) Day 0: 1.138 ± 0.78; 12w: 0.604 ± 0.38; (SRP+prob) Day 0: 1.274 ± 0.63; 12w: 0.636 ± 0.32.	(SRP+plac) Day 0: 0.902 ± 0.17; 12w: 0.540 ± 0.24; (SRP+prob) Day 0: 0.871 ± 0.30; 12w: 0.714 ± 0.22.	(Aa) (SRP+plac) Day 0: 10500 ± 14740; 12w: 0 ± 0; (SRP+prob) Day 0: 19000 ± 41160; 12w: 0 ± 0; (Pg) (SRP+plac) Day 0: 12400 ± 10400; 12w: 0 ± 0; (SRP+prob) Day 0: 18400	None	PI is reported according to mean of Silness & Loe index 1964 BOP is reported according to mean of Ainamo & Bay index 1975

											± 23000; 12w: 538 ± 1050; (Pi) (SRP+plac) Day 0: 4181 ± 8931; 12w: 0 ± 0; (SRP+prob) Day 0: 1846 ± 3105; 12w: 0 ± 0;		
Pelekos2020 (Pelekos et al., 2020)	59 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 52.76 SRP+prob: 51.14	SRP+plac: 10/10 SRP+prob: 4/16	L. reuteri DSM17938 and L. reuteri ATCC PTA5289 with 10^8 CFU for each strain (Prodentis, Biogaia, Sweden).	Lozenges	28d	(SRP+plac) Day 0: 8.02 ± 2.32; 180d: 7.50 ± 2.58; (SRP+prob) Day 0: 7.61 ± 1.99; 180d: 7.07 ± 2.20.	(SRP+plac) Day 0: 6.38 ± 1.68; 180d: 4.97 ± 1.91; (SRP+prob) Day 0: 5.95 ± 1.19; 180d: 4.55 ± 1.37.	Not reported	(SRP+plac) Day 0: 221(93.2%); 180d: 145 (61.2%)); (SRP+prob) Day 0: 184 (87.6%); 180d: 110 (52.4%).	Not reported	Not reported	-
Penala2016(Penala et al., 2016)	29 (SRP+plac: 14; SRP+prob:15)	SRP+plac: 35.5 ± 9.17 SRP+prob: 37.2 ± 9.79	Not reported	Lactobacillus salivarius (2 × 109 CFU) and Lactobacillus reuteri (2 × 109 CFU) per capsule	Mouth wash	14d	(SRP+plac) Day 0: 2.88 ± 0.40; 3m: gráfico; (SRP+prob) Day 0:2.98 ± 0.78; 3m: gráfico.	(SRP+plac) Day 0: 3.19 ± 0.44; 3m: gráfico; (SRP+prob) Day 0: 3.12 ± 0.71; 3m: gráfico.	(SRP+plac) Day 0: 2.16 ± 0.35; 3m: 0.72 ± 0.39; (SRP+prob) Day 0: 1.81 ± 0.47; 3m: 0.35 ± 0.18.	(SRP+plac) Day 0: 1.79 ± 0.11; 3m: 0-71 ± 0.43. (SRP+prob) Day 0: 1.65 ± 0.38; 3m: 0.31 ± 0.14.	Not reported	None	Also report data relative to moderate and depp pockets; also data relative to halitosis; Data from PI are presented in % but the method is not explained
Pudgar2021 (Pudgar et al., 2021)	40 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 46.7 (11.0) SRP+prob: 45.9 (8.0)	SRP+plac: 11/9 SRP+prob: 7/13	6.0 × 109 CFU/ml of L. brevis (CECT7480) [8] and 6.0 × 109 CFU/ml of L. plantarum (CECT7481) [8], while the probiotic lozenges contained 1.2 × 109 CFU/ml of each bacterium (ProlacSan, CMS Dental, Copenhagen, Denmark)	Lozenges	3m	(SRP+plac) Day 0: 4.5 (4.0; 5.9); 3m: 3.7 (3.3; 4.9); (SRP+prob) Day 0: 4.3 (3.8; 4.9); 3m: 3.6 (3.1; 4.2).	(SRP+plac) Day 0: 4.0 (3.6; 4.3); 3m: 3.1 (2.8; 3.3); (SRP+prob) Day 0: 3.9 (3.7; 4.2; 3m: 3.0 (2.9; 3.2).	(SRP+plac) Day 0: 23.5 (14.0; 36.5) 3m: 12.5 (5.5; 23.5); (SRP+prob) Day 0: 24.5 (17.5; 38.0); 3m: 9.0 (6.0; 13.5).	(SRP+plac) Day 0: 63.0 (44.0; 74.5) 3m: 24.5 (15.5; 30.0); (SRP+prob) Day 0: 63.0 (45.0; 77.5); 3m: 27.0 (18.5; 31.0).	Not reported	None	Also report data relative to gingival recession Data relative to PI is reported by median (Q1; Q3)
Ranjith2021(Ranjith et al., 2022)	60 (SRP+plac: 27; SRP+prob: 28)	SRP+plac: 37.95 ± 6.94 SRP+prob: 39.48 ± 7.65	SRP+plac: 16/14 SRP+prob: 17/13	Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Sachet (2x/d)	1m	(SRP+plac) Day 0: 2.9 ± 0.16; 90d: 2.72 ± 0.10; (SRP+prob) Day 0: 3.48 ± 0.2; 90d: 2.25 ± 0.11.	(SRP+plac) Day 0: 3.0 ± 0.16; 90d: 2.74 ± 0.15; (SRP+prob) Day 0: 3.4 ± 0.28; 90d: 2.65 ± 0.11.	(SRP+plac) Day 0: 1.57 ± 0.87; 90d: 1.06 ± 0.06; (SRP+prob) Day 0: 1.7 ± 0.87; 90d: 1.09 ± 0.07. (Silness & Loe)	Not reported	Not reported	No adverse events were reported and compliance was satisfactory in both groups.	-
Tekce2015(Tekce et al., 2015)	40 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 41.40 ± 8.86 SRP+prob: 43 ± 5.01	SRP+plac: 10/10 SRP+prob: 8/12	L. reuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289 (Prodentis; BioGaia, Lund, Sweden)	Lozenges	3w	Not reported	(SRP+plac) Day 0: 5.36 ± 0.72; 360d: 4.80 ± 0.70; (SRP+prob) Day 0: 5.23 ± 0.68; 360d: 3.49 ± 0.87.	(SRP+plac) Day 0: 2.30 ± 0.41; 360d: 1.39 ± 0.28; (SRP+prob) Day 0: 2.29 ± 0.28; 360d: 0.73 ± 0.24.	(SRP+plac) Day 0: 88.65 ± 4.11; 360d: 19.05 ± 4.84; (SRP+prob) Day 0: 88.90 ± 7.66; 360d: 11.05 ± 3.99.	(SRP+plac) Day 0: 41.5 (14–81); 360d: 40.5 (12–78); (SRP+prob) Day 0: 35.5 (26–43); 360d: 35 (25–42).	None	Also report data relative to gingival index; PI is reported according to mean of Silness & Loe index 1964; CFU presented with median, (min-max)
Teughels2013(Teughels et al., 2013)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 45.7 ± 6.2 SRP+prob: 46.6 ± 4.5	SRP+plac: 8/7 SRP+prob: 7/8	L. reuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289 (Prodentis; BioGaia, Lund, Sweden)	Lozenges	12w	(SRP+plac) Day 0: 4.97 ± 0.61; 12w: 4.21 ± 0.67; (SRP+prob) Day 0: 4.97 ± 1.01; 12w: 3.97 ± 0.97.	(SRP+plac) Day 0: 4.32 ± 0.50; 12w: 2.93 ± 0.40; (SRP+prob) Day 0: 4.15 ± 0.71; 12w: 2.73 ± 0.57.	(SRP+plac) Day 0: 99.66 ± 0.99; 12w: 24.88 ± 33.26; (SRP+prob) Day 0: 95 ± 10.27; 12w: 16.34 ± 19.19.	(SRP+plac) Day 0: 67.53% ± 11.37; 12w: 16.58% ± 10.54; (SRP+prob) Day 0: 70.70% ± 14.53; 12w: 15.51% ± 11.92.	(Aa) (SRP+plac) Day 0: 3.57 ± 1.97; 12w: 1.86 ± 2.12; (SRP+prob) Day 0: 3.84 ± 2.70; 12w: 1.98 ± 2.38; (Fn) (SRP+plac) Day 0: 7.40 ± 1.16; 12w: 5.87 ± 1.08; (SRP+prob) Day 0: 7.70 ± 1.11; 12w: 5.45 ± 2.05; (Pg) (SRP+plac) Day 0: 6.37± 1.7; 12w: 5.43 ± 1.73; (SRP+prob) Day 0: 6.67 ± 1.5; 12w: 4.87 ± 1.21; (Pi) (SRP+plac) Day 0: 6.17 ± 2.73; 12w: 4.81 ± 2.44; (SRP+prob) Day 0: 6.345 ± 2.14; 12w: 4.22 ± 2.07; (Tf) (SRP+plac) Day 0:6.56 ± 0.89; 12w: 5.24 ± 1.17; (SRP+prob) Day 0: 5.95 ± 1.82 12w: 8.49 ± 0.82;	None	Also report data relative to moderate and deep pockets separately and individually for specific bacteria *(Aa, Fn, Pg, Pi, Tf)*

											(Total load) (SRP+plac) Day 0: 10.11 ± 0.86; 12w: 8.99 ± 0.99; (SRP+prob) Day 0: 9.9 ± 0.52; 12w: 8.49 ± 0.82;		
Theodoro2019(Theodoro et al., 2019)	34 (SRP+plac: 14; SRP+prob: 14)	SRP+plac: 45.07 ± 6.31 SRP+prob: 47.25 ± 7.10	SRP+plac: 10/4 SRP+prob: 5/9	L. reuteri DSM 17938, with 1×10^8 cfu (BioGaia™, 450 mg, Laboratórios Ferrring Ltda, São Paulo, SP, Brazil)	Lozenges	21d	(SRP+plac) Day 0: 4.23 ± 0.56; 90d: 4.17 ± 0.42; (SRP+prob) Day 0: 4.39 ± 0.86; 90d: 3.96 ± 0.89.	(SRP+plac) Day 0: 3.81 ± 0.44; 90d: 3.66 ± 0.36; (SRP+prob) Day 0: 3.23 ± 0.44; 90d:2.98 ± 0.54.	Not reported	(SRP+plac) Day 0: 74.10 ± 22.08; 90d: 65.13 ± 20.65; (SRP+prob) Day 0: 45.74 ± 20.65; 90d:23.51 ± 14.15.	Not reported	None	Also report data relative to moderate and deep pockets separately and % deep pockets + BOP; and gingivel recession
Tsubura2009(Tsubura et al., 2009)	54 (SRP+cont:27; SRP+prob: 27)	53.4 (44-62)	21/33	Bacillus subtilis	Mouth wash	30d	Not reported	(SRP+cont) Day 0: 4.7±0.72; 30d: 3.5±0.51; (SRP+prob) Day 0: 4.8±0.75; 30d: 4.2±0.60.	Not reported	(SRP+cont) Day 0: 1.6±0.50; 30d: 0.8±0.62; (SRP+prob) Day 0: 1.6±0.51; 30d: 0.5±0.51.	Not reported	Not reported	Also report data relative to GI and BANA score
Vicario2013 (Vicario et al., 2013)	19 (SRP+plac: 9; SRP+prob: 10)	SRP+plac: 53.8 (44.3–63.1) SRP+prob: 58.0 (51.4–64.7)	SRP+plac: 4/5 SRP+prob: 8/2	Lactobacillus reuteri (ATCC 55730 and ATCCPTA 5289) (2X10^8 living cells of L.reuteri Prodentis)	Not reported	Not reported	Not reported	% sites with pocket probing depths 4–5 mm. (SRP+plac) Day 0: 38.1 ± 16.37; 30d: 45.3 ± 10.38; (SRP+prob) Day 0: 50.1 ± 17.92; 30d: 40.4 ± 17.76. % sites with pocket probing depths ≥ 6 mm. (SRP+plac) Day 0: 13.7 ± 16.42; 30d: 13.4 ± 13.31; (SRP+prob) Day 0: 12.3 ± 16.13; 30d: 7.5 ± 11.40.	(SRP+plac) Day 0: 62.9 ± 24.21; 30d: 67.4 ± 16.57; (SRP+prob) Day 0: 69.5 ± 16.95; 30d: 52.5 ± 14.25.	(SRP+plac) Day 0: 40.0 ± 23.36; 30d: 47.0 ± 17.43; (SRP+prob) Day 0: 55.3 ± 16.39; 30d: 29.3 ± 15.04.	Not reported	None	-

%: percentage; *Aa: Aggregatibacter actinomycetemcomitans;* atb: antibiotic; BOP: bleeding on probing; CAL: clinical attachment level; CFU: colony forming units; CHX: chlorhexidine; d: day; F: female; *Fn: Fusobacterium nucleatum;* GCF: gingival crevicular fluid; GI: gingival index; m: months; M: male; mm: millimeter; NR: not reported; *Pg: Porphyromonas gingivalis; Pi: Prevotella intermedia;* PI: plaque index; plac: placebo; PPD: periodontal probing depth; prob: probiotic; SD: standard deviation; SRP: scaling and root planning; tetra: tetracycline fibers; *Tn: Tannerella forsythia; Td: Treponema denticola;* w: week

Appendix 5: Statistical methods in detail

PPD

Table 5 - Summary measures of treatment effect of PPD outcome

studlab	treat1.long	treat2.long	treat1	treat2	*n1*	*n2*	TE (treat1)	seTE (treat1)	TE (treat2)	seTE (treat2)	TEglobal	seTE (global)
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP	Sbbif	10	10	-1.360	0.143	-1.270	0.181	0.090	0.073
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + CHX	SRP	SChx	10	10	-1.360	0.143	-1.090	0.175	0.270	0.071
Abuazab2021(Abuazab et al., 2021)	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP + CHX	Sbbif	SChx	10	10	-1.270	0.181	-1.090	0.175	0.180	0.080
Alshareef2020(Alshareef et al., 2020)	SRP	SRP + Lacidophilus, Lcasei, Bbifidum, Lrhamnosus, and Lsalivarius	SRP	SLacidLcasBbifLrhamLsal	10	15	-0.275	0.190	-0.356	0.094	-0.081	0.055
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SChx	SBifLactt	20	20	-0.080	0.371	-1.210	0.250	-1.130	0.100
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SChx	SBifLacttg	20	20	-0.080	0.371	-2.050	0.224	-1.970	0.097
Butera2020(Butera et al., 2020)	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SBifLactt	SBifLacttg	20	20	-1.210	0.250	-2.050	0.224	-0.840	0.075
Chandra2016(Chandra et al., 2016)	SRP	SRP + Saccharomyces boulardii (≥ 5 billion CFU)	SRP	Ssbou	27	28	-1.910	0.235	-3.470	0.168	-1.560	0.055
Costacurta2018(Costacurta et al., 2018)	SRP	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	SRP	SLreutDA	20	20	-0.600	0.165	-0.650	0.246	-0.050	0.066
deOliveira2022(deOliveira et al., 2022)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-0.580	0.105	-0.640	0.111	-0.060	0.033
Dhaliwal2017(Dhaliwal et al., 2017)	SRP	Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU	SRP	SfaeCbutBmesLspo	13	14	-0.820	0.264	-0.920	0.456	-0.100	0.145
El-bagoory2021(El-Bagoory et al., 2021)	SRP	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	SRP	SLreutD	6	6	-1.000	0.336	-1.800	0.236	-0.800	0.168
Ghasemi2020(Ghasemi et al., 2020)	SRP + placebo	SRP + 15×10^9 probiotic units per capsule), Blactis, Lacidophilus, Bbifidum, Lrhamnosus	Splac	SBlacLacidBbifLrham	18	18	-0.810	0.209	-1.360	0.215	-0.550	0.071

Grover(Grover)	SRP	SRP + Bifilac lozenges (Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU)	SRP	SfaeCbutBmesLspo	15	15	-0.820	0.246	-0.920	0.440	-0.100	0.130
Ikram2019(Ikram et al., 2019)	SRP + placebo	SRP + L. reuteri 1.2 billion CFU/g	Splac	Slreut	14	14	-0.300	0.365	-1.780	0.280	-1.480	0.123
Ince2015(Ince et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-0.560	0.144	-1.700	0.180	-1.140	0.060
Invernici2018(Invernici et al., 2018)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	21	20	-0.250	0.120	-0.520	0.085	-0.270	0.033
Invernici2020(Invernici et al., 2020)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Jebin2021(Jebin et al., 2021)	SRP	SRP + Lreuteri UBLRu-87 (0.5 billion CFU)	SRP	SLreutU	13	14	-0.850	0.153	-1.670	0.199	2.520	0.069
Kanagaraj2019(Kanagaraj et al., 2019)	SRP + placebo	SRP + Lsporogenes 100 million, Sfaecalis Scientific Name Search PC 60 million, Clostridium butyrium TO-A 4 million, and Bmesentericus TO-A JPC 2 million	Splac	LspoSfaeCbutBmes	30	30	-2.630	0.100	-3.500	0.107	-0.870	0.027
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	Splac	SLreutsingle	15	15	-1.640	0.208	-1.860	0.239	-0.220	0.082
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	Splac	Slreutincrem	15	15	-1.640	0.208	-1.720	0.270	-0.080	0.088
Kumar2021(Kumar et al., 2021)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	SLreutsingle	Slreutincrem	15	15	-1.860	0.239	-1.720	0.270	0.140	0.093
Laleman2015(Laleman et al., 2015)	SRP + placebo	SRP + Soralis KJ3, Suberis KJ2 and Srattus JH145(≥ 10^8 CFU)	Splac	SSoralubeerrat	24	24	-1.610	0.143	-1.510	0.142	0.100	0.041
Meenakshi2020(Meenakshi & Varghese, 2018)	SRP	SRP + Lcasei (dosage not specified)	SRP	SLcas	10	10	-0.320	0.316	-1.140	0.203	-0.820	0.119
Minic2020(Minic et al., 2022)	SRP	SRP + 6.5 billion live L acidophilus, concentration of 107 CFU, at least 107 CFU Binfantis and at least 106 CFU Efaecium colony-forming	SRP	SRPLacidBinfEfae	40	40	-0.500	0.105	-1.220	0.081	-0.720	*0.021*
Morales2016(Morales et al., 2016)	SRP + placebo	SRP + LrhamanosusSP1 (2X10^7 CFU)	Splac	SLrham	14	14	-0.500	0.096	-0.600	0.209	-0.100	0.061
Oliveira2021(Oliveira et al., 2021)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-0.580	0.105	-0.640	0.111	-0.060	0.033
Özener2023(Ozener et al., 2023)	SRP + placebo	SRP + B. lactis DN-173010, ≥108 CFU	Splac	SBlactDN	15	15	-0.530	0.143	-0.710	0.135	-0.180	0.051
Paul2019(Paul et al., 2019)	SRP + placebo	SRP + Lbrevis (dosage not reported)	Splac	Slbrevis	13	14	-0.803	0.343	-0.707	0.274	0.096	0.119
Pelekos2020(Pelekos et al., 2020)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-1.410	0.569	-1.400	0.406	0.010	0.156
Penala2016(Penala et al., 2016)	SRP + placebo	SRP + L salivarius (2 × 109 CFU) and Lreuteri (2 × 109 CFU)	Splac	SLsalreut	14	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

Pudgar2021(Pudgar et al., 2021)	SRP + placebo	SRP + Lbrevis (CECT7480) and Lplantarum (CECT7481) (1.2 × 109 CFU/ml of each bacterium)	Splac	SLbreviseplant	20	20	-0.900	0.143	-0.900	0.096	0.000	0.039
Ranjith2021(Ranjith et al., 2022)	SRP + placebo	SRP + Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Splac	SLacidLrhaBlongSboul	27	28	-0.260	0.042	-0.750	0.057	-0.490	0.014
Tekce2015(Tekce et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-0.560	0.225	-1.740	0.247	-1.180	0.075
Teughels2013(Teughels et al., 2013)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-1.390	0.165	-1.420	0.235	-0.030	0.074
Theodoro2019(Theodoro et al., 2019)	SRP + placebo	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	Splac	SLreutD	14	14	-0.150	0.152	-0.250	0.186	-0.100	0.064
Tsubura2009(Tsubura et al., 2009)	SRP + control	SRP + B subtilis: E-300	Scont	Sbsub	27	27	-1.200	0.170	-0.600	0.185	0.600	0.048
Vicario2013(Vicario et al., 2013)	SRP + placebo	SRP + L reuteri ATCC 55730 and ATCCPTA 5289) (2X10^8 CFU)	Splac	SLreutAA	9	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

CFU: colony forming units; CHX: chlorhexidine; SRP: scaling and root planning.

CAL

Table 6 - Summary measures of treatment effect of CAL outcome

studlab	treat1.long	treat2.long	treat1	treat2	*n1*	*n2*	TE (treat1)	seTE (treat1)	TE (treat2)	seTE (treat2)	TEglobal	seTE (global)
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP	Sbbif	10	10	-0.530	0.148	-0.920	0.168	-0.390	0.071
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + CHX	SRP	SChx	10	10	-0.530	0.148	-0.610	0.168	-0.080	0.071
Abuazab2021(Abuazab et al., 2021)	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP + CHX	Sbbif	SChx	10	10	-0.920	0.168	-0.610	0.168	0.310	0.075
Alshareef2020(Alshareef et al., 2020)	SRP	SRP + Lacidophilus, Lcasei, Bbifidum, Lrhamnosus, and Lsalivarius	SRP	SLacidLcasBbifLrhamLsal	10	15	-0.344	0.294	-0.425	0.214	-0.081	0.101
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SChx	SBifLactt	20	20	-0.260	0.568	-1.200	0.698	-0.940	0.201
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SChx	SBifLacttg	20	20	-0.260	0.568	-1.900	0.388	-1.640	0.154
Butera2020(Butera et al., 2020)	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SBifLactt	SBifLacttg	20	20	-1.200	0.698	-1.900	0.388	-0.700	0.179
Chandra2016(Chandra et al., 2016)	SRP	SRP + Saccharomyces boulardii (≥ 5 billion CFU)	SRP	Ssbou	27	28	-1.720	0.227	-2.960	0.178	-1.240	0.055
Costacurta2018(Costacurta et al., 2018)	SRP	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	SRP	SLreutDA	20	20	-0.650	0.171	-0.620	0.283	0.030	0.074
deOliveira2022(deOliveira et al., 2022)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-0.290	0.221	-0.570	0.272	-0.280	0.076
Dhaliwal2017(Dhaliwal et al., 2017)	SRP	Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU	SRP	SfaeCbutBmesLspo	13	14	-0.960	0.365	-1.290	0.514	-0.330	0.173
El-bagoory2021(El-Bagoory et al., 2021)	SRP	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	SRP	SLreutD	6	6	-1.000	0.336	-1.800	0.236	-0.800	0.168
Ghasemi2020(Ghasemi et al., 2020)	SRP + placebo	SRP + 15×10^9 probiotic units per capsule), Blactis, Lacidophilus, Bbifidum, Lrhamnosus	Splac	SBlacLacidBbifLrham	18	18	-0.640	0.230	-1.060	0.225	-0.420	0.076
Grover(Grover)	SRP	SRP + Bifilac lozenges (Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU)	SRP	SfaeCbutBmesLspo	15	15	-0.960	0.339	-1.290	0.497	-0.330	0.155
Ikram2019(Ikram et al., 2019)	SRP + placebo	SRP + L. reuteri 1.2 billion CFU/g	Splac	Slreut	14	14	-0.260	0.253	-0.840	0.217	-0.580	0.089

Ince2015(Ince et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Invernici2018(Invernici et al., 2018)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	21	20	-0.180	0.162	-0.490	0.122	-0.310	0.045
Invernici2020(Invernici et al., 2020)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Jebin2021(Jebin et al., 2021)	SRP	SRP + Lreuteri UBLRu-87 (0.5 billion CFU)	SRP	SLreutU	13	14	-0.670	0.080	-1.020	0.176	-0.350	0.053
Kanagaraj2019(Kanagaraj et al., 2019)	SRP + placebo	SRP + Lsporogenes 100 million, Sfaecalis Scientific Name Search PC 60 million, Clostridium butyrium TO-A 4 million, and Bmesentericus TO-A JPC 2 million	Splac	LspoSfaeCbutBmes	30	30	-1.820	0.079	-2.550	0.089	-0.730	0.022
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	Splac	SLreutsingle	15	15	-1.130	0.287	-1.450	0.248	-0.320	0.098
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	Splac	Slreutincrem	15	15	-1.130	0.287	-1.560	0.253	-0.430	0.099
Kumar2021(Kumar et al., 2021)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	SLreutsingle	Slreutincrem	15	15	-1.450	0.248	-1.560	0.253	-0.110	0.091
Laleman2015(Laleman et al., 2015)	SRP + placebo	SRP + Soralis KJ3, Suberis KJ2 and Srattus JH145(≥ 10^8 CFU)	Splac	SSoralubeerrat	24	24	-0.760	0.134	-0.710	0.118	0.050	0.036
Meenakshi2020(Meenakshi & Varghese, 2018)	SRP	SRP + Lcasei (dosage not specified)	SRP	SLcas	10	10	-0.350	0.242	-0.940	0.210	-0.590	0.101
Minic2020(Minic et al., 2022)	SRP	SRP + 6.5 billion live L acidophilus, concentration of 107 CFU, at least 107 CFU Binfantis and at least 106 CFU Efaecium colony-forming	SRP	SRPLacidBinfEfae	40	40	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Morales2016(Morales et al., 2016)	SRP + placebo	SRP + LrhamanosusSP1 (2X10^7 CFU)	Splac	SLrham	14	14	-0.100	0.491	-0.100	0.360	0.000	0.163
Oliveira2021(Oliveira et al., 2021)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-0.290	0.221	-0.570	0.271	-0.280	0.076
Özener2023(Ozener et al., 2023)	SRP + placebo	SRP + B. lactis DN-173010, ≥108 CFU	Splac	SBlactDN	15	15	-0.510	0.163	-0.670	0.150	-0.160	0.057
Paul2019(Paul et al., 2019)	SRP + placebo	SRP + Lbrevis (dosage not reported)	Splac	Slbrevis	13	14	-0.808	0.282	-0.447	0.407	0.361	0.136
Pelekos2020(Pelekos et al., 2020)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-0.520	0.776	-0.540	0.663	-0.020	0.228
Penala2016(Penala et al., 2016)	SRP + placebo	SRP + L salivarius (2 × 109 CFU) and Lreuteri (2 × 109 CFU)	Splac	SLsalreut	14	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Pudgar2021(Pudgar et al., 2021)	SRP + placebo	SRP + Lbrevis (CECT7480) and Lplantarum (CECT7481) (1.2 × 109 CFU/ml of each bacterium)	Splac	SLbreviseplant	20	20	-0.800	0.413	-0.700	0.256	0.100	0.109
Ranjith2021(Ranjith et al., 2022)	SRP + placebo	SRP + Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Splac	SLacidLrhaBlongSboul	27	28	-0.180	0.036	-1.230	0.043	-1.050	0.011

Tekce2015(Tekce et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Teughels2013(Teughels et al., 2013)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-0.760	0.234	-1.000	0.362	-0.240	0.111
Theodoro2019(Theodoro et al., 2019)	SRP + placebo	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	Splac	SLreutD	14	14	-0.060	0.187	-0.430	0.331	-0.370	0.102
Tsubura2009(Tsubura et al., 2009)	SRP + control	SRP + B subtilis: E-300	Scont	Sbsub	27	27	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Vicario2013(Vicario et al., 2013)	SRP + placebo	SRP + L reuteri ATCC 55730 and ATCCPTA 5289) (2X10^8 CFU)	Splac	SLreutAA	9	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

CFU: colony forming units; CHX: chlorhexidine; SRP: scaling and root planning.

BOP

Table 7 - Summary measures of treatment effect of BOP outcome

studlab	treat1.long	treat2.long	treat1	treat2	*n1*	*n2*	TE (treat1)	seTE (treat1)	TE (treat2)	seTE (treat2)	TEglobal	seTE (global)
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP	Sbbif	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + CHX	SRP	SChx	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Abuazab2021(Abuazab et al., 2021)	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP + CHX	Sbbif	SChx	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Alshareef2020(Alshareef et al., 2020)	SRP	SRP + Lacidophilus, Lcasei, Bbifidum, Lrhamnosus, and Lsalivarius	SRP	SLacidLcasBbifLrhamLsal	10	15	-8.935	6.072	-8.600	3.308	0.335	1.875
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SChx	SBifLactt	20	20	-2.250	4.966	-34.000	7.203	-31.750	1.956
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SChx	SBifLacttg	20	20	-2.250	4.966	-44.650	8.733	-42.400	2.246
Butera2020(Butera et al., 2020)	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SBifLactt	SBifLacttg	20	20	-34.000	7.203	-44.650	8.733	-10.650	2.531
Chandra2016(Chandra et al., 2016)	SRP	SRP + Saccharomyces boulardii (≥ 5 billion CFU)	SRP	Ssbou	27	28	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Costacurta2018(Costacurta et al., 2018)	SRP	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	SRP	SLreutDA	20	20	-30.300	3.166	-56.050	4.861	-25.750	1.297
deOliveira2022(deOliveira et al., 2022)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-20.400	4.587	-21.100	6.790	-0.700	1.762
Dhaliwal2017(Dhaliwal et al., 2017)	SRP	Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU	SRP	SfaeCbutBmesLspo	13	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
El-bagoory2021(El-Bagoory et al., 2021)	SRP	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	SRP	SLreutD	6	6	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Ghasemi2020(Ghasemi et al., 2020)	SRP + placebo	SRP + 15×10^9 probiotic units per capsule), Blactis, Lacidophilus, Bbifidum, Lrhamnosus	Splac	SBlacLacidBbifLrham	18	18	-24.100	2.890	-29.490	3.163	-5.390	1.010
Grover(Grover)	SRP	SRP + Bifilac lozenges (Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU)	SRP	SfaeCbutBmesLspo	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Ikram2019(Ikram et al., 2019)	SRP + placebo	SRP + L. reuteri 1.2 billion CFU/g	Splac	Slreut	14	14	-25.700	6.892	-56.580	3.271	-30.880	2.039

Ince2015(Ince et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-69.650	1.756	-77.300	2.274	-7.650	0.742
Invernici2018(Invernici et al., 2018)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	21	20	-4.290	8.292	-12.000	6.114	-7.710	2.285
Invernici2020(Invernici et al., 2020)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	15	15	-1.970	2.954	-3.250	2.542	-1.280	1.006
Jebin2021(Jebin et al., 2021)	SRP	SRP + Lreuteri UBLRu-87 (0.5 billion CFU)	SRP	SLreutU	13	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Kanagaraj2019(Kanagaraj et al., 2019)	SRP + placebo	SRP + Lsporogenes 100 million, Sfaecalis Scientific Name Search PC 60 million, Clostridium butyrium TO-A 4 million, and Bmesentericus TO-A JPC 2 million	Splac	LspoSfaeCbutBmes	30	30	-0.340	0.116	-1.110	0.118	-0.770	0.030
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	Splac	SLreutsingle	15	15	-38.340	7.689	-58.330	6.577	-19.990	2.613
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	Splac	Slreutincrem	15	15	-38.340	7.689	-61.650	5.600	-23.310	2.456
Kumar2021(Kumar et al., 2021)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	SLreutsingle	Slreutincrem	15	15	-58.330	6.577	-61.650	5.600	-3.320	2.230
Laleman2015(Laleman et al., 2015)	SRP + placebo	SRP + Soralis KJ3, Suberis KJ2 and Srattus JH145(≥ 10^8 CFU)	Splac	SSoralubeRrat	24	24	-55.440	2.586	-60.460	2.269	-5.020	0.702
Meenakshi2020(Meenakshi & Varghese, 2018)	SRP	SRP + Lcasei (dosage not specified)	SRP	SLcas	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Minic2020(Minic et al., 2022)	SRP	SRP + 6.5 billion live L acidophilus, concentration of 107 CFU, at least 107 CFU Binfantis and at least 106 CFU Efaecium colony-forming	SRP	SRPLacidBinfEfae	40	40	-1.050	0.064	-1.620	0.056	-0.570	0.013
Morales2016(Morales et al., 2016)	SRP + placebo	SRP + LrhamanosusSP1 (2X10^7 CFU)	Splac	SLrham	14	14	-8.400	5.108	-11.800	5.523	-3.400	2.011
Oliveira2021(Oliveira et al., 2021)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-20.400	4.587	-21.100	6.790	0.000	2.105
Özener2023(Ozener et al., 2023)	SRP + placebo	SRP + B. lactis DN-173010, ≥108 CFU	Splac	SBlactDN	15	15	-26.820	4.124	-42.120	5.734	-15.300	1.824
Paul2019(Paul et al., 2019)	SRP + placebo	SRP + Lbrevis (dosage not reported)	Splac	Slbrevis	13	14	-0.362	0.082	-0.157	0.099	0.205	0.035
Pelekos2020(Pelekos et al., 2020)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Penala2016(Penala et al., 2016)	SRP + placebo	SRP + L salivarius (2 × 109 CFU) and Lreuteri (2 × 109 CFU)	Splac	SLsalreut	14	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Pudgar2021(Pudgar et al., 2021)	SRP + placebo	SRP + Lbrevis (CECT7480) and Lplantarum (CECT7481) (1.2 × 109 CFU/ml of each bacterium)	Splac	SLbreviseplant	20	20	-38.500	5.593	-36.000	5.767	2.500	1.796
Ranjith2021(Ranjith et al., 2022)	SRP + placebo	SRP + Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Splac	SLacidLrhaBlongSboul	27	28	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

Tekce2015(Tekce et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-69.600	1.420	-77.850	1.931	-8.250	0.536
Teughels2013(Teughels et al., 2013)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-50.950	4.003	-55.190	4.853	-4.240	1.624
Theodoro2019(Theodoro et al., 2019)	SRP + placebo	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	Splac	SLreutD	14	14	-8.970	8.080	-22.230	6.690	-13.260	2.804
Tsubura2009(Tsubura et al., 2009)	SRP + control	SRP + B subtilis: E-300	Scont	Sbsub	27	27	-0.800	0.153	-1.100	0.139	-0.300	0.040
Vicario2013(Vicario et al., 2013)	SRP + placebo	SRP + L reuteri ATCC 55730 and ATCCPTA 5289) (2X10^8 CFU)	Splac	SLreutAA	9	10	7.000	9.715	-26.000	7.034	-33.000	3.861

CFU: colony forming units; CHX: chlorhexidine; SRP: scaling and root planning.

PI

Table 8 - Summary measures of treatment effect of PI outcome.

studlab	treat1.long	treat2.long	treat1	treat2	*n1*	*n2*	TE (treat1)	seTE (treat1)	TE (treat2)	seTE (treat2)	TEglobal	seTE (global)
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP	Sbbif	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + CHX	SRP	SChx	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Abuazab2021(Abuazab et al., 2021)	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP + CHX	Sbbif	SChx	10	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Alshareef2020(Alshareef et al., 2020)	SRP	SRP + Lacidophilus, Lcasei, Bbifidum, Lrhamnosus, and Lsalivarius	SRP	SLacidLcasBbifLrhamLsal	10	15	-10.009	6.229	-8.269	4.704	1.740	2.185
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SChx	SBifLactt	20	20	-3.000	7.759	-34.350	5.931	-31.350	2.184
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SChx	SBifLacttg	20	20	-3.000	7.759	-42.000	6.058	-39.000	2.201
Butera2020(Butera et al., 2020)	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SBifLactt	SBifLacttg	20	20	-34.350	5.931	-42.000	6.058	-7.650	1.896
Chandra2016(Chandra et al., 2016)	SRP	SRP + Saccharomyces boulardii (≥ 5 billion CFU)	SRP	Ssbou	27	28	-0.870	0.087	-0.940	0.083	-0.070	0.023
Costacurta2018(Costacurta et al., 2018)	SRP	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	SRP	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
deOliveira2022(deOliveira et al., 2022)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Dhaliwal2017(Dhaliwal et al., 2017)	SRP	Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU	SRP	SfaeCbutBmesLspo	13	14	-0.400	0.118	-0.390	0.105	0.010	0.043
El-bagoory2021(El-Bagoory et al., 2021)	SRP	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	SRP	SLreutD	6	6	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Ghasemi2020(Ghasemi et al., 2020)	SRP + placebo	SRP + 15×10^9 probiotic units per capsule), Blactis, Lacidophilus, Bbifidum, Lrhamnosus	Splac	SBlacLacidBbifLrham	18	18	-28.610	2.542	-31.170	3.148	-2.560	0.954
Grover(Grover)	SRP	SRP + Bifilac lozenges (Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU)	SRP	SfaeCbutBmesLspo	15	15	-0.400	0.110	-0.390	0.102	0.010	0.039
Ikram2019(Ikram et al., 2019)	SRP + placebo	SRP + L. reuteri 1.2 billion CFU/g	Splac	Slreut	14	14	-50.910	3.324	-58.950	2.460	-8.040	1.105

Ince2015(Ince et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-0.800	0.091	-1.490	0.089	-0.690	0.033
Invernici2018(Invernici et al., 2018)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	21	20	0.430	5.447	-2.200	4.513	-2.630	1.567
Invernici2020(Invernici et al., 2020)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	15	15	0.160	3.393	-0.440	5.417	-0.600	1.650
Jebin2021(Jebin et al., 2021)	SRP	SRP + Lreuteri UBLRu-87 (0.5 billion CFU)	SRP	SLreutU	13	14	-0.520	0.109	-0.740	0.109	-0.220	0.042
Kanagaraj2019(Kanagaraj et al., 2019)	SRP + placebo	SRP + Lsporogenes 100 million, Sfaecalis Scientific Name Search PC 60 million, Clostridium butyrium TO-A 4 million, and Bmesentericus TO-A JPC 2 million	Splac	LspoSfaeCbutBmes	30	30	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	Splac	SLreutsingle	15	15	-1.380	0.113	-1.370	0.086	0.010	0.037
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	Splac	Slreutincrem	15	15	-1.380	0.113	-1.740	0.121	-0.360	0.043
Kumar2021(Kumar et al., 2021)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	SLreutsingle	Slreutincrem	15	15	-1.370	0.086	-1.740	0.121	-0.370	0.038
Laleman2015(Laleman et al., 2015)	SRP + placebo	SRP + Soralis KJ3, Suberis KJ2 and Srattus JH145(≥ 10^8 CFU)	Splac	SSoralubeRrat	24	24	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Meenakshi2020(Meenakshi & Varghese, 2018)	SRP	SRP + Lcasei (dosage not specified)	SRP	SLcas	10	10	-0.360	0.170	-1.130	0.168	-0.770	0.076
Minic2020(Minic et al., 2022)	SRP	SRP + 6.5 billion live L acidophilus, concentration of 107 CFU, at least 107 CFU Binfantis and at least 106 CFU Efaecium colony-forming	SRP	SRPLacidBinfEfae	40	40	-1.310	0.084	-1.900	0.089	-0.590	0.019
Morales2016(Morales et al., 2016)	SRP + placebo	SRP + LrhamanosusSP1 (2X10^7 CFU)	Splac	SLrham	14	14	-16.600	6.316	-30.000	7.556	-13.400	2.632
Oliveira2021(Oliveira et al., 2021)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	-17.200	4.271	-13.300	5.347	3.900	1.483
Özener2023(Ozener et al., 2023)	SRP + placebo	SRP + B. lactis DN-173010, ≥108 CFU	Splac	SBlactDN	15	15	-1.440	0.109	-1.630	0.063	-0.190	0.033
Paul2019(Paul et al., 2019)	SRP + placebo	SRP + Lbrevis (dosage not reported)	Splac	Slbrevis	13	14	-0.534	0.241	-0.638	0.189	-0.104	0.083
Pelekos2020(Pelekos et al., 2020)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Penala2016(Penala et al., 2016)	SRP + placebo	SRP + L salivarius (2 × 109 CFU) and Lreuteri (2 × 109 CFU)	Splac	SLsalreut	14	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Pudgar2021(Pudgar et al., 2021)	SRP + placebo	SRP + Lbrevis (CECT7480) and Lplantarum (CECT7481) (1.2 × 109 CFU/ml of each bacterium)	Splac	SLbreviseplant	20	20	-11.000	4.773	-15.500	3.617	-4.500	1.339
Ranjith2021(Ranjith et al., 2022)	SRP + placebo	SRP + Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Splac	SLacidLrhaBlongSboul	27	28	-0.510	0.168	-0.610	0.165	-0.100	0.045

Tekce2015(Tekce et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-0.910	0.111	-1.560	0.082	-0.650	0.031
Teughels2013(Teughels et al., 2013)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	-74.780	8.591	-78.660	5.620	-3.880	2.651
Theodoro2019(Theodoro et al., 2019)	SRP + placebo	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	Splac	SLreutD	14	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Tsubura2009(Tsubura et al., 2009)	SRP + control	SRP + B subtilis: E-300	Scont	Sbsub	27	27	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Vicario2013(Vicario et al., 2013)	SRP + placebo	SRP + L reuteri ATCC 55730 and ATCCPTA 5289) (2X10^8 CFU)	Splac	SLreutAA	9	10	4.500	9.779	-17.000	7.003	-21.500	3.871

CFU: colony forming units; CHX: chlorhexidine; SRP: scaling and root planning.

CFU

Table 9 - Summary measures of treatment effect of CFU outcome.

studlab	treat1.long	treat2.long	treat1	treat2	*n1*	*n2*	TE (treat1)	seTE (treat1)	TE (treat2)	seTE (treat2)	TEglobal	seTE (global)
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP	Sbbif	10	10	***Pg*** -12.000 ***Pi*** -13.000 ***Total load*** -353.000	***Pg*** 3.265 ***Pi*** 2.989 ***Total load*** 69.986	***Pg*** -23.000 ***Pi*** -24.000 ***Total load*** -423.500	***Pg*** 4.585 ***Pi*** 3.654 ***Total load*** 80.146	***Pg*** -11.000 ***Pi*** -11.000 ***Total load*** -70.500	***Pg*** 1.780 ***Pi*** 1.493 ***Total load*** 33.647
Abuazab2021(Abuazab et al., 2021)	SRP	SRP + CHX	SRP	SChx	10	10	***Pg*** -12.000 ***Pi*** -13.000 ***Total load*** -353.000	***Pg*** 3.265 ***Pi*** 2.989 ***Total load*** 69.986	***Pg*** -19.000 ***Pi*** -21.000 ***Total load*** -303.000	***Pg*** 5.576 ***Pi*** 5.932 ***Total load*** 81.644	***Pg*** -7.000 ***Pi*** -8.000 ***Total load*** 50.000	***Pg*** 2.043 ***Pi*** 2.101 ***Total load*** 34.006
Abuazab2021(Abuazab et al., 2021)	SRP + Bbifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12	SRP + CHX	Sbbif	SChx	10	10	***Pg*** -23.000 ***Pi*** -24.000 ***Total load*** -423.500	***Pg*** 4.585 ***Pi*** 3.654 ***Total load*** 80.146	***Pg*** -19.000 ***Pi*** -21.000 ***Total load*** -303.000	***Pg*** 5.576 ***Pi*** 5.932 ***Total load*** 81.644	***Pg*** 4.000 ***Pi*** 3.000 ***Total load*** 120.500	***Pg*** 2.283 ***Pi*** 2.203 ***Total load*** 36.179
Alshareef2020(Alshareef et al., 2020)	SRP	SRP + Lacidophilus, Lcasei, Bbifidum, Lrhamnosus, and Lsalivarius	SRP	SLacidLcasBbifLrhamLsal	10	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SChx	SBifLactt	20	20	***Aa*** -217.400 ***Pg*** -2051.550 ***Tf*** 6977.490 ***Td*** -2688.820 ***Pi*** -	***Aa*** 385.986 ***Pg*** 4214.588 ***Tf*** 12899.660 ***Td*** 4480.986 ***Pi*** 2605.431 ***Fn*** 6850.22	***Aa*** 206.500 ***Pg*** -1481.900 ***Tf*** -32034.000 ***Td*** 4926.630 ***Pi*** - 6184.10	***Aa*** 527.624 ***Pg*** 7052.556 ***Tf*** 23012.070 ***Td*** 4202.883 ***Pi*** 1431.302 ***Fn*** 2623.84	***Aa*** 423.900 ***Pg*** 569.650 ***Tf*** -39011.490 ***Td*** 7615.450 ***Pi*** -3996.100 ***Fn***	***Aa*** 146.180 ***Pg*** 1837.135 ***Tf*** 5898.969 ***Td*** 1373.744 ***Pi*** 664.714 ***Fn*** 1640.277

							2188.000 ***Fn*** -1308.480 ***Total*** -1087500.000	7 ***Total*** 580221.837	0 ***Fn*** -11537.600 ***Total*** -615195.000	3 ***Total*** 512217.926	-10229.120 ***Total*** 472305.000	***Total*** 173064.234
Butera2020(Butera et al., 2020)	SRP + CHX toothpaste	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SChx	SBifLacttg	20	20	***Aa*** -217.400 ***Pg*** -2051.550 ***Tf*** 6977.490 ***Td*** -2688.820 ***Pi*** -2188.000 ***Fn*** -1308.480 ***Total*** -1087500.000	***Aa*** 385.986 ***Pg*** 4214.588 ***Tf*** 12899.660 ***Td*** 4480.986 ***Pi*** 2605.431 ***Fn*** 6850.227 ***Total*** 580221.837	***Aa*** -244.050 ***Pg*** 11644 ***Tf*** 3893988.100 ***Td*** 543.380 ***Pi*** -4956.050 ***Fn*** -10841.220 ***Total*** 1289616.000	***Aa*** 323.070 ***Pg*** 6293.792 ***Tf*** 17469.062 ***Td*** 6083.094 ***Pi*** 1201.180 ***Fn*** 2785.310 ***Total*** 1315478.847	***Aa*** -26.650 ***Pg*** 13695.550 ***Tf*** 3887010.610 ***Td*** 3232.200 ***Pi*** -2768.050 ***Fn*** -9532.740 ***Total*** 2377116.000	***Aa*** 112.552 ***Pg*** 1693.732 ***Tf*** 4855.766 ***Td*** 1689.427 ***Pi*** 641.526 ***Fn*** 1653.535 ***Total*** 321491.989
Butera2020(Butera et al., 2020)	SRP + Bifidobacterium, Lactobacillus (toothpaste)	SRP + Bifidobacterium, Lactobacillus (toothpaste+chewing gum)	SBifLactt	SBifLacttg	20	20	***Aa*** 206.500 ***Pg*** -1481.900 ***Tf*** -32034.000 ***Td*** 4926.630 ***Pi***	***Aa*** 527.624 ***Pg*** 7052.556 ***Tf*** 23012.070 ***Td*** 4202.883 ***Pi*** 1431.302	***Aa*** -244.050 ***Pg*** 11644 ***Tf*** 3893988.100 ***Td*** 543.380 ***Pi*** -4956.050	***Aa*** 323.070 ***Pg*** 6293.792 ***Tf*** 17469.062 ***Td*** 6083.094 ***Pi*** 1201.180	***Aa*** -450.550 ***Pg*** 13125.900 ***Tf*** 3926022.100 ***Td*** -4383.250 ***Pi***	***Aa*** 138.340 ***Pg*** 2113.650 ***Tf*** 6460.354 ***Td*** 1653.304 ***Pi*** 417.819 ***Fn***

							-6184.100 ***Fn*** -11537.600 ***Total*** -615195.000	***Fn*** 2623.843 ***Total*** 512217.926	***Fn*** -10841.220 ***Total*** 1289616.000	***Fn*** 2785.310 ***Total*** 1315478.847	1228.050 ***Fn*** 696.380 ***Total*** 1904811.000	855.643 ***Total*** 315662.145
Chandra2016(Chandra et al., 2016)	SRP	SRP + Saccharomyces boulardii (≥ 5 billion CFU)	SRP	Ssbou	27	28	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Costacurta2018(Costacurta et al., 2018)	SRP	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	SRP	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
deOliveira2022(deOliveira et al., 2022)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Dhaliwal2017(Dhaliwal et al., 2017)	SRP	Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU	SRP	SfaeCbutBmesLspo	13	14	***Aa*** 0.500 ***Pg*** -13.930 ***Pi*** 1.860	***Aa*** 8.030 ***Pg*** 10.419 ***Pi*** 2.291	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 5.690	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 5.690	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 3.830	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 2.187
El-bagoory2021(El-Bagoory et al., 2021)	SRP	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	SRP	SLreutD	6	6	5.090	2.496	-10.070	1.424	-15.160	1.173
Ghasemi2020(Ghasemi et al., 2020)	SRP + placebo	SRP + 15×10^9 probiotic units per capsule), Blactis, Lacidophilus, Bbifidum, Lrhamnosus	Splac	SBlacLacidBbifLrham	18	18	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Grover(Grover)	SRP	SRP + Bifilac lozenges (Sfaecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bmesentericus TO-A JPC-1million CFU and Lsporogenes IHS-50 million CFU)	SRP	SfaeCbutBmesLspo	15	15	***Aa*** 0.500 ***Pg*** -13.930 ***Pi*** 1.860	***Aa*** 7.476 ***Pg*** 9.700 ***Pi*** 2.133	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 5.690	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 7.304	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 3.830	***Aa*** not applicable ***Pg*** not applicable ***Pi*** 1.965
Ikram2019(Ikram et al., 2019)	SRP + placebo	SRP + L. reuteri 1.2 billion CFU/g	Splac	Slreut	14	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Ince2015(Ince et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

Invernici2018(Invernici et al., 2018)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	21	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Invernici2020(Invernici et al., 2020)	SRP + placebo	SRP + Bifidobacterium lactis HN019 (1X10^9 CFU)	Splac	SBlactis	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Jebin2021(Jebin et al., 2021)	SRP	SRP + Lreuteri UBLRu-87 (0.5 billion CFU)	SRP	SLreutU	13	14	-1.890	0.224	-2.660	0.190	-0.770	0.080
Kanagaraj2019(Kanagaraj et al., 2019)	SRP + placebo	SRP + Lsporogenes 100 million, Sfaecalis Scientific Name Search PC 60 million, Clostridium butyrium TO-A 4 million, and Bmesentericus TO-A JPC 2 million	Splac	LspoSfaeCbutBmes	30	30	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	Splac	SLreutsingle	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Kumar2021(Kumar et al., 2021)	SRP + placebo	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	Splac	Slreutincrem	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Kumar2021(Kumar et al., 2021)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (single application)	SRP + 5.9 billion CFU) of Lreuteri per gram and maltodextrin as a carrier (incremental application)	SLreutsingle	Slreutincrem	15	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Laleman2015(Laleman et al., 2015)	SRP + placebo	SRP + Soralis KJ3, Suberis KJ2 and Srattus JH145(≥ 10^8 CFU)	Splac	SSoralubeerrat	24	24	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Meenakshi2020(Meenakshi & Varghese, 2018)	SRP	SRP + Lcasei (dosage not specified)	SRP	SLcas	10	10	-41.400	14.939	-70.500	12.110	-29.100	6.081
Minic2020(Minic et al., 2022)	SRP	SRP + 6.5 billion live L acidophilus, concentration of 107 CFU, at least 107 CFU Binfantis and at least 106 CFU Efaecium colony-forming	SRP	SRPLacidBinfEfae	40	40	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Morales2016(Morales et al., 2016)	SRP + placebo	SRP + LrhamanosusSP1 (2X10^7 CFU)	Splac	SLrham	14	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Oliveira2021(Oliveira et al., 2021)	SRP + placebo	SRP + Lactobacillus spp. and 3 of Bifidobacterium spp.	Splac	SLsppBspp	23	19	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Özener2023(Ozener et al., 2023)	SRP + placebo	SRP + B. lactis DN-173010, ≥108 CFU	Splac	SBlactDN	15	15	-50.740	13.232	-62.000	22.171	-11.260	6.667
Paul2019(Paul et al., 2019)	SRP + placebo	SRP + Lbrevis (dosage not reported)	Splac	Slbrevis	13	14	***Aa*** not applicable ***Pg*** not applicable ***Pi*** not applicable	***Aa*** not applicable ***Pg*** not applicable ***Pi*** not applicable	***Aa*** not applicable ***Pg*** -17862.000 ***Pi*** not applicable	***Aa*** not applicable ***Pg*** 6153.411 ***Pi*** not applicable	***Aa*** not applicable ***Pg*** not applicable ***Pi*** not applicable	***Aa*** not applicable ***Pg*** not applicable ***Pi*** not applicable
Pelekos2020(Pelekos et al., 2020)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Penala2016(Penala et al., 2016)	SRP + placebo	SRP + L salivarius (2 × 109 CFU) and Lreuteri (2 × 109 CFU)	Splac	SLsalreut	14	15	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

Pudgar2021(Pudgar et al., 2021)	SRP + placebo	SRP + Lbrevis (CECT7480) and Lplantarum (CECT7481) (1.2 × 109 CFU/ml of each bacterium)	Splac	SLbreviseplant	20	20	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Ranjith2021(Ranjith et al., 2022)	SRP + placebo	SRP + Darolac, Aristo pharmaceuticals, India containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.	Splac	SLacidLrhaBlongSboul	27	28	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Tekce2015(Tekce et al., 2015)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	20	20	-1.000	15.578	-0.300	3.981	0.700	3.595
Teughels2013(Teughels et al., 2013)	SRP + placebo	SRP + Lreuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289	Splac	SLreutDA	15	15	***Aa*** -1.710 ***Fn*** -1.530 ***Pg*** -0.940 ***Pi*** -1.360 ***Tf*** -1.320 ***Total load*** -1.120	***Aa*** 0.747 ***Fn*** 0.409 ***Pg*** 0.626 ***Pi*** 0.945 ***Tf*** 0.380 ***Total load*** 0.339	***Aa*** -1.860 ***Fn*** -2.250 ***Pg*** -1.800 ***Pi*** -2.120 ***Tf*** -0.990 ***Total load*** -1.410	***Aa*** ***0.929*** ***Fn*** 0.602 ***Pg*** 0.498 ***Pi*** 0.769 ***Tf*** 0.657 ***Total load*** 0.251	***Aa*** -3.570 ***Fn*** -0.720 ***Pg*** -0.860 ***Pi*** ***-0.760*** ***Tf*** 0.330 ***Total load*** -0.290	***Aa*** 0.308 ***Fn*** 0.188 ***Pg*** 0.207 ***Pi*** 0.315 ***Tf*** 0.196 ***Total load*** 0.109
Theodoro2019(Theodoro et al., 2019)	SRP + placebo	SRP + Lreuteri DSM 17938 (1×10^8 CFU)	Splac	SLreutD	14	14	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Tsubura2009(Tsubura et al., 2009)	SRP + control	SRP + B subtilis: E-300	Scont	Sbsub	27	27	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*
Vicario2013(Vicario et al., 2013)	SRP + placebo	SRP + L reuteri ATCC 55730 and ATCCPTA 5289) (2X10^8 CFU)	Splac	SLreutAA	9	10	*NA*	*NA*	*NA*	*NA*	*NA*	*NA*

Aa: *Aggregatibacter actinomycetemcomitans*; CFU: colony forming units; CHX: chlorhexidine; Fn: *Fusobacterium nucleatum;* Pg: *Porphyromonas gingivalis*; Pi: *Prevotella intermedia*; SRP: scaling and root planning; Tn: *Tannerella forsythia*; Td: *Treponema denticola.*

Appendix 6: Risk of bias across studies, publication bias and evaluation of the confidence in the results of the network meta-analysis using the CINeMA framework

Table 10 - CINeMA for the primary outcome "PPD"

COMPARISON	NUMBER OF STUDIES	WITHIN-STUDY BIAS	REPORTING BIAS	INDIRECTNESS	IMPRECISION	HETEROGENEITY	INCOHERENCE	CONFIDENCE RATING	REASON(S) FOR DOWNGRADING
MIXED EVIDENCE									
Lsposfaecbutbmes:Splac	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Study limitations, Heterogeneity, Serious Incoherence
SBLACLACIDBBIFLRHAM:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTDN:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SRP	2	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Study limitations and Serious Incoherence
SBBIF:SCHX	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	Study limitations, Major imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SRP	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVISEPLANT:SPLAC	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLCAS:SRP	1	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Major concerns	very low	Study limitations, heterogeneity, Serious Incoherence
SLREUTD:SRP	2	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	Study limitations, Imprecision, Heterogeneity, Incoherence

SLREUTD:SPLAC	1	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	Heterogeneity and Incoherence
SLREUTDA:SRP	1	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	very low	Study limitations, Imprecision, Heterogeneity
SLREUTDA:SPLAC	5	No concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	low	Heterogeneity
SLREUTU:SRP	1	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLREUTINCREM:SLREUTSINGLE	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTSINGLE:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLRHAM:SPLAC	3	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLSPPBSPP:SPLAC	2	No concerns	Some concerns	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SRP:SRPLACIDBINFEFAE	1	Major concerns	Low risk	Some concerns	Some concerns	No concerns	Major concerns	very low	Study limitations and Serious Incoherence
SBBIF:SRP	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	Study limitations, Major imprecision, Incoherence
SFAECBUTBMESLSPO:SRP	2	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Major concerns	very low	Study limitations, Imprecision, Heterogeneity, serious Incoherence
SRP:SSBOU	1	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SPLAC:SSORALUBERRAT	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SPLAC	1	No concerns	Some concerns	No concerns	No concerns	Some concerns	Major concerns	very low	Study limitations, Heterogeneity, Serious Incoherence
SLREUTINCREM:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

INDIRECT EVIDENCE									
LSPOSFAECBUTBMES:SBLACLACIDBBIFLRHAM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SBLACTDN	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SBLACTIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLBREVISEPLANT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SLCAS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLREUTDA	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations and Serious Incoherence
LSPOSFAECBUTBMES:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
LSPOSFAECBUTBMES:SLSPPBSPP	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SRP	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

LSPOSFAECBUTBMES:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	Some concerns	No concerns	Major concerns	very low	Study limitations, heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SBBIF	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SFAECBUTBMESLSPO	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLBREVIS	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Study limitations, Imprecision, serious Incoherence
LSPOSFAECBUTBMES:SLREUT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
LSPOSFAECBUTBMES:SLREUTINCREM	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
LSPOSFAECBUTBMES:SSBOU	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACLACIDBBIFLRHAM:SBLACTDN	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SLCAS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SBLACLACIDBBIFLRHAM :SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SBLACLACIDBBIFLRHAM :SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SLRHAM	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACLACIDBBIFLRHAM :SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACLACIDBBIFLRHAM :SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SBLACLACIDBBIFL RHAM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SLBREVIS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACLACIDBBIFLRHAM :SLREUT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACLACIDBBIFLRHAM :SSBOU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SBLACTDN:SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SBLACTDN:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLCAS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTDN:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLREUTDA	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTDN:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SBLACTDN:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTDN:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SBLACTDN	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SLBREVIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SBLACTDN:SLREUT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTDN:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTDN:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SBLACTIS:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLCAS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTIS:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SBLACTIS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLRHAM	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTIS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SBLACTIS:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SBLACTIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLBREVIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SLREUT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBLACTIS:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBLACTIS:SSBOU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SCHX:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLBREVISEPLANT	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLCAS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLREUTDA	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations and Serious Incoherence
SCHX:SLREUTSINGLE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLRHAM	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

SCHX:SLSPPBSPP	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SLBREVIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SLREUT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SLREUTINCREM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SCHX:SPLAC	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SCHX:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLCAS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTDA	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	Study limitations and Serious Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SLACIDLCASBBIFLRHAMLSAL:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLCASBBIFLRHAMLSAL:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLBREVIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SPLAC	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLCASBBIFLRHAMLSAL:SSBOU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	Study limitations and Serious Incoherence
SLACIDLRHABLONGSBOUL:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLCAS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence

SLACIDLRHABLONGSBOUL:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLRHAM	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLRHABLONGSBOUL:SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLRHABLONGSBOUL:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLBREVIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SLREUT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLACIDLRHABLONGSBOUL:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLACIDLRHABLONGSBOUL:SSBOU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLBREVISEPLANT:SLCAS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVISEPLANT:SLREUTD	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVISEPLANT:SLREUTDA	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVISEPLANT:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence

SLBREVISEPLANT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SLSPPBSPP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SRP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SRPLACIDBINFEFAE	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVISEPLANT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLBREVISEPLANT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SLREUT	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLBREVISEPLANT:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVISEPLANT:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLCAS:SLREUTD	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLCAS:SLREUTDA	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLCAS:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Serious Incoherence
SLCAS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

SLCAS:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Serious Incoherence
SLCAS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLCAS:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLCAS:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Serious Incoherence
SBBIF:SLCAS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SFAECBUTBMESLSPO:SLCAS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVIS:SLCAS	0	No concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Serious Incoherence
SLCAS:SLREUT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLCAS:SLREUTINCREM	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLCAS:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLCAS:SSBOU	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTD:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTD:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Serious Incoherence
SLREUTD:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTD:SLRHAM	0	No concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTD:SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

SLREUTD:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTD:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SLREUTD	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUT:SLREUTD	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTD:SLREUTINCREM	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTD:SSBOU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTDA:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Serious Incoherence
SLREUTDA:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTDA:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTDA:SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTDA:SRPLACIDBINFEFAE	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTDA:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SLREUTDA	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLREUTDA	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence

SLBREVIS:SLREUTDA	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUT:SLREUTDA	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTDA:SLREUTINCREM	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTDA:SSBOU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTSINGLE:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUTU:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUTU:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUTU:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLREUTU:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SBBIF:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SFAECBUTBMESLSPO:SLREUTU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLBREVIS:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUT:SLREUTU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLREUTINCREM:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUTU:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLREUTU:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence

SLREUTSINGLE:SLRHAM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTSINGLE:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTSINGLE:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTSINGLE:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTSINGLE:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLREUTSINGLE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUTSINGLE:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLRHAM:SLSPPBSPP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLRHAM:SRP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLRHAM:SRPLACIDBINFEFAE	0	Some concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLRHAM:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLRHAM	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SFAECBUTBMESLSPO:SLRHAM	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

SLBREVIS:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTINCREM:SLRHAM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLRHAM:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLSPPBSPP:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLSPPBSPP:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLSPPBSPP:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLSPPBSPP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTINCREM:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLSPPBSPP:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SRP:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SRP	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence

SLREUTINCREM:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SPLAC:SRP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SRPLACIDBINFEFAE:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Serious Incoherence
SBBIF:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SRPLACIDBINFEFAE	0	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLBREVIS:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SLREUT:SRPLACIDBINFEFAE	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUTINCREM:SRPLACIDBINFEFAE	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SPLAC:SRPLACIDBINFEFAE	0	Some concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SRPLACIDBINFEFAE:SSBOU	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SSORALUBERRAT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLREUT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLREUTINCREM:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SSBOU:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence

SBBIF:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLBREVIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SLREUT	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SLREUTINCREM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SBBIF:SPLAC	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SBBIF:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SFAECBUTBMESLSPO:SLBREVIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SLREUT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SFAECBUTBMESLSPO:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SFAECBUTBMESLSPO:SPLAC	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence
SFAECBUTBMESLSPO:SSBOU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	Study limitations, Serious Incoherence
SLBREVIS:SLREUT	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	Heterogeneity and serious Incoherence
SLBREVIS:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	Serious Imprecision and Incoherence
SLBREVIS:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SLREUT:SLREUTINCREM	0	No concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	very low	Imprecision, Serious Incoherence
SLREUT:SSBOU	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	Imprecision, Heterogeneity, Serious Incoherence

SLREUTINCREM:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence
SPLAC:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	Serious Incoherence

Only for confidence rating ranging from 'very low' to 'moderate' the reasons for the downgrade were presented, since there were constraints in at least one of the six domains assessed by CINeMA.

Table 11 - CINeMA for the primary outcome "CAL"

COMPARISON	NUMBER OF STUDIES	WITHIN-STUDY BIAS	REPORTING BIAS	INDIRECTNESS	IMPRECISION	HETEROGENEITY	INCOHERENCE	CONFIDENCE RATING	REASON(S) FOR DOWNGRADING
MIXED EVIDENCE									
Lsposfaecbutbmes:Splac	1	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBIFLACTT:SBIFLACTTG	1	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBIFLACTT:SCHX	1	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBIFLACTTG:SCHX	1	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBLACLACIDBBIFLRHAM:SPLAC	1	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	incoherence
SBLACTDN:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	incoherence
SBLACTIS:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	incoherence
SCHX:SRP	2	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	serious study limitations, imprecision
SBBIF:SCHX	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	very low	study limitations, imprecision, heterogeneity
SLACIDLCASBBIFLRHAMLSAL:SRP	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	study limitations, incoherence
SLACIDLRHABLONGSBOUL:SPLAC	1	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLBREVISEPLANT:SPLAC	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SRP	1	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SLREUTD:SRP	2	Some concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	very low	study limitations, incoherence

SLREUTD:SPLAC	1	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUTDA:SRP	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	very low	study limitations, serious imprecision
SLREUTDA:SPLAC	3	No concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	very low	study limitations, serious heterogeneity
SLREUTU:SRP	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	study limitations, incoherence
SLREUTINCREM:SLREUTSINGLE	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTSINGLE:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, incoherence
SLRHAM:SPLAC	3	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLSPPBSPP:SPLAC	2	No concerns	Some concerns	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SBBIF:SRP	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	low	heterogeneity
SFAECBUTBMESLSPO:SRP	2	Some concerns	Some concerns	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SRP:SSBOU	1	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SPLAC:SSORALUBERRAT	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SPLAC	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLREUT:SPLAC	1	No concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	low	heterogeneity
SLREUTINCREM:SPLAC	1	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
INDIRECT EVIDENCE									

LSPOSFAECBUTBMES:SBIFLACTT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SBIFLACTTG	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
LSPOSFAECBUTBMES:SBLACLACIDBBIFLRHAM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SBLACTDN	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
LSPOSFAECBUTBMES:SBLACTIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
LSPOSFAECBUTBMES:SCHX	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
LSPOSFAECBUTBMES:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
LSPOSFAECBUTBMES:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SLBREVISEPLANT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
LSPOSFAECBUTBMES:SLCAS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	study limitations, incoherence
LSPOSFAECBUTBMES:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SLREUTDA	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	study limitations, incoherence
LSPOSFAECBUTBMES:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious heterogeneity, incoherence
LSPOSFAECBUTBMES:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
LSPOSFAECBUTBMES:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
LSPOSFAECBUTBMES:SLSPPBSPP	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence

LSPOSFAECBUTBMES:SRP	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	study limitations, heterogeneity, incoherence
LSPOSFAECBUTBMES:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
LSPOSFAECBUTBMES:SBBIF	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SFAECBUTBMESLSPO	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SLBREVIS	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
LSPOSFAECBUTBMES:SLREUT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
LSPOSFAECBUTBMES:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SBLACLACIDBBIFLRHAM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SBIFLACTT:SBLACTDN	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SBLACTIS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTT:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBIFLACTT:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBIFLACTT:SLCAS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBIFLACTT:SLREUTD	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence

SBIFLACTT:SLREUTDA	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTT:SLREUTU	0	Some concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	study limitations, heterogeneity, incoherence
SBIFLACTT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBIFLACTT:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SRP	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBBIF:SBIFLACTT	0	Some concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SBIFLACTT:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SBIFLACTT:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTT:SLREUT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTT:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SBIFLACTT:SPLAC	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTT:SSBOU	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SBLACLACIDBBIFLRHAM	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBIFLACTTG:SBLACTDN	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence

SBIFLACTTG:SBLACTIS	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBIFLACTTG:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBIFLACTTG:SLBREVISEPLANT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLCAS	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLREUTD	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLREUTDA	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLREUTU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTTG:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBIFLACTTG:SLSPPBSPP	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBIFLACTTG:SRP	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBBIF:SBIFLACTTG	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLBREVIS	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence

SBIFLACTTG:SLREUT	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBIFLACTTG:SPLAC	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SBIFLACTTG:SSBOU	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACLACIDBBIFLRHAM:SBLACTDN	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBLACLACIDBBIFLRHAM:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SBLACLACIDBBIFLRHAM:SLCAS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLREUTU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence

SBLACLACIDBBIFLRHAM:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SBBIF:SBLACLACIDBBIFLRHAM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBLACLACIDBBIFLRHAM:SLREUT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACLACIDBBIFLRHAM:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBLACTDN:SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBLACTDN:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLCAS	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SBLACTDN:SLREUTD	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence

SBLACTDN:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLREUTU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SBLACTDN	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTDN:SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLBREVIS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTDN:SLREUT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTDN:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBLACTIS:SCHX	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence

SBLACTIS:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTIS:SLCAS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTIS:SLREUTD	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTIS:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLREUTU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLRHAM	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBLACTIS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBBIF:SBLACTIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SFAECBUTBMESLSPO	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SBLACTIS:SLREUT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBLACTIS:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence

SCHX:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SCHX:SLBREVISEPLANT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SCHX:SLCAS	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SCHX:SLREUTD	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SCHX:SLREUTDA	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLREUTSINGLE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLRHAM	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SCHX:SLSPPBSPP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SSORALUBERRAT	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SCHX:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLBREVIS	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SCHX:SLREUT	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SLREUTINCREM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SCHX:SPLAC	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence

SCHX:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLCASBBIFLRHAMLSAL:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLCAS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTD	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTDA	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTU	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLACIDLCASBBIFLRHAMLSAL	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUT	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence

SLACIDLCASBBIFLRHAMLSAL:SPLAC	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLCASBBIFLRHAMLSAL:SSBOU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SLACIDLRHABLONGSBOUL:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SLACIDLRHABLONGSBOUL:SLCAS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLACIDLRHABLONGSBOUL:SLREUTD	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLACIDLRHABLONGSBOUL:SLREUTDA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLRHABLONGSBOUL:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLACIDLRHABLONGSBOUL:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLRHABLONGSBOUL:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SLACIDLRHABLONGSBOUL:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLRHABLONGSBOUL:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLRHABLONGSBOUL:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	low	incoherence
SBBIF:SLACIDLRHABLONGSBOUL	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SFAECBUTBMESLSPO:SLACIDLRHABLONGSBOUL	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLACIDLRHABLONGSBOUL:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLACIDLRHABLONGSBOUL:SLREUT	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence

SLACIDLRHABLONGSBOUL:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SLACIDLRHABLONGSBOUL:SSBOU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVISEPLANT:SLCAS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLBREVISEPLANT:SLREUTD	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLBREVISEPLANT:SLREUTDA	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLBREVISEPLANT:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	incoherence
SLBREVISEPLANT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVISEPLANT:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVISEPLANT:SLSPPBSPP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLBREVISEPLANT:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVISEPLANT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLBREVISEPLANT	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SFAECBUTBMESLSPO:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SLBREVIS:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVISEPLANT:SLREUT	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SLBREVISEPLANT:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence

SLBREVISEPLANT:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLCAS:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SLREUTDA	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLCAS:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLCAS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLCAS:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBBIF:SLCAS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLCAS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLCAS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLCAS:SLREUT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLCAS:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SLCAS:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	study limitations, heterogeneity, incoherence
SLREUTD:SLREUTDA	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	study limitations, heterogeneity, incoherence

SLREUTD:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTD:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLREUTD:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUTD:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLREUTD:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBBIF:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLREUTD	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLREUTD	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUT:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTD:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTD:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SLREUTDA:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTDA:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTDA:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLREUTDA:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTDA:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence

SBBIF:SLREUTDA	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SFAECBUTBMESLSPO:SLREUTDA	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLREUTDA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUT:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTDA:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTDA:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUTSINGLE:SLREUTU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTU:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	incoherence
SLREUTU:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTU:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SBBIF:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLREUTU	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLREUTU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUT:SLREUTU	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTINCREM:SLREUTU	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTU:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	serious heterogeneity, incoherence

SLREUTU:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SLREUTSINGLE:SLRHAM	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLREUTSINGLE:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTSINGLE:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTSINGLE:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLREUTSINGLE	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SLREUT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTSINGLE:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLRHAM:SLSPPBSPP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLRHAM:SRP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLRHAM:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLRHAM	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SFAECBUTBMESLSPO:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SLBREVIS:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence

SLREUT:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SLREUTINCREM:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLRHAM:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLSPPBSPP:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLSPPBSPP:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SBBIF:SLSPPBSPP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUT:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUTINCREM:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLSPPBSPP:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SRP:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLBREVIS:SRP	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	low	heterogeneity, incoherence
SLREUT:SRP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLREUTINCREM:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SPLAC:SRP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence

SBBIF:SSORALUBERRAT	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence
SFAECBUTBMESLSPO:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity, incoherence
SLBREVIS:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SLREUTINCREM:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	very low	imprecision, heterogeneity, incoherence
SSBOU:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SBBIF:SFAECBUTBMESLSPO	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLBREVIS	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBBIF:SLREUT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SLREUTINCREM	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SBBIF:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SBBIF:SSBOU	0	Some concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	low	study limitations, incoherence
SFAECBUTBMESLSPO:SLBREVIS	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SFAECBUTBMESLSPO:SLREUT	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SFAECBUTBMESLSPO:SPLAC	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	very low	heterogeneity, incoherence

SFAECBUTBMESLSPO:SSBOU	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	Some concerns	very low	study limitations, incoherence
SLBREVIS:SLREUT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLBREVIS:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLBREVIS:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUT:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	very low	serious imprecision, incoherence
SLREUT:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SLREUTINCREM:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence
SPLAC:SSBOU	0	No concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	moderate	incoherence

Only for confidence rating ranging from 'very low' to 'moderate' the reasons for the downgrade were presented, since there were constraints in at least one of the six domains assessed by CINeMA.

Table 12 - CINeMA for the secondary outcome "BOP"

COMPARISON	NUMBER OF STUDIES	WITHIN-STUDY BIAS	REPORTING BIAS	INDIRECTNESS	IMPRECISION	HETEROGENEITY	INCOHERENCE	CONFIDENCE RATING	REASON(S) FOR DOWNGRADING
MIXED EVIDENCE									
SBLACLACIDBBIFLRHAM:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SPLAC	1	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTIS:SPLAC	2	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLACIDLCASBBIFLRHAMLSAL:SRP	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SPLAC	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTAA:SPLAC	1	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTD:SRP	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	very low	study limitations and serious heterogeneity
SLREUTD:SPLAC	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	low	serious imprecision
SLREUTDA:SRP	1	Some concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	study limitations, serious incoherence
SLREUTDA:SPLAC	3	No concerns	Some concerns	No concerns	No concerns	Major concerns	Some concerns	very low	serious heterogeneity
SLREUTINCREM:SLREUTSINGLE	1	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTSINGLE:SPLAC	1	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLRHAM:SPLAC	3	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLSPPBSPP:SPLAC	2	No concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence

SPLAC:SSORALUBERRAT	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SPLAC	1	No concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLREUTINCREM:SPLAC	1	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
INDIRECT EVIDENCE									
SBLACLACIDBBIFLRHAM :SBLACTDN	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLACIDLCASBBIFLRHAM LSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLREUTAA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SBLACLACIDBBIFLRHAM :SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACLACIDBBIFLRHAM :SRP	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	imprecision, heterogeneity, serious incoherence
SBLACLACIDBBIFLRHAM :SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence

SBLACLACIDBBIFLRHAM:SLREUT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SBLACLACIDBBIFLRHAM:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTDN:SBLACTIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTDN:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTDN:SLREUTAA	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	imprecision, heterogeneity, serious incoherence
SBLACTDN:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTDN:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTDN:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SBLACTDN:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLREUT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTDN:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLACIDLCASBBIFLRHAMLSAL	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence

SBLACTIS:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLREUTAA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SBLACTIS:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLREUTDA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTIS:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SRP	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SBLACTIS:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SBLACTIS:SLREUT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SBLACTIS:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLBREVISEPLANT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTAA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTD	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTDA	0	Some concerns	Low risk	Some concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence

SLACIDLCASBBIFLRHAMLSAL:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLACIDLCASBBIFLRHAMLSAL:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUT	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLACIDLCASBBIFLRHAMLSAL:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLACIDLCASBBIFLRHAMLSAL:SPLAC	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SLREUTAA	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLBREVISEPLANT:SLREUTD	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SLREUTDA	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLBREVISEPLANT:SLRHAM	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SLSPPBSPP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLBREVISEPLANT:SLREUT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLBREVISEPLANT:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence

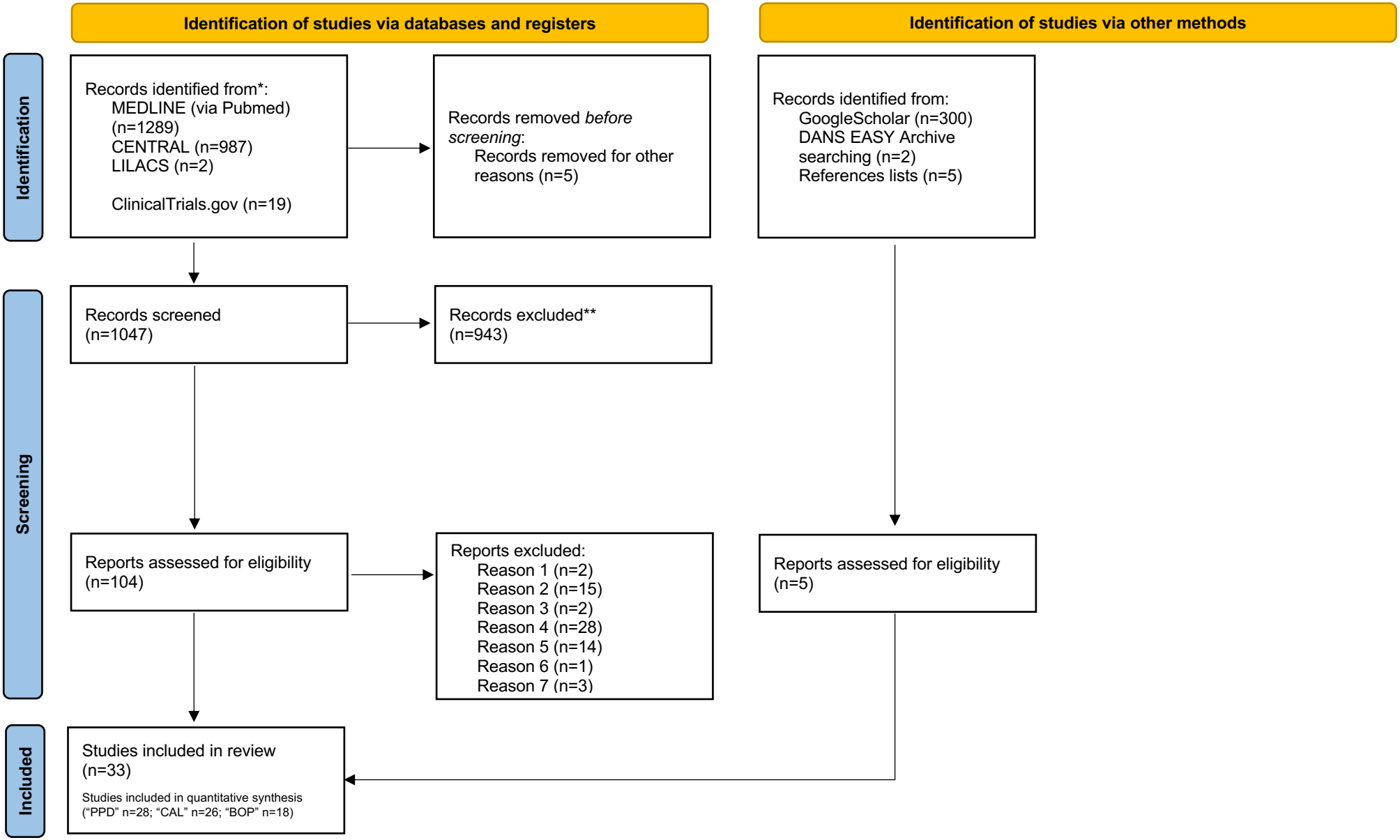
SLREUTAA:SLREUTD	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTAA:SLREUTDA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTAA:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTAA:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLREUTAA:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTAA:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTAA:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLREUT:SLREUTAA	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTAA:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTD:SLREUTDA	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTD:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTD:SLRHAM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTD:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTD:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SLREUTD	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTD:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence

SLREUTDA:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTDA:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLREUTDA:SLSPPBSPP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUTDA:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SLREUTDA	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTDA:SLREUTINCREM	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLREUTSINGLE:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	very low	heterogeneity and serious incoherence
SLREUTSINGLE:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLREUTSINGLE:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTSINGLE:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SLREUTSINGLE	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLRHAM:SLSPPBSPP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLRHAM:SRP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLRHAM:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SLRHAM	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLREUTINCREM:SLRHAM	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence

SLSPPBSPP:SRP	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLSPPBSPP:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence
SLREUT:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTINCREM:SLSPPBSPP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SRP:SSORALUBERRAT	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	very low	imprecision, serious incoherence
SLREUT:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SLREUTINCREM:SRP	0	No concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	low	serious incoherence
SPLAC:SRP	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLREUT:SSORALUBERRAT	0	No concerns	Low risk	Some concerns	No concerns	No concerns	Major concerns	very low	serious incoherence
SLREUTINCREM:SSORALUBERRAT	0	No concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	very low	serious heterogeneity and incoherence
SLREUT:SLREUTINCREM	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	very low	serious imprecision and incoherence

Only for confidence rating ranging from 'very low' to 'moderate' the reasons for the downgrade were presented, since there were constraints in at least one of the six domains assessed by CINeMA.

Appendix 7: Flow Diagram summarizing the search strategy and study selection



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Appendix 8: Summary of the included RCTs

Table 13 - Main characteristics and results of the included RCTs

studlab	*sample size*	*age ± SD*	*gender (M/F)*	*intervention*	*probiotic strain and concentration*	*comparison*	*CAL (mm)*	*PPD (mm)*	*PI (%)*	*BOP (%)*	*CFU*	*adverse effects*	*smoking habits*	*follow-up period*
Abuazab2021(Abuazab et al., 2021)	30 (SRP:10; SRP+CHX:10 SRP+Prob:10)	30-50	12 males; 18 females	Group I: SRP + probiotic	Bifidobacterium bifidum, EMCC #: 1334, Designation: DSM 20082, E 319f, JCM 12, isolated from intestine of adults and supplied as actively growing cultures.	Group II: SRP + CHX gel Group III: SRP only	(SRP) Day 0: 2.78 ± 0.31; 6w: 2.25 ± 0.35; (SRP+CHX) Day 0: 2.57 ± 0.34; 6w: 1.96 ± 0.41; (SRP+prob) Day 0: 2.79 ± 0.34; 6w: 1.87 ± 0.41.	(SRP) Day 0: 3.28 ± 0.39; 6w: 1.92 ± 0.23; (SRP+CHX) Day 0: 3.06 ± 0.45; 6w: 1.97 ± 0.32; (SRP+prob) Day 0: 3.29 ± 0.39; 6w: 2.02 ± 0.42.	(SRP) Day 0: 2.33 ± 0.21; 6w: 0.826 ± 0.109; (SRP+CHX) Day 0: 2.49 ± 0.245; 6w: 0.889 ± 0.138; (SRP+prob) Day 0: 2.34 ± 0.24; 6w: 0.766 ± 0.096.	NR	(Pg) (SRP) Day 0: 29.0 ± 10.15; 6w: 17.0 ± 1.9; (SRP+CHX) Day 0: 28.0 ± 17.52; 6w: 9.0 ± 2.0; (SRP+prob) Day 0: 30.0 ± 14.43; 6w: 7.0 ± 1.4; (Pi) (SRP) Day 0: 32.0 ± 8.93; 6w: 19.0 ± 3.1; (SRP+CHX) Day 0: 33.0 ± 18.7; 6w: 12.0 ± 1.5; (SRP+prob) Day 0: 35.0 ± 11.28; 6w: 11.0 ± 2.5; (Total load) (SRP) Day 0: 965.0 ± 166.02; 6w: 612.0 ± 146.35; (SRP+CHX) Day 0: 884.0 ± 187.39; 6w: 581.0 ± 177.60; (SRP+prob) Day 0: 928.50 ± 183.88; 6w: 505 ± 174.42.	None	All non-smokers	6 weeks
Alshareef2020(Alshareef et al., 2020)	25 (SRP: 10; SRP+prob: 15)	29 ± 96	NR	SRP + probiotic	Each probiotic lozenge contains five bifid bacteria including Lactobacillus acidophilus,	SRP alone	(SRP) Day 0: 3.4930 ± 0.66101; 30d: 3.1490 ± 0.65514; . (SRP+prob) Day 0: 3.5740 ± 0.58024;	(SRP) Day 0: 2.6130 ± 0.41508; 30d: 2.3380 ± 0.43235; . (SRP+prob) Day 0: 2.5533 ± 0.23654;	(SRP) Day 0: 47.3250 ± 15.38717; 30d: 37.3160 ± 12.29990; . (SRP+prob) Day 0: 44.0127 ±	(SRP) Day 0: 49.7550 ± 13.93193; 30d: 40.8200 ± 13.21242; . (SRP+prob) Day 0: 40.7533 ±	NR	NR	NR	30 days

					Lactobacillus casei, Bifidobacterium bifidum, Lactobacillus rhamnosus, and Lactobacillus salivarius.		30d: 3.1487 ± 0.59010.	30d: 2.1973 ± 0.27830.	10.06966; 30d: 35.7433 ± 15.18255.	9.58256; 30d: 32.1533 ± 8.50200.				
Butera2020(Butera et al., 2020)	60 (SRP+CHX: 20; SRP+probTo othpaste:20; SRP+probTo othpaste&gum: 20)	SRP+CHX: 55 SRP+probTo othpaste: 49 SRP+probTo othpaste&gum: 55	SRP+CHX: 9/11 SRP+probTo othpaste: 13/7 SRP+probTo othpaste&gum: 10/10	SRP + Probiotic toothpaste SRP + Probiotic toothpaste+chewing gum	Toothpaste: Bifidobacterium *, Lactobacillus * Chewing gum: L. reuteri (SGL 01), L. salivarius (SGL 03), L. plantarum (SGL 07)	SRP + Curasept CHX toothpaste	(CHXtoothpaste) Day 0: 5.83 ± 1.87; 6m: 5.57 ± 1.72; (ProbToothpaste) Day 0: 5.64 ± 2.27; 6m: 4.44 ± 2.14; (ProbToothpaste+gum) Day 0: 5.36 ± 1.46; 6m: 3.46 ± 0.94.	(CHXtoothpaste) Day 0: 5.88 ± 1.26; 6m: 5.80 ± 1.08; (ProbToothpaste) Day 0: 5.67 ± 0.74; 6m: 4.46 ± 0.84; (ProbToothpaste+gum) Day 0: 5.57 ± 0.85; 6m: 3.52 ± 0.53.	(CHXtoothpaste) Day 0: 70.00 ± 26.56; 6m: 67.00 ± 22.33; (ProbToothpaste) Day 0: 68,50 ± 22.48; 6m: 34.15 ± 14.08; (ProbToothpaste+gum) Day 0: 70.50 ± 20.38; 6m: 28.50 ± 17.85.	(CHXtoothpaste) Day 0: 66.25 ± 17.23; 6m: 64.00 ± 14.01; (ProbToothpaste) Day 0: 67.00 ± 24.94; 6m: 33.00 ± 20.39; (ProbToothpaste+gum) Day 0: 66.15 ± 34.89; 6m: 21.50 ± 17.55.	*(Aa)* (CHXtoothpaste) Day 0: 1247.48 ± 1238.52; 6m: 1030.08 ± 1202.40; (ProbToothpaste) Day 0: 528 ± 1121.42; 6m: 734.5 ± 2076.09; (ProbToothpaste+gum) Day 0: 650.25 ± 1114.43; 6m: 406.2 ± 919.53; *(Pg)* (CHXtoothpaste) Day 0: 10530.55 ± 18424.41; 6m: 8479 ± 3974.44; (ProbToothpaste) Day 0: 9107.65 ± 21882.53; 6m: 7625.75 ± 22714.00; (ProbToothpaste+gum) Day 0: 11644.1 ± 23306.05; 6m: 7553.641 ± 15781.77; *(Tf)* (CHXtoothpaste) Day 0: 34012.51 ± 54134.03; 6m: 40990 ± 19938.19; (ProbToothpaste) Day 0: 57690.4 ± 90873,28; 6m: 25656.4 ± 48302.74; (ProbToothpaste+gum) Day 0: 35091.9 ± 40463.06;	NR	NR	6 months

											6m: 3929080 ± 66828.91; *(Td)* (CHXtoothpaste) Day 0: 7339.82 ± 19922.95; 6m: 4651 ± 2158.87; (ProbToothpaste) Day 0: 5318 ± 10086.63; 6m: 10244.63 ± 15860.15; (ProbToothpaste+gum) Day 0: 5521.75 ± 18720.46; 6m: 6065.13 ± 19738.92; *(Pi)* (CHXtoothpaste) Day 0: 11018 ± 10208.32; 6m: 8830 ± 5617.44; (ProbToothpaste) Day 0: 9720.1 ± 2405.66; 6m: 3536 ± 5931.72; (ProbToothpaste+gum) Day 0: 7476.55 ± 4787.82; 6m: 2520.5 ± 2435.87; *(Fn)* (CHXtoothpaste) Day 0: 17607.3 ± 25342.18; 6m: 16298.82 ± 17212.96; (ProbToothpaste) Day 0: 19381.2 ± 10360.37; 6m: 7843.6 ± 5509.43; (ProbToothpaste+gum) Day 0: 18053 ± 10931.75; 6m: 7211.78 ± 5971.25; *(Total Bacteria Count)* (CHXtoothpaste) Day 0:			

											1648650 ± 2571189.00; 6m: 561150 ± 349477.80; (ProbToothpaste) Day 0: 1150665 ± 2270115.00; 6m: 535470 ± 306466.90; (ProbToothpaste+gum) Day 0: 808115 ± 1619913.00; 6m: 2097731 ± 5655579.00;			
Chandra2016(Chandra et al., 2016)	30 (SRP: 27; SRP+prob:30)	25-50	NR	SRP + probiotic	(250 mg; Florafi x®, Unique Biotech, Hyderabad, India) + The probiotic was mixed with a prebiotic (fructooligosaccharide, FOS; Mitushi Pharma, Ahmedabad, India), in the ratio of 4:1 to induce growth and activity in S boulardii. Briefl y, 30 preparations of 1 g S boulardii-FOS mixture were made by stirring 200 mg of FOS and 800 mg of probiotic with a spatula. containing approximatel y 5 billion colony forming units (CFU) of the yeast Saccharomyces boulardii.	SRP	(SRP) Day 0: 3.52 ± 0.74; 6m: 1.80 ± 0.92; (SRP+prob) Day 0: 3.57 ± 0.74; 6m: 0.61 ± 0.58.	(SRP) Day 0: 5.52 ± 0.74; 6m: 3.61 ± 0.97; (SRP+prob) Day 0: 5.66 ± 0.73; 6m: 2.19 ± 0.51.	(SRP) Day 0: 1.79 ± 0.36; 6m: 0.92 ± 0.27; (SRP+prob) Day 0: 1.58 ± 0.34; 6m: 0.64 ± 0.28.	NR	NR	NR	All non-smokers	6 months
Costacurta2018(Costacurta et al., 2018)	40 (SRP: 20; SRP+prob: 20)	SRP: 51.8±14.94 SRP+prob: 41.3±11.85	SRP: F:60%, M:40% SRP+prob: F:40%, M:60%	SRP + probiotic	probiotic containing 10 8 CFU of Lactobacillus reuteri DSM 17938 and 10	SRP alone	(SRP) Day 0: 4.95 ± 0.56; 4w: 4.3 ± 0.52; (SRP+prob) Day 0: 4.56 ±	(SRP) Day 0: 4.51 ± 0.54; 4w: 3.91 ± 0.50; (SRP+prob) Day 0: 4.12 ±	NR	(SRP) Day 0: 88.45 ± 9.63; 4w: 58.15±10.38; (SRP+prob) Day 0:	NR	NR	NR	4 weeks

					8 CFU of Lactobacillus reuteri ATCC PTA 5289		0.94; 4w: 3.94 ± 0.85.	0.89; 4w: 3.47 ± 0.65.		87.5±14.75; 4w: 31.45±15.97.				
deOliveira2022(de Oliveira et al., 2022)	48 (SRP+plac: 23; SRP+prob: 19)	NR	NR	SRP + probiotic	Dive strains of Lactobacillus spp. and three of Bifidobacterium spp.	SRP + placebo	(SRP+plac) Day 0: 3.18 ± 0.785; 2m: 2.89 ± 0.711; (SRP+prob) Day 0: 3.31 ± 0.830; 2m: 2.74 ± 0.844.	(SRP+plac) Day 0: 2.82 ± 0.460; 2m: 2.24 ± 0.207; (SRP+prob) Day 0: 3.00 ± 0.363; 2m: 2.36 ± 0.319.	NR	(SRP+plac) Day 0: 45.10 ± 16.333; 2m: 24.70 ± 14.740; (SRP+prob) Day 0: 53.30 ± 24.148; 2m: 32.20 ± 17.111. (%)	NR	Most patients reported feeling well during treat-ments; however, gastrointestinal symptoms were morefrequently reported in the probiotic than placebo group,in particular the occurrence of soft stools	All non-smokers	2 months
Dhaliwal2017(Dhaliwal et al., 2017)	27 (SRP: 13; SRP+prob: 14)	SRP: 31 ± 8.07 SRP+prob: 33.46 ± 6.63	20 males (74.07%) and 7 females (25.93%)	SRP + probiotic	Bifi lac lozenges (Tablets India Private Limited, Chennai).It is a commercially available probiotic preparation combined with prebiotics to enhance its action. Each tablet contains Streptococcus faecalis T-110 JPC -30 million CFU, Clostridium butyricum TO-A IHS-2 million CFU, Bacillus mesentericus TO-A JPC-1million CFU and Lactobacillus sporogenes IHS-50 million CFU.	SRP alone	(SRP) Day 0: 9.17 ± 0.75; 3m: 8.21 ± 1.08; (SRP+prob) Day 0: 9.45 ± 1.14; 3m: 8.16 ± 1.55.	(SRP) Day 0: 4.97 ± 0.61; 3m: 4.15 ± 0.73; (SRP+prob) Day 0: 5.54 ± 1.08; 3m: 4.62 ± 1.32.	(SRP) Day 0: 1.51 ± 0.40; 3m: 1.11 ± 0.15; (SRP+prob) Day 0: 1.59 ± 0.34; 3m: 1.20 ± 0.20.	NR	(Aa) (SRP) Day 0: 10.57 ± 16.15; 3m:11.07 ± 24.03; (SRP+prob) Day 0: 5.82 ± 10.60; 3m: 0.00 ± 0.00; (Pg) (SRP) Day 0: 28.29± 30.68; 3m: 14.36 ± 21.68; (SRP+prob) Day 0: 21.38 ± 22.51; 3m: 0.00 ± 0.00; (Pi) (SRP) Day 0: 0.71 ± 1.86; 3m: 2.57 ± 8.05; (SRP+prob) Day 0: 2.00 ± 5.54; 3m: 7.69 ± 27.74;	None	NR	3 months
El-bagoory2021 (El-Bagoory et al., 2021)	12 (SRP: 6; SRP+prob:6)	SRP: 39.33 ± 3.20 SRP+prob: 39.33 ± 3.20	SRP:1/5 SRP+prob: 2/4	SRP + probiotic	L. reuteri DSM 17938 [1 × 108 CFU]	SRP alone	(SRP) Day 0: 3.30 ± 0.48; 6m: 2.30 ± 0.67; (SRP+prob) Day 0: 3.10 ± 0.32;	(SRP) Day 0: 5.30 ± 0.48; 6m: 4.30 ± 0.67; (SRP+prob) Day 0: 5.10 ± 0.32;	NR	NR	(Pg) (SRP) Day 0: 31.01 ± 5.43; 6m: 36.10 ± 2.81; (SRP+prob) Day 0: 34.41 ± 1.13;	None	All non-smokers	6 months

							6m: 1.30 ± 0.48.	6m: 3.30 ± 0.48.			6m: 24.34 ± 3.30.			
Ghasemi2020(Ghasemi et al., 2020)	36 (SRP+plac:18; SRP+prob:18)	SRP+plac: 44.35 SRP+prob: 44.81	SRP+plac: 60%/40%; SRP+prob: 55%/45%	SRP + probiotic	Prokid capsule (15×10 9 probiotic units per capsule), which contained a combination of bacterial strains, i.e., Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus rhamnosus, which were purchased from Gostaresh Milad Pharmed Co	SRP + placebo	(SRP+plac) Day 0: 5.33±0.69; 3m: 4.69±0.69; (SRP+prob) Day 0: 5.31±0.58; 3m: 4.25±0.76.	(SRP+plac) Day 0: 5.78±0.57; 3m: 4.97±0.68; (SRP+prob) Day 0: 5.65±0.57; 3m: 4.29±0.71.	(SRP+plac) Day 0: 48.72±7.71; 3m: 20.11±7.54; (SRP+prob) Day 0: 50.76±7.87; 3m: 19.59±10.79.	(SRP+plac) Day 0: 47.55±8.14; 3m: 23.45±9.17; (SRP+prob) Day 0: 48.95±7.73; 3m: 19.46±10.97.	NR	NR	All non-smokers	3 months
Grover(Grover)	30 (SRP: 15; SRP+prob: 15)	SRP: 31 ± 8.07 (A) SRP+prob: 33.46 ± 6.63 (B)	population: 20/7	SRP + probiotic	Bifilac lozenges (Streptococcus faecalis T-110 JPC -30 millionCFU; Clostridium butyricum TO-A IHS-2 million CFU; Bacillus mesentericus TO-A JPC-1million CFU;Lactobacillus sporogenes IHS-50 million CFU)	SRP alone	(SRP) Day 0: 9.17 ± 0.75; 3m: 8.21 ± 1.08; (SRP+prob) Day 0: 9.45 ± 1.14; 3m: 8.16 ± 1.55.	(SRP) Day 0: 4.97 ± 0.61; 3m: 4.15 ± 0.73; (SRP+prob) Day 0: 5.54 ± 1.08; 3m: 4.62 ± 1.32.	(SRP) Day 0: 1.51 ± 0.40; 3m: 1.11 ± 0.15; (SRP+prob) Day 0: 1.59 ± 0.34; 3m: 1.20 ± 0.20.	NR	(Aa) (SRP) Day 0: 10.57 ± 16.15; 3m: 11.07 ± 24.03; (SRP+prob) Day 0: 5.82 ± 10.60; 3m: 0 ± 0; (Pg) (SRP) Day 0: 28.29 ± 30.68; 3m: 14.36 ± 21.68; (SRP+prob) Day 0: 21.38 ± 22.51; 3m: 0 ± 0; (Pi) (SRP Day 0: 0.71 ± 1.86; 3m: 2.57 ± 8.05; (SRP+prob) Day 0: 2.00 ± 5.54; 3m: 7.69 ± 27.74	None	NR	3 months
Ikram2019(Ikram et al., 2019)	67 (SRP+plac: 14; SRP+prob: 14)	SRP+plac: 40.14 ± 2.64; SRP+prob: 41.78 ± 3.58;	SRP+plac: 8/6 SRP+prob: 9/5	SRP + probiotic	L. reuteri (doesn't mention dosage), but protocol has L. reuteri 1.2 billion CFU/g	SRP + placebo	(SRP+plac) Day 0: 4.12 ± 0.74; 84d: 3.86 ± 0.59; (SRP+prob) Day 0: 4.08 ± 0.66;	(SRP+plac) Day 0: 4.25 ± 1.12; 84d: 3.95 ± 0.78; (SRP+prob) Day 0: 4.32 ±0.91;	(SRP+plac) Day 0: 84.58 ± 8.06; 84d: 33.67 ± 9.47; (SRP+prob) Day 0: 85.23 ± 8.23;	(SRP+plac) Day 0: 71.94 ± 23.13; 84d: 46.24 ± 11.40; (SRP+prob) Day 0: 70.47 ± 11.8;	NR	NR	All non-smokers	84 dias

							84d: 3.24 ± 0.47.	84d: 2.54 ± 0.52.	84d: 26.28 ± 4.12.	84d: 13.89 ± 3.25.				
Ince2015(Ince et al., 2015)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 42.20 ± 2.78 SRP+prob: 41 ± 3.17	SRP+plac: 8/7 SRP+prob: 9/6	SRP + probiotic	L. reuteri DSM17938 and L. reuteri ATCC PTA5289 with 10^8 CFU for each strain (Prodentis, Biogaia, Sweden).	SRP + placebo	NR	(SRP+plac) Day 0: 5.57 ± 0.39; 360d: 5.01 ± 0.40; (SRP+prob) Day 0: 5.85 ± 0.54; 360d: 4.15 ± 0.44.	(SRP+plac) Day 0: 2.23 ± 0.24; 360d: 1.43 ± 0.26; (SRP+prob) Day 0: 2.25 ± 0.25; 360d: 0.76 ± 0.24.	(SRP+plac) Day 0: 88.65 ±4 .11; 360d: 19.00 ± 5.42; (SRP+prob) Day 0: 88.90 ± 7.66; 360d: 11.60 ± 4.35.	NR	None	All non-smokers	1 year
Invernici2018(Invernici et al., 2018)	41 (SRP+plac: 21; SRP+prob: 20)	NR	NR	SRP + probiotic	Bifidobacterium animalis subsp. lactis (B. lactis) HN019 (HOWARU® Bifido LYO 40 DCUS, DuPont™ Danisco® Sweeteners Oy, Kantvik, Finland) (10^9 colony-forming units (CFUs))	SRP + placebo	(SRP+plac) Day 0: 3.42 ± 0.54; 90d: 3.24 ± 0.51; (SRP+prob) Day 0: 3.26 ± 0.39; 90d: 2.77 ± 0.38.	(SRP+plac) Day 0: 3.10 ± 0.43; 90d: 2.85 ± 0.34; (SRP+prob) Day 0: 3.01 ± 0.27; 90d: 2.49 ± 0.27.	(SRP+plac) Day 0: 26.71 ± 16.60; 90d: 27.14 ± 18.64; (SRP+prob) Day 0: 23.85 ± 15.33; 90d: 21.65 ± 13.13.	(SRP+plac) Day 0: 35.00 ± 25.84; 90d: 30.71 ± 27.86; (SRP+prob) Day 0: 30.80 ± 22.07; 90d: 18.80 ± 16.14.	NR	None	All non-smokers	90 days
Invernici2020(Invernici et al., 2020)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 47.67 ± 9.49 SRP+prob: 47.60 ± 9.97	SRP+plac: 8/7 SRP+prob: 5/10	SRP + probiotic	10^9 colony-forming units (CFUs) of B. lactis HN019 (HOWARU1 Bifido LYO 40 DCU-S, DuPont™ Danisco1 Sweeteners Oy, Kantvik, Finland)	SRP + placebo	NR	NR	(SRP+plac) Day 0: 22.50 ± 8.54; 90d: 22.66 ± 9.99; (SRP+prob) Day 0: 18.71 ± 12.14; 90d: 18.27 ± 17.11.	(SRP+plac) Day 0: 14.07 ± 7.99; 90d: 12.10 ± 8.19; (SRP+prob) Day 0: 9.17 ± 7.71; 90d: 5.92 ± 6.12.	NR	None	All non-smokers	90 days
Jebin2021(Jebin et al., 2021)	27 (SRP:13; SRP+prob:14)	SRP: 37.8 ± 7.90 SRP+prob: 37.5 ± 7.12	SRP: 10/3 SRP+prob:11/3	SRP + probiotic	L. reuteri UBLRu-87, 0.5 billion CFU, Unique Biotech Ltd, Hyderabad, India	SRP alone	(SRP) Day 0: 4.17 ± 0.20; 3m: 3.50 ± 0.21; (SRP+prob) Day 0: 3.99 ± 0.56; 3m: 2.97 ± 0.35.	(SRP) Day 0: 5.20 ± 0.40; 3m: 4.35 ± 0.38; (SRP+prob) Day 0: 5.27 ± 0.49; 3m: 3.6 ± 0.56.	(SRP) Day 0: 1.80 ± 0.32; 3m: 1.28 ± 0.23; (SRP+prob) Day 0: 1.69 ± 0.36; 3m: 0.95 ± 0.19.	NR	(SRP) Day 0: 6.43±0.64; 3m: 4.54±0.49; (SRP+prob) Day 0: 6.60±0.63; 3m: 3.94±0.33.	None	All non-smokers	3 months
Kanagaraj2019(Kanagaraj et al., 2019)	60 (SRP+plac: 30; SRP+prob: 30)	25-50	NR	SRP + probiotic	BIFILAC-lozenges) contains Lactobacillus sporogenes 100 million, Streptococcus faecalis T-110 JPC 60 million, Clostridium butyrium TO-A 4 million	SRP + placebo	(SRP+plac) Day 0: 3.09 ± 0.21; 6w: 1.27 ± 0.38; (SRP+prob) Day 0: 3.05 ± 0.13; 6w: 0.50 ± 0.47.	(SRP+plac) Day 0: 5.13 ± 0.10; 6w: 2.50 ± 0.54; (SRP+prob) Day 0: 5.19 ± 0.14; 6w: 1.69 ± 0.57.	(SRP+plac) Day 0: 2.12 ± 0.51; 6w: 1.92 ± 0.43; (SRP+prob) Day 0: 2.15 ± 0.48; 6w: 1.04 ± 0.51.	(SRP+plac) Day 0: 2.30 ± 0.47; 6w: 1.96 ± 0.43; (SRP+prob) Day 0:2 .24 ± 0.42; 6w: 1.13 ± 0.49.	In evaluating the presence of Porphyromonas gingivalis, more positive bands of P gingivalis was seen in both Group I and Group II at Day 0 and there was	None	All non-smokers	6 weeks

					and Bacillus mesentericus TO-A JPC 2 million.						much reduction after 3 weeks in Group II after post therapy compared to Group I as shown in Fig. 3.			
Kumar2021(Kumar et al., 2021)	48 (SRP+plac: 15; SRP+prob: 15; SRP+pprob: 15)	SRP+plac: 42.87 ± 3.42 SRP+prob: 41.79 ± 2.37 SRP+pprob: 39.74 ± 2.97	SRP+plac: 7/8 SRP+prob: 6/9 SRP+pprob: 8/7	SRP+single application of probiotic (G2); SRP+incremental application of probiotic (G3)	5.9 billion CFU of L. reuteri per gram and maltodextrin as a carrier (batch No. LR 12, Meteoric Lifesciences, Ahmedabad, India)	SRP+placebo (G1)	(SRP+plac) Day 0: 5.92 ± 0.65; 24w: 4.79 ± 0.90; (SRP+prob) Day 0: 6.27 ± 0.75; 24w: 4.82 ± 0.60; (SRP+pprob) Day 0: 6.44 ± 0.79; 24w: 4.88 ± 0.58.	(SRP+plac) Day 0: 6.72 ± 0.63; 24w: 5.08 ± 0.50; (SRP+prob) Day 0: 6.78 ± 0.72; 24w: 4.92 ± 0.58; (SRP+pprob) Day 0: 6.63 ± 0.75; 24w: 4.91 ± 0.73.	(SRP+plac) Day 0: 2.08 ± 0.18; 24w: 0.70 ± 0.40; (SRP+prob) Day 0: 2.10 ± 0.23; 24w: 0.73 ± 0.24; (SRP+pprob) Day 0: 2.20 ± 0.43; 24w: 0.46 ± 0.19.	(SRP+plac) Day 0: 81.67 ± 19.97; 24w: 43.33 ± 22.09; (SRP+prob) Day 0: 93.33 ± 11.44; 24w: 35.00 ± 22.76; (SRP+pprob) Day 0: 92.8 6 ±15.28; 24w: 31.21 ± 15.39.	NR	None	All non-smokers	24 weeks
Laleman2015(Laleman et al., 2015)	48 (SRP+plac: 24; SRP+prob: 24)	SRP+plac: 46.0 ±- 5,0 SRP+prob: 47.0 ± 5.0	SRP+plac: 14/10 SRP+prob: 12/12	SRP + probiotic	S. oralis KJ3, S. uberis KJ2 and S. rattus JH145 (Probiora3,;Oragenics, Alachua, FL, USA) were added (at least 108 CFU of each strain/tablet)	SRP + placebo	(SRP+plac) Day 0: 5.36 ± 0.45; 24w: 4.60 ± 0.48; (SRP+prob) Day 0: 5.22 ± 0.41; 24w: 4.51 ± 0.41.	(SRP+plac) Day 0: 4.59 ± 0.52; 24w: 2.98 ± 0.47; (SRP+prob) Day 0: 4.50 ± 0.51; 24w: 2.99 ± 0.47.	NR	(SRP+plac) Day 0: 85.55 ± 7.29 24w: 30.11 ± 10.36; (SRP+prob) Day 0: 87.44 ± 6.03; 24w: 26.98 ± 9.34.	NR	None	NR	24 weeks
Meenakshi2020(Meenakshi & Varghese, 2018)	20 (SRP:10; SRP+prob:10)	NR	NR	SRP + probiotic	Yakult containing *Lactobacillus casei* strain Shirota	SRP alone	(SRP) Day 0: 4.89±0.55; 1m: 4.54±0.53; (SRP+prob) Day 0: 4.95±0.40; 1m: 4.01±0.53.	(SRP) Day 0: 4.46±0.75; 1m: 4.14±0.66; (SRP+prob) Day 0: 4.57±0.51; 1m: 3.43±0.39.	(SRP) Day 0: 1.76±0.41; 1m: 1.40±0.35; (SRP+prob) Day 0: 1.93±0.40; 1m: 0.80±0.35.	NR	(SRP) Day 0: 163.9±37.6; 1m: 122.5±28.6; (SRP+prob) Day 0: 169.4±34.7; 1m: 98.9±16.2.	NR	All non-smokers	1 month
Minic2020(Minic et al., 2022)	80 (SRP: 40; SRP+prob: 40)	35-55	NR	SRP + probiotic	6.5 billion live Lactobacillus acidophilus, concentration of 107 CFU, at least 107 CFU Bifidobacterium infantis and at least 106 CFU Enterococcus faecium colony-forming	SRP alone	NR	(SRP) Day 0: 5.22 ± 0.56; 30d: 4.72 ± 0.36; (SRP+prob) Day 0: 5.30 ± 0.46; 30d: 4.08 ± 0.22.	(SRP) Day 0: 1.92 ± 0.53; 30d: 0.61 ± 0.03; (SRP+prob) Day 0: 2.00 ± 0.56; 30d: 0.10 ± 0.04.	(SRP) Day 0: 1.87 ± 0.38; 30d: 0.82 ± 0.13; (SRP+prob) Day 0: 1.80 ± 0.35; 30d: 0.18 ± 0.06.	NR	None	NR	30 days

					units per capsule									
Morales2016 (Morales et al., 2016)	28 (SRP+plac: 14; SRP+prob:14)	SRP+plac: 46.9 ±- 10.3 SRP+prob: 52.7 ± 7.3	SRP+plac: 7/7 SRP+prob: 7/7	SRP + probiotic	L. rhamanosus SP1 (2 × 10^7 CFU/day) (Macrofood SA, Santiago, Chile)	SRP + placebo	(SRP+plac) Day 0: 4.9 ± 1.3; 12m: 4.8 ± 1.3; (SRP+prob) Day 0: 4.2 ± 0.9; 12m: 4.1 ± 1.0.	(SRP+plac) Day 0: 2.5 ± 0.3; 12m: 2.0 ± 0.2; (SRP+prob) Day 0: 2.7 ± 0.6; 12m: 2.1 ± 0.5.	(SRP+plac) Day 0: 52.1 ± 20.7; 12m: 35.5 ± 11.4; (SRP+prob) Day 0: 63.1 ± 18.59. 12m: 33.1 ± 21.3.	(SRP+plac) Day 0: 33.8 ± 16.1; 12m: 25.4 ± 10.3; (SRP+prob) Day 0: 41.1 ± 16.3; 12m: 29.3 ± 12.7.	NR	None	NR	12 months
Oliveira2021 (Oliveira et al., 2021)	48 (SRP+plac: 23; SRP+prob: 19)	SRP+plac: 53.0 (12.0) SRP+prob: 49.0 (10.0)	SRP+plac: 9/14 SRP+prob: 10/9	SRP + probiotic	The probiotic selected * contained 5 strains of Lactobacillus spp. and 3 of Bifidobacterium spp.	SRP + placebo	(SRP+plac) Day 0: 3.18 (1.06); 2m: 2.89 (0.96); (SRP+prob) Day 0: 3.31 (1.12); 2m: 2.74 (1.14).	(SRP+plac) Day 0: 2.82 (0.62); 2m: 2.24 (0.28); (SRP+prob) Day 0: 3.00 (0.49); 2m: 2.36 (0.43).	(SRP+plac) Day 0: 62.10 (20); 2m: 44.90 (19.10); (SRP+prob) Day 0: 61.30 (22.10); 2m: 47.90 (22.40).	(SRP+plac) Day 0: 45.10 (22.05); 2m: 24.70 (19.90); (SRP+prob) Day 0: 53.30 (32.60); 2m: 32.20 (23.10).	Change in mean counts, 41 bacteria, but only in graphics Not reported on other way	The 42 individuals who finished the study reported full adherence to the prescribed products, but 3 did not fill the side effects form correctly. Most patients reported feeling well during treatments; however, gastrointestinal symptoms were more frequently reported in the probiotic than placebo group, in particular the occurrence of sooft stools. Median (IQR)	NR	2 months
Özener2023(Ozener et al., 2023)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 42.27±8.8; SRP+prob: 41.40±6.8	SRP+plac:7/8 SRP+prob:8/7	SRP + probiotic	B. lactis DN-173010, $\geq 10^8$ CFU	SRP + placebo	(SRP+plac) Day 0: 2.67±0.46; 3m: 2.16±0.43; (SRP+prob) Day 0: 2.93±0.37; 3m: 2.26±0.45.	(SRP+plac) Day 0: 2.59±0.43; 3m: 2.06±0.35c; (SRP+prob) Day 0: 2.76±0.38; 3m: 2.05±0.36.	(SRP+plac) Day 0: 1.79±0.36 ; 3m: 0.35±022 ; (SRP+prob) Day 0: 1.81±0.23; 3m: 0.18±0.08.	(SRP+plac) Day 0: 49.16±15.09; 3m: 22.34±5.23; (SRP+prob) Day 0: 52.70±21.98; 3m: 10.58±3.16.	(SRP+plac) Day 0: 75.64±42.72; 3m: 24.90±28.31; (SRP+prob) Day 0: 93.95±76.18; 3m: 31.95±39.62.	None	All non-smokers	3 months
Paul2019(Paul et al., 2019)	30 (SRP+plac: 13; SRP+prob:14)	38.1	13/17	SRP + probiotic	Lactobacillus brevis (dosage not reported)	SRP + placebo	(SRP+plac) Day 0: 3.584 ± 0.73; 12w: 2.776 ± 0.71; (SRP+prob) Day 0: 3.580 ± 1.00; 12w: 3.133 ± 1.15.	(SRP+plac) Day 0: 3.420 ± 0.77; 12w: 2.617 ± 0.97; (SRP+prob) Day 0: 3.280 ± 0.83; 12w: 2.57 3 ±0.60.	(SRP+plac) Day 0: 1.138 ± 0.78; 12w: 0.604 ± 0.38; (SRP+prob) Day 0: 1.274 ± 0.63; 12w: 0.636 ± 0.32.	(SRP+plac) Day 0: 0.902 ± 0.17; 12w: 0.540 ± 0.24; (SRP+prob) Day 0: 0.871 ± 0.30; 12w: 0.714 ± 0.22.	(Aa) (SRP+plac) Day 0: 10500 ± 14740; 12w: 0 ± 0; (SRP+prob) Day 0: 19000 ± 41160; 12w: 0 ± 0; (Pg) (SRP+plac)	None	All non-smokers	12 weeks

											Day 0: 12400 ± 10400; 12w: 0 ± 0; (SRP+prob) Day 0: 18400 ± 23000; 12w: 538 ± 1050; (Pi) (SRP+plac) Day 0: 4181 ± 8931; 12w: 0 ± 0; (SRP+prob) Day 0: 1846 ± 3105; 12w: 0 ± 0;			
Pelekos2020(Pelekos et al., 2020)	59 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 52.76 SRP+prob: 51.14	SRP+plac: 10/10 SRP+prob: 4/16	SRP + probiotic	L. reuteri DSM17938 and L. reuteri ATCC PTA5289 with 10^8 CFU for each strain (Prodentis, Biogaia, Sweden).	SRP + placebo	(SRP+plac) Day 0: 8.02 ± 2.32; 180d: 7.50 ± 2.58; (SRP+prob) Day 0: 7.61 ± 1.99; 180d: 7.07 ± 2.20.	(SRP+plac) Day 0: 6.38 ± 1.68; 180d: 4.97 ± 1.91; (SRP+prob) Day 0: 5.95 ± 1.19; 180d: 4.55 ± 1.37.	NR	(SRP+plac) Day 0: 221(93.2%); 180d: 145 (61.2%)); (SRP+prob) Day 0: 184 (87.6%); 180d: 110 (52.4%).	NR	NR	All non-smokers	180 days
Penala2016(Penala et al., 2016)	29 (SRP+plac: 14; SRP+prob:15)	SRP+plac: 35.5 ± 9.17 SRP+prob: 37.2 ± 9.79	NR	SRP + probiotic	Lactobacillus salivarius (2 × 109 CFU) and Lactobacillus reuteri (2 × 109 CFU) per capsule	SRP + placebo	(SRP+plac) Day 0: 2.88 ± 0.40; 3m: gráfico; (SRP+prob) Day 0:2.98 ± 0.78; 3m: gráfico.	(SRP+plac) Day 0: 3.19 ± 0.44; 3m: gráfico; (SRP+prob) Day 0: 3.12 ± 0.71; 3m: gráfico.	(SRP+plac) Day 0: 2.16 ± 0.35; 3m: 0.72 ± 0.39; (SRP+prob) Day 0: 1.81 ± 0.47; 3m: 0.35 ± 0.18.	(SRP+plac) Day 0: 1.79 ± 0.11; 3m: 0-71 ± 0.43. (SRP+prob) Day 0: 1.65 ± 0.38; 3m: 0.31 ± 0.14.	NR	None	All non-smokers	3 months
Pudgar2021(Pudgar et al., 2021)	40 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 46.7 (11.0) SRP+prob: 45.9 (8.0)	SRP+plac: 11/9 SRP+prob: 7/13	SRP + probiotic	6.0 × 109 CFU/ml of L. brevis (CECT7480) [8] and 6.0 × 109 CFU/ml of L. plantarum (CECT7481) [8], while the probiotic lozenges contained 1.2 × 109 CFU/ml of each bacterium (ProlacSan, CMS Dental, Copenhagen, Denmark)	SRP + placebo	(SRP+plac) Day 0: 4.5 (4.0; 5.9); 3m: 3.7 (3.3; 4.9); (SRP+prob) Day 0: 4.3 (3.8; 4.9); 3m: 3.6 (3.1; 4.2).	(SRP+plac) Day 0: 4.0 (3.6; 4.3); 3m: 3.1 (2.8; 3.3); (SRP+prob) Day 0: 3.9 (3.7; 4.2; 3m: 3.0 (2.9; 3.2).	(SRP+plac) Day 0: 23.5 (14.0; 36.5) 3m: 12.5 (5.5; 23.5); (SRP+prob) Day 0: 24.5 (17.5; 38.0); 3m: 9.0 (6.0; 13.5).	(SRP+plac) Day 0: 63.0 (44.0; 74.5) 3m: 24.5 (15.5; 30.0); (SRP+prob) Day 0: 63.0 (45.0; 77.5); 3m: 27.0 (18.5; 31.0).	NR	None	Smokers and non-smokers	3 months
Ranjith2021(Ranjith et al., 2022)	60 (SRP+plac: 27;	SRP+plac: 37.95 ± 6.94 SRP+prob: 39.48 ± 7.65	SRP+plac: 16/14 SRP+prob: 17/13	SRP + probiotic	Darolac, Aristo pharmaceutic als, India	SRP + placebo	(SRP+plac) Day 0: 2.9 ± 0.16; 90d: 2.72 ±	(SRP+plac) Day 0: 3.0 ± 0.16; 90d: 2.74 ±	(SRP+plac) Day 0: 1.57 ± 0.87; 90d: 1.06 ±	NR	NR	No adverse events were reported and compliance	All non-smokers	90 days

	SRP+prob: 28)				containing 1 g powder of 1.25 billion freeze-dried combination of a mixture of L. acidophilus, L. rhamnosus, B. longum and S. boulardii.		0.10; (SRP+prob) Day 0: 3.48 ± 0.2; 90d: 2.25 ± 0.11.	0.15; (SRP+prob) Day 0: 3.4 ± 0.28; 90d: 2.65 ± 0.11.	0.06; (SRP+prob) Day 0: 1.7 ± 0.87; 90d: 1.09 ± 0.07. (Silness & Loe)			was satisfactory in both groups.		
Tekce2015(Tekce et al., 2015)	40 (SRP+plac: 20; SRP+prob: 20)	SRP+plac: 41.40 ± 8.86 SRP+prob: 43 ± 5.01	SRP+plac: 10/10 SRP+prob: 8/12	SRP + probiotic	L. reuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289 (Prodentis; BioGaia, Lund, Sweden)	SRP + placebo	NR	(SRP+plac) Day 0: 5.36 ± 0.72; 360d: 4.80 ± 0.70; (SRP+prob) Day 0: 5.23 ± 0.68; 360d: 3.49 ± 0.87.	(SRP+plac) Day 0: 2.30 ± 0.41; 360d: 1.39 ± 0.28; (SRP+prob) Day 0: 2.29 ± 0.28; 360d: 0.73 ± 0.24.	(SRP+plac) Day 0: 88.65 ± 4.11; 360d: 19.05 ± 4.84; (SRP+prob) Day 0: 88.90 ± 7.66; 360d: 11.05 ± 3.99.	(SRP+plac) Day 0: 41.5 (14–81); 360d: 40.5 (12–78); (SRP+prob) Day 0: 35.5 (26–43); 360d: 35 (25–42).	None	All non-smokers	360 dyas
Teughels2013(Teughels et al., 2013)	30 (SRP+plac: 15; SRP+prob: 15)	SRP+plac: 45.7 ± 6.2 SRP+prob: 46.6 ± 4.5	SRP+plac: 8/7 SRP+prob: 7/8	SRP + probiotic	L. reuteri (1x10^8 CFU) for DSM17938 and ATCC PTA5289 (Prodentis; BioGaia, Lund, Sweden)	SRP + placebo	(SRP+plac) Day 0: 4.97 ± 0.61; 12w: 4.21 ± 0.67; (SRP+prob) Day 0: 4.97 ± 1.01; 12w: 3.97 ± 0.97.	(SRP+plac) Day 0: 4.32 ± 0.50; 12w: 2.93 ± 0.40; (SRP+prob) Day 0: 4.15 ± 0.71; 12w: 2.73 ± 0.57.	(SRP+plac) Day 0: 99.66 ± 0.99; 12w: 24.88 ± 33.26; (SRP+prob) Day 0: 95 ± 10.27; 12w: 16.34 ± 19.19.	(SRP+plac) Day 0: 67.53% ± 11.37; 12w: 16.58% ± 10.54; (SRP+prob) Day 0: 70.70% ± 14.53; 12w: 15.51% ± 11.92.	(Aa) (SRP+plac) Day 0: 3.57 ± 1.97; 12w: 1.86 ± 2.12; (SRP+prob) Day 0: 3.84 ± 2.70; 12w: 1.98 ± 2.38; (Fn) (SRP+plac) Day 0: 7.40 ± 1.16; 12w: 5.87 ± 1.08; (SRP+prob) Day 0: 7.70 ± 1.11; 12w: 5.45 ± 2.05; (Pg) (SRP+plac) Day 0: 6.37± 1.7; 12w: 5.43 ± 1.73; (SRP+prob) Day 0: 6.67 ± 1.5; 12w: 4.87 ± 1.21; (Pi) (SRP+plac) Day 0: 6.17 ± 2.73; 12w: 4.81 ± 2.44; (SRP+prob) Day 0: 6.345 ± 2.14;	None	All non-smokers	12 weeks

											12w: 4.22 ± 2.07; (Tf) (SRP+plac) Day 0:6.56 ± 0.89; 12w: 5.24 ± 1.17; (SRP+prob) Day 0: 5.95 ± 1.82 12w: 8.49 ± 0.82; (Total load) (SRP+plac) Day 0: 10.11 ± 0.86; 12w: 8.99 ± 0.99; (SRP+prob) Day 0: 9.9 ± 0.52; 12w: 8.49 ± 0.82;			
Theodoro2019(Theodoro et al., 2019)	34 (SRP+plac: 14; SRP+prob: 14)	SRP+plac: 45.07 ± 6.31 SRP+prob: 47.25 ± 7.10	SRP+plac: 10/4 SRP+prob: 5/9	SRP + probiotic	L. reuteri DSM 17938, with 1×10^8 cfu (BioGaia™, 450 mg, Laboratórios Ferrring Ltda, São Paulo, SP, Brazil)	SRP + placebo	(SRP+plac) Day 0: 4.23 ± 0.56; 90d: 4.17 ± 0.42; (SRP+prob) Day 0: 4.39 ± 0.86; 90d: 3.96 ± 0.89.	(SRP+plac) Day 0: 3.81 ± 0.44; 90d: 3.66 ± 0.36; (SRP+prob) Day 0: 3.23 ± 0.44; 90d:2.98 ± 0.54.	NR	(SRP+plac) Day 0: 74.10 ± 22.08; 90d: 65.13 ± 20.65; (SRP+prob) Day 0: 45.74 ± 20.65; 90d:23.51 ± 14.15.	NR	None	All smokers	90 days
Tsubura2009 (Tsubura et al., 2009)	54 (SRP+cont:27; SRP+prob: 27)	53.4 (44-62)	21/33	SRP + probiotic (Extraction 300E (containing Bacillus subtilis: E-300)	Bacillus subtilis	SRP + control (NG - Neosteline Green (NG), containing benzethonium chloride 0.2 g/100 ml)	NR	(SRP+cont) Day 0: 4.7±0.72; 30d: 3.5±0.51; (SRP+prob) Day 0: 4.8±0.75; 30d: 4.2±0.60.	NR	(SRP+cont) Day 0: 1.6±0.50; 30d: 0.8±0.62; (SRP+prob) Day 0: 1.6±0.51; 30d: 0.5±0.51.	NR	NR	All non-smokers	30 days
Vicario2013(Vicario et al., 2013)	19 (SRP+plac: 9; SRP+prob: 10)	SRP+plac: 53.8 (44.3–63.1) SRP+prob: 58.0 (51.4–64.7)	SRP+plac: 4/5 SRP+prob: 8/2	SRP + probiotic	Lactobacillus reuteri (ATCC 55730 and ATCCPTA 5289) (2X10^8 living cells of L.reuteri Prodentis)	SRP + placebo	NR	% sites with pocket probing depths 4–5 mm. (SRP+plac) Day 0: 38.1 ± 16.37; 30d: 45.3 ± 10.38; (SRP+prob) Day 0: 50.1 ± 17.92; 30d: 40.4 ± 17.76. % sites with pocket probing depths ≥ 6 mm.	(SRP+plac) Day 0: 62.9 ± 24.21; 30d: 67.4 ± 16.57; (SRP+prob) Day 0: 69.5 ± 16.95; 30d: 52.5 ± 14.25.	(SRP+plac) Day 0: 40.0 ± 23.36; 30d: 47.0 ± 17.43; (SRP+prob) Day 0: 55.3 ± 16.39; 30d: 29.3 ± 15.04.	NR	None	All non-smokers	30 days

								(SRP+plac) Day 0: 13.7 ± 16.42; 30d: 13.4 ± 13.31; (SRP+prob) Day 0: 12.3 ± 16.13; 30d: 7.5 ± 11.40.						

%: percentage; *Aa: Aggregatibacter actinomycetemcomitans;* atb: antibiotic; BOP: bleeding on probing; CAL: clinical attachment level; CFU: colony forming units; CHX: chlorhexidine; d: day; F: female; *Fn: Fusobacterium nucleatum;* GCF: gingival crevicular fluid; GI: gingival index; m: months; M: male; mm: millimeter; NR: not reported; *Pg: Porphyromonas gingivalis; Pi: Prevotella intermedia;* PI: plaque index; plac: placebo; PPD: periodontal probing depth; prob: probiotic; SD: standard deviation; SRP: scaling and root planning; tetra: tetracycline fibers; *Tn: Tannerella forsythia; Td: Treponema denticola;* w: week.

Appendix 9: Risk of bias within individual studies

9.1. Risk of bias in individual studies

Abuazab 2021(Abuazab et al., 2021) ***(Mansoura Journal of Dentistry)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1 shows *n*, and analyzed data (coincident with *n* in the recruitment phase)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Alshareef 2020(Alshareef et al., 2020) ***(European Journal of Dentistry)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Unclear risk of bias	Publication bias?

Butera 2020(Butera et al., 2020) ***(Microorganisms)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	By means of a block randomization table, the data analyst provided a randomization sequence, considering a permuted block of 20 participants.
Allocation concealment (selection bias)	Low risk of bias	The operator who enrolled participants also assigned them to the respective domiciliary treatment using sequentially numbered and sealed envelopes with the allocation cards previously prepared; blinding him was not technically possible.
Blinding of participants and personnel (performance bias)	Low risk of bias	Patients were not blinded but personnel was blinded.
Blinding of outcome assessment (detection bias)	Low risk of bias	Professional oral procedures and outcomes assessment were executed by another operator. Microbiological tests were conducted by a microbiologist in an external laboratory. Operator/data assessor, microbiologist and data analyst were

		always blinded during the study since none of them knew the treatment administered to each participant.
Incomplete outcome data (attrition bias)	Low risk of bias	Data presented and analyzed are coincident with n in the recruitment phase.
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Chandra 2016(Chandra et al., 2016) ***(Journal of the International Academy of Periodontology)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Randomization included computerized generation of the allocation sequence in random permuted blocks. Allocation was performed by assigning the block of sites to study and control sites according to the specified sequence.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Low risk of bias	All the therapies were performed by a designated operator (TS) for the sake of uniformity, whereas the relevant readings were recorded by another operator (YSHSC) who was blinded to the nature of the site. The blind was not broken until this clinical trial was finished.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)- reason for loss of follow up also presented
Selective reporting (reporting bias)	Low risk of bias	Data coincident with was defined in the protocol (NCT02645669)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Costacurta 2018(Costacurta et al., 2018) ***(ORAL & Implantology)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Allocation concealment (selection bias)	Low risk of bias	A person not involved in the clinical trial carried out the randomization
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1 and 2
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Unclear risk of bias	Publication bias?

Dhaliwal 2017(Dhaliwal et al., 2017) ***(Journal of the International Academy of Periodontology)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Patients were randomly assigned (coin-toss method) to 2 groups of 15 patients each.

Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Of 30 patients enrolled in the study, 27 patients (20 males and 7 females) completed the study. Two patients from the test group and one patient from the control group failed to attend the subsequent recall examinations and their data were excluded from the study.
Selective reporting (reporting bias)	Unclear risk of bias	The study protocol is not available. All the outcomes are not analyzed and discussed in the respective section for that.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

El-bagoory 2021(El-Bagoory et al., 2021) ***(J Indian Soc Periodontol)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk of bias	Investigator GH K screened the patients and randomly assigned them to test and control groups and performed the treatment procedures for all participants.
Allocation concealment (selection bias)	Unclear risk of bias	"Investigator M.Sh recorded the clinical
Blinding of participants and personnel (performance bias)	Low risk of bias	Investigator M. Sh recorded the clinical parameters, and she was masked to the randomization for the extent of the study.
Blinding of outcome assessment (detection bias)	Low risk of bias	Investigator M. Sh recorded the clinical parameters, and she was masked to the randomization for the extent of the study.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Ghasemi 2020 (Ghasemi et al., 2020) ***(J Adv Periodontol Implant Dent)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Computer-generated random numbers were used to assign the patients to the test and control groups (n=18)
Allocation concealment (selection bias)	Low risk of bias	To ensure allocation, the patients codes were preserved by a researcher based on the serial number
Blinding of participants and personnel (performance bias)	Low risk of bias	Placebo and probiotic capsules were labeled in the same containers
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1. First sentence of results
Selective reporting (reporting bias)	Low risk of bias	Data coincident with was defined in the protocol (IRCT20180630040290N2)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Grover (Grover) ***(Thesis File)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Unclea risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'. - For this study, qualified patients were randomly categorized into 2 groups as follows:
Allocation concealment (selection bias)	Unclea risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclea risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclea risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Out of 30 patients enrolled in the study 27 patients (20 males and 7 females) completed the study. Two patients from group B and one patient from group A failed to attend the subsequent recall examination whose data was excluded from the study.
Selective reporting (reporting bias)	Low risk of bias	The findings of all parameters were evaluated and put to statistical analysis.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Ikram 2019(Ikram et al., 2019) ***(Annals Abbasi Shaheed Hospital & Karachi Medical & Dental College)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	Participants were asked by the appointed research assistant to pick one envelope containing the name of the therapy which was provided to them after the baseline periodontal examination and recording the clinical periodontal parameters.
Allocation concealment (selection bias)	Low risk of bias	To randomization sealed opaque envelopes were used.
Blinding of participants and personnel (performance bias)	Low risk of bias	Participants were asked by the appointed research assistant to pick one envelope containing the name of the therapy which was provided to them after the baseline periodontal examination and recording the clinical periodontal parameters. Throughout the study period full blinding was maintained with the help of research assistant who held all the details related to the study groups and treatment strategy till the completion of the trial and complete analysis of the research data. Both probiotic and placebo powder were similar in color and texture.
Blinding of outcome assessment (detection bias)	Low risk of bias	Throughout the study period full blinding was maintained with the help of research assistant who held all the details related to the study groups and treatment strategy till the completion of the trial and complete analysis of the research data.
Incomplete outcome data (attrition bias)	Low risk of bias	Data presented and analyzed are coincident with n in the recruitment phase.
Selective reporting (reporting bias)	Unclear risk of bias	Data from the study protocol not coincident with the study. Data from Change in bacterial load of Porphyromonas gingivalis was not analyzed or presented (primary outcome) (NCT03499184).

Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Ince 2015(Ince et al., 2015) ***(J Periodontoly)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	Patients who were eligible for the study were randomly assigned into 2 treatment groups according to a computer-based randomization program.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Low risk of bias	Identical bottles were presented to the researcher who performed the SRP procedure (GIN) by the study leader (SY). All researchers involved in this study were blind to the treatment groups.
Blinding of outcome assessment (detection bias)	Low risk of bias	See justification above
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Invernici 2018(Invernici et al., 2018) ***(J Clin Periodontol)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	According to a random numeric table generated by computer software, the study coordinator (M.R.M.) allocated each patient to one of the following groups: Control (SRP+Placebo; 21 patients) or Test (SRP+Probiotic therapy, 20 patients).
Allocation concealment (selection bias)	Low risk of bias	Before the study began, the selected individuals were identified by a numeric code that designated the experimental group to which they belonged. The study coordinator (M.R.M.) revealed the meaning of each code only after conducting the statistical analysis of the experimental data.
Blinding of participants and personnel (performance bias)	Low risk of bias	The coded bottles were given to the examiner (M.S.M.S.), who distributed them to the patients and did not have any access to information about the content of the lozenges. In addition, the patients were blinded to the content of the lozenges and treatment assignment during the study.
Blinding of outcome assessment (detection bias)	Low risk of bias	The study coordinator (M.R.M.) revealed the meaning of each code only after conducting the statistical analysis of the experimental data.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	There is no information about data for changes in the levels of immunoglobulin A in saliva and Changes in the expression of beta-defensin-3, toll like receptor-4, cluster of differentiation (CD)-4 and CD-8, pre-defined in protocol (NCT03408548) -

		secondary outcome (reported on the RCT of 2020)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Invernici 2020(Invernici et al., 2020) ***(PLOS ONE)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	According to a random numeric table generated by a computer software, the study coordinator (M.R.M.) allocated each patient to one of the following groups: Control (Scaling and root planing–SRP + placebo; 15 patients) or Test (SRP + probiotic therapy, 15 patients).
Allocation concealment (selection bias)	Low risk of bias	Before the study began, the selected individuals were identified by a numeric code that designated the experimental group to which they belonged. The study coordinator (M.R.M.) broke the code only after conducting the statistical analysis of the experimental data.
Blinding of participants and personnel (performance bias)	Low risk of bias	The same pharmacy prepared identical probiotic and placebo lozenges (i.e., same appearance, taste, and color). Identical plastic bottles containing the probiotic/placebos were sent to the study coordinator (M.R.M.), who wrote the number code of each patient on each bottle, according to the therapy to which they were assigned. The coded bottles were given to the examiner (M.S.M.S.), who was blinded to the content of the lozenges and distributed them to the patients. In addition, the patients were also blinded to the content of the lozenges and treatment assignment during the study.
Blinding of outcome assessment (detection bias)	Low risk of bias	All patients received immunological and clinical monitoring at baseline, at 30 days, and at 90 days. The evaluations (pre- and post-intervention) were conducted by a single trained and calibrated examiner (M.S.M.S.), who was blinded to the experimental groups.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	There is no information about data for changes PPD, levels of IL and CL, pre-defined in protocol (NCT03408548) - secondary outcome (reported on the RCT of 2018)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Jebin 2021(Jebin et al., 2021) ***(Contemp Clin Dent.)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	High risk of bias	(…) following which patients were allocated randomly into both treatment groups, based on their sequence of reporting to the department by the study coordinator.

Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'. Besides classification of double-blind. Not sure about patients; The primary investigator performed SRP in all the patients using ultrasonic scaler (DTE D1 Ultrasonic scaler, Guilin woodpecker) and in deeper areas using hand instruments (Gracey curettes, Hu Friedy Mfg.) in a single session, following which patients were allocated randomly into both treatment groups, based on their sequence of reporting to the department by the study coordinator.
Blinding of outcome assessment (detection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Incomplete outcome data (attrition bias)	Low risk of bias	Thirty, systemically healthy, mild-to-moderate CP patients (with age between 20 and 60 years, including 24 males and 6 females) were included in the study of which three patients were dropped out of the study due to personal reasons. Hence, the final statistical analysis was performed using 14 test group patients and 13 control group patients. The baseline clinical parameters and the Pg levels for the patients were comparable for both treatment groups ($P > 0.05$).
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Kanagaraj 2019(Kanagaraj et al., 2019) ***(International Journal of Oral Health Dentistry)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	(…) 60 participants assigned to test and control group using lottery method.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome (only said single blind, but it isn't clear in the text)
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Unclear risk of bias	Insufficient reporting of attrition/exclusions to permit judgement of 'Low risk' or 'High risk' (no reasons for missing data provided)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Kumar 2021(Kumar et al., 2021) ***(Journal of Periodontal & Implant Science)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Random assignment was performed by the study coordinator (RS) in ascending order at the enrollment visit. A biostatistician provided codes through a computer-generated randomization table for 1 of the 3 treatment protocols. A balanced random-

		permuted block approach (9-unit block size) was used to prepare the randomization table.
Allocation concealment (selection bias)	Low risk of bias	The study coordinator (RS) allocated randomization codes to patients and was kept completely masked from any other details of the study. At treatment visits, an investigator (VJ) unaware of the code that had been assigned to a particular subject was provided with the sequential probiotic/placebo-containing tube by RS to be locally applied in subjects.
Blinding of participants and personnel (performance bias)	Low risk of bias	Three identical, sterile, dry Eppendorf tubes numbered 1, 2, and 3 (representing the treatment sequence) were prepared to contain color- and texture-matched placebo or probiotic powder in equal volumes. A biochemical technician who was blinded to the study protocol prepared these tubes. The tubes were placed in coded, sealed, non-labeled envelopes following randomization charts and codes. The non-labeled coded envelopes were dispensed to the study coordinator (RS). Disclosure of the assigned groups was done after completion of the statistical analysis.
Blinding of outcome assessment (detection bias)	Low risk of bias	See justification above
Incomplete outcome data (attrition bias)	Low risk of bias	The study flow chart is depicted in Figure 1. Forty-five of the 48 subjects were evaluated for clinical parameters and biochemical analysis. The dropouts did not affect the power of the study, as we recruited beyond the minimum sample size to counter study attrition. Demographic characteristics were analyzed after study completion, and the groups were found to be matched for non-modifiable characteristics at baseline (P>0.05) (Table 1).
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. All the outcomes are not analyzed and discussed in the respective section for that.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Laleman 2015(Laleman et al., 2015) ***(J Clin Periodontol)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Randomization of the patients was done by block randomization (version 2.7.3; StatsDirect).
Allocation concealment (selection bias)	Unclear risk of bias	Except for the study coordinator, all patients and study personnel were blinded to the study group allocation.
Blinding of participants and personnel (performance bias)	Low risk of bias	See justification above and - The probiotic and placebo tablets were identical in shape, texture, taste, and composition.
Blinding of outcome assessment (detection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1

Selective reporting (reporting bias)	Low risk of bias	Data coincident with was defined in the protocol (NCT02403960)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Meenakshi 2020(Meenakshi & Varghese, 2018) ***(Drug Invention Today)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	Patients who were eligible for participation were randomly assigned by the flip of a coin into one of the two groups.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Selective reporting (reporting bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Other sources of bias (other bias)	Unclear risk of bias	Insufficient information to assess whether an important risk of bias exists

Minić 2020(Minic et al., 2022) ***(Int J Dent Hygiene)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1 and table 2
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Unclear risk of bias	Due to study methodology

Morales 2016(Morales et al., 2016) ***(Journal of Periodontology)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	Participants with chronic periodontitis were randomized by the study coordinator over the two treatment groups: control [C] (SRP + placebo) or test [T] (SRP + probiotic). Randomization was computer-generated. Eligible individuals were allocated randomly to the test and control groups according to gender, age, and smoking status after the basal examination, using a randomization table (Jorge Gamonal).
Allocation concealment (selection bias)	Low risk of bias	Randomization was computer-generated, with allocation concealment by opaque sequentially numbered sealed envelopes. Study coordinator was responsible for allocation concealment.
Blinding of participants and personnel (performance bias)	Low risk of bias	Except for the study coordinator (Jorge Gamonal), all study personnel and patients were blinded to the study group assignment. Only after study completion,

		the designation of the different groups was revealed.
Blinding of outcome assessment (detection bias)	Low risk of bias	Except for the study coordinator (Jorge Gamonal), all study personnel and patients were blinded to the study group assignment. Only after study completion, the designation of the different groups was revealed.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	There is no information about data for levels of Interleukin and levels of periodontal pathogens changes, pre-defined in protocol (NCT02283736) - secondary outcome
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Oliveira 2021(Oliveira et al., 2021) ***(J Periodontol)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Eligible individuals were randomly allocated into the SI+probiotic or SI+placebo group per a computer-generated list using sequentially numbered sealed envelopes by an independent researcher (L.C.P.E).
Allocation concealment (selection bias)	Low risk of bias	Eligible individuals were randomly allocated into the SI+probiotic or SI+placebo group per a computer-generated list using sequentially numbered sealed envelopes by an independent researcher (L.C.P.E).
Blinding of participants and personnel (performance bias)	Low risk of bias	Participants and professional (A.M.O.) were blind to group assignment. Identical probiotics * and placebo † capsules were prepacked in the same opaque vials, containing 30 capsules each.
Blinding of outcome assessment (detection bias)	Low risk of bias	The codes of the groups were revealed only after completion of all clinical and laboratory proceedings.
Incomplete outcome data (attrition bias)	Low risk of bias	2 months after allocation, 6 individuals on placebo and 5 in probiotic were excluded due to antibiotic use
Selective reporting (reporting bias)	Unclear risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed, but not mention on the discussion phase.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Oliveira 2022(de Oliveira et al., 2022) ***(J Periodontol.)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Eligible individuals were randomly allocated into the SI+probiotic or SI+placebo group per a computer-generated list using sequentially numbered sealed envelopes by an independent researcher (LCPE).
Allocation concealment (selection bias)	Low risk of bias	(…) using sequentially numbered sealed envelopes by an independent researcher (LCPE). The codes of the groups were

		revealed only after completion of all clinical and laboratory proceedings. Participants and professional (AMO) were blind to group assignment.
Blinding of participants and personnel (performance bias)	Low risk of bias	Identical probiotics and placebo capsules were prepacked in the same opaque vials, containing 30 capsules each. The codes of the groups were revealed only after completion of all clinical and laboratory proceedings.
Blinding of outcome assessment (detection bias)	Low risk of bias	Participants and professional (AMO) were blind to group assignment. AMO performed the statistical analysis
Incomplete outcome data (attrition bias)	Low risk of bias	After the initial contact and clinical screening, 48 periodontitis individuals were eligible, six were excluded during the therapeutic phase due to antibiotic use, and 42completed the study
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Ozener 2022(Ozener et al., 2023) ***(J Clin Oral Investig)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Thirty participants were randomly assigned in two treatment groups by a computer-assisted randomization program. Each patient was assigned a number (1–30) and a code.
Allocation concealment (selection bias)	Low risk of bias	The coordinator of the study (BEK) distributed the coded yogurt container to the patients at baseline. Prior to statistical analysis, the coordinator cracked the code to allocate the patients to the proper groups.
Blinding of participants and personnel (performance bias)	Low risk of bias	The study personnel and participants were unaware of the study group assignment, except for the study coordinator.
Blinding of outcome assessment (detection bias)	Low risk of bias	Prior to statistical analysis, the coordinator cracked the code to allocate the patients to the proper groups.
Incomplete outcome data (attrition bias)	Low risk of bias	Tabel 1
Selective reporting (reporting bias)	Low risk of bias	The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Paul 2019(Paul et al., 2019) ***(Journal of Health and Research)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	The random numbers were generated by computerized random number, in permuted blocks of 6. The randomization list and numbered packing of the intervention were prepared by a person not involved in the study.
Allocation concealment (selection bias)	Low risk of bias	All the randomization numbers were concealed in separate envelopes and

		marked by patient number on the outer envelope. The individually sealed envelope method was used to maintain blinding of the investigators and study participants.
Blinding of participants and personnel (performance bias)	Low risk of bias	The individually sealed envelope method was used to maintain blinding of the investigators and study participants.
Blinding of outcome assessment (detection bias)	Low risk of bias	See justification above
Incomplete outcome data (attrition bias)	Unclear risk of bias	Insufficient reporting of attrition/exclusions to permit judgement of 'Low risk' or 'High risk' (e.g. number randomized not stated, no reasons for missing data provided)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of all parameters were evaluated and statistically analyzed.
Other sources of bias (other bias)	Unclear risk of bias	Publication bias - they don't specify the number of sample size needed to have power on statistical analysis.

Pelekos 2020(Pelekos et al., 2020) ***(Journal of Clinical Periodontology)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk', but we presume that the methodology was equal to Pelekos G., 2019.
Allocation concealment (selection bias)	Low risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Low risk of bias	The study did not address this outcome (only said single blind, but it isn't clear in the text), although is classified as double blind
Blinding of outcome assessment (detection bias)	Low risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	High risk of bias	Recruitment involved 59 participants, and then data is analyzed only in 40 patients.
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. The findings of secondary outcome 'visible plaque' are not presented.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Penala 2016(Penala et al., 2016) ***(Journal of Research in Pharmacy Practice)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Randomization was done based on computer generated random numbers by a biostatistician to allocate patients to one of the treatment groups.
Allocation concealment (selection bias)	Low risk of bias	To ensure allocation concealment, the codes for the patients based on the serial number were maintained by one of the investigators. The same investigator dispensed the probiotic and placebo capsules to the investigator doing all the interventions.
Blinding of participants and personnel (performance bias)	Low risk of bias	Probiotic and placebo capsules were provided in identically labeled containers and were given code as A and B.

Blinding of outcome assessment (detection bias)	Low risk of bias	The same investigator dispensed the probiotic and placebo capsules to the investigator doing all the interventions.
Incomplete outcome data (attrition bias)	Low risk of bias	Three patients were lost to follow-up, one in the test group and the rest in the control group as one of the patients did not turn up for further appointments due to time constraints, and others migrated to some other place as mentioned in the study flow chart.
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed.
Other sources of bias (other bias)	Unclear risk of bias	Publication bias??

Pudgar 2020(Pudgar et al., 2021) ***(Clinical Oral Investigations)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Whether a subject received test medication or placebo was determined using a computer generated randomization table provided by the company and disclosed to the examiner and operator upon the last follow-up visit of the last patient. Simple randomization procedure based on a single sequence of random assignments was utilized.
Allocation concealment (selection bias)	Low risk of bias	Allocation concealment was insured by CMS Dental, Copenhagen, Denmark. The company marked the boxes containing probiotic/placebo vials and lozenges with sequential numbers and insured that all were identical in appearance. The allocation of subjects into treatment groups was revealed to the therapist (P. P.) and evaluator (R. G.) by uncovering a randomization code after the last patient had been re-evaluated.
Blinding of participants and personnel (performance bias)	Low risk of bias	The company marked the boxes containing probiotic/placebo vials and lozenges with sequential numbers and insured that all were identical in appearance.
Blinding of outcome assessment (detection bias)	Low risk of bias	See justification above
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 and table 1
Selective reporting (reporting bias)	Low risk of bias	Data coincident with was defined in the protocol (NCT04137419)
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Ranjith 2021(Ranjith et al., 2022) ***(Int J Dent Hygiene)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Selected subjects were randomly allotted into test group and control group (1:1 ratio) using block randomization method.
Allocation concealment (selection bias)	Low risk of bias	Allocations were prepared by the statistician, which were kept in sealed opaque envelopes, which was opened at the time of procedure by the clinical assistant who distributed the sachet.
Blinding of participants and personnel (performance bias)	Low risk of bias	Triple blind

Blinding of outcome assessment (detection bias)	Unclear risk of bias	Although they say it is a triple blind RCT, the allocation was prepared by the statistician.
Incomplete outcome data (attrition bias)	Low risk of bias	2 patients from test group and 1 patient from control group were excluded from the study due to the use of anti-inflammatory drugs during the study period. 2 patients in control group could not be contacted for follow up.
Selective reporting (reporting bias)	Low risk of bias	Data reported according pre-stablished protocol (CTRI/2019/10/021630)
Other sources of bias (other bias)	Low risk of bias	

Tekce 2015(Tekce et al., 2015) ***(J Clin Periodontol)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Patients who were eligible for study participation were randomly assigned to one of the two treatment groups according to a computer-based randomization program (www.random-izer.org/Copyright ©1997–2011 by Geoffrey C. Urbaniak and Scott Plous).
Allocation concealment (selection bias)	High risk of bias	Probably not done
Blinding of participants and personnel (performance bias)	Low risk of bias	The study leader (SY)presented identical bottles to the researcher, who performed the SRP procedure (GIN).
Blinding of outcome assessment (detection bias)	Low risk of bias	The study leader (SY)presented identical bottles to the researcher, who performed the SRP procedure (GIN).
Incomplete outcome data (attrition bias)	Low risk of bias	The remaining 40 systemically healthy patients with chronic periodontitis included 18 males and 22 females between 35 and 50 years of age. The baseline clinical and microbiological parameters for these patients were similar for both groups ($p > 0.05$) (Table 1). No adverse effects were observed throughout the study period. All subjects completed the 360-day study period and were compliant with the study requirements.
Selective reporting (reporting bias)	Unclear risk of bias	The study protocol is not available. Presented primary outcomes are all measured but not analyzed and discussed in the respective section for that.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Teughels 2013(Teughels et al., 2013) ***(J Clin Periodontol)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	Randomization of the 30 patients, fulfilling the inclusion/exclusion criteria and willing to participate in this study, over the two different treatment groups was done by block randomization (version 2.7.3; Stats-Direct).
Allocation concealment (selection bias)	Low risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk' - "Coded bottles were given by the study coordinator (MCH) to the

		examiner (OO) at the patient's first initial treatment, 3, 6 and 9 week visit."
Blinding of participants and personnel (performance bias)	Low risk of bias	Except for the study coordinator, all study personnel and patients were blinded to the study group assignment.
Blinding of outcome assessment (detection bias)	Low risk of bias	Prior to sending the data to the biostatistician, the code was partially broken by MCH to group the different patients over the two treatments. Only after the statistical analysis, the designation of the different groups was revealed.
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (coincident)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed.
Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Theodoro 2019(Theodoro et al., 2019) ***(Beneficial Microbes)***

Bias	**Author's Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk of bias	After inclusion in the present study, patients underwent the randomization process, in which patients were randomly divided into two groups using an online randomization system (www.sealedenvelope.com).
Allocation concealment (selection bias)	Unclear risk of bias	After randomization, envelopes were created regarding the treatment of each patient by a professional who did not perform the evaluation of the patients nor the treatments (LHT), which were opened only after treatment. They do not specify if the envelops are époque and correctly sealed.
Blinding of participants and personnel (performance bias)	Low risk of bias	All probiotic tablets were removed from their packaging and placed in vials identified with the same pattern as the placebo group. Although the vials containing probiotics and placebos were identical, they had different descriptions on the packaging label, for the professional to differentiate them. The SRP procedures were performed under anesthesia using the regional block technique by two specialists (MAAN, DMJM), different from the professional who performed the clinical examinations and who were unaware of the results of the randomization until the scaling was completed.
Blinding of outcome assessment (detection bias)	Low risk of bias	See justification above
Incomplete outcome data (attrition bias)	Low risk of bias	Figure 1 shows n, lost in follow-up, complete data, analyzed data (missing data were considered and the groups are balanced)
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed.

Other sources of bias (other bias)	Low risk of bias	The study appears to be free of other sources of bias.

Tsubura 2009(Tsubura et al., 2009) ***(Eur J Clin Microbiol Infect Dis)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Allocation concealment (selection bias)	Unclear risk of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'.
Blinding of participants and personnel (performance bias)	Unclear risk of bias	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk of bias	The study did not address this outcome
Incomplete outcome data (attrition bias)	Low risk of bias	Fifty-four participants were examined according to the protocol and all of them completed the study.
Selective reporting (reporting bias)	Unclear risk of bias	The study protocol is not available. All the outcomes are not analyzed and discussed in the respective section for that.
Other sources of bias (other bias)	Unclear risk of bias	Due to study methodology and publication bias?

Vicario 2013(Vicario et al., 2013) ***(Acta Odontologica Scandinavica,)***

Bias	Author's Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk of bias	Subjects were assigned in ascending order at the enrolment visit and were randomly assigned by a computer-generated table to receive one of the two treatments. A balanced random permuted block approach (5-unit block size) was used to prepare randomization tables in order to avoid unequal balance between the two treatments.
Allocation concealment (selection bias)	Low risk of bias	The randomization code was not open until all data had been collected and analyzed.
Blinding of participants and personnel (performance bias)	Low risk of bias	The randomization table was sent to the manufacturer (GUM, Sunstar) in Switzerland, which prepared the tablets containing Lactobacillus reuteri Prodenti and the placebo tablets with the same appearance color and shape.
Blinding of outcome assessment (detection bias)	Low risk of bias	The randomization code was not open until all data had been collected and analyzed.
Incomplete outcome data (attrition bias)	Low risk of bias	Table 1 and 20 patients participated in the study. One patient from the placebo group was withdrawn because she had to take antibiotics during the study period.
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available. Presented primary outcomes are all measured and analyzed.
Other sources of bias (other bias)	Unclear risk of bias*	Publication bias?? - they don't refer how to calculate the sample size

9.2. Overall appraisal of included studies

Author_year	"Low risk of bias" answer (%)	Final classification
Abuazab_2021	42.86	High
Alshareef_2020	14.29	High
Butera_2020	100	Low
Chandra_2016	71.43	Low
Costacurta_2018	42.86	High
Dhaliwal_2017	42.86	High
El-bagoory_2021	71.43	Low
Ghasemi_2020	85.71	Low
Grover [thesis file]	42.86	High
Ikram_2019	85.71	Low
Ince_2015	85.71	Low
Invernici_2018	100	Low
Invernici_2020	100	Low
Jebin_2021	42.86	High
Kanagaraj_2019	42.86	High
Kumar_2021	100	Low
Laleman_2015	71.43	Low
Meenakshi_2020	14.29	High
Minić_2020	28.57	High
Morales_2016	100	Low
Oliveira_2021	85.71	Low
Oliveira_2022	100	Low
Ozener_2023	100	Low
Paul_2019	71.43	Low
Pelekos_2020	85.71	Low
Penala_2016	85.71	Low
Pudgar_2021	100	Low
Ranjith_2021	85.71	Low
Tekce_2015	71.43	Low
Teughels_2013	100	Low
Theodoro_2019	85.71	Low
Tsubura_2009	14.29	High
Vicario_2013	85.71	Low

Appendix 10: SIDE analysis

PPD (short-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
LspoSfaeCbutBmes:Sbbif	0	0	0.9800	.	0.9800		.	.
LspoSfaeCbutBmes:SBlacLacidBbifLrham	0	0	0.3200	.	0.3200		.	.
LspoSfaeCbutBmes:SBlactDN	0	0	0.6900	.	0.6900		.	.
LspoSfaeCbutBmes:SBlactis	0	0	0.6000	.	0.6000		.	.
LspoSfaeCbutBmes:SChx	0	0	1.1600	.	1.1600		.	.
LspoSfaeCbutBmes:SfaeCbutBmesLspo	0	0	0.7900	.	0.7900		.	.
LspoSfaeCbutBmes:SLacidLcasBbifLrhamLsal	0	0	0.8090	.	0.8090		.	.
LspoSfaeCbutBmes:SLacidLrhaBlongSboul	0	0	0.3800	.	0.3800		.	.
LspoSfaeCbutBmes:Slbrevis	0	0	0.9660	.	0.9660		.	.
LspoSfaeCbutBmes:SLbreviseplant	0	0	0.8700	.	0.8700		.	.
LspoSfaeCbutBmes:SLcas	0	0	0.0700	.	0.0700		.	.
LspoSfaeCbutBmes:Slreut	0	0	-0.6100	.	-0.6100		.	.
LspoSfaeCbutBmes:SLreutD	0	0	0.7700	.	0.7700		.	.
LspoSfaeCbutBmes:SLreutDA	0	0	0.8400	.	0.8400		.	.
LspoSfaeCbutBmes:SLreutU	0	0	3.4100	.	3.4100		.	.
LspoSfaeCbutBmes:SLsppBspp	0	0	0.8100	.	0.8100		.	.
LspoSfaeCbutBmes:Splac	1	1.00	0.8700	0.8700	.		.	.
LspoSfaeCbutBmes:SRP	0	0	0.8900	.	0.8900		.	.
LspoSfaeCbutBmes:SRPLacidBinfEfae	0	0	0.1700	.	0.1700		.	.
Sbbif:SBlacLacidBbifLrham	0	0	-0.6600	.	-0.6600		.	.
Sbbif:SBlactDN	0	0	-0.2900	.	-0.2900		.	.
Sbbif:SBlactis	0	0	-0.3800	.	-0.3800		.	.
Sbbif:SChx	1	1.00	0.1800	0.1800	.		.	.
Sbbif:SfaeCbutBmesLspo	0	0	-0.1900	.	-0.1900		.	.
Sbbif:SLacidLcasBbifLrhamLsal	0	0	-0.1710	.	-0.1710		.	.
Sbbif:SLacidLrhaBlongSboul	0	0	-0.6000	.	-0.6000		.	.
Sbbif:Slbrevis	0	0	-0.0140	.	-0.0140		.	.
Sbbif:SLbreviseplant	0	0	-0.1100	.	-0.1100		.	.
Sbbif:SLcas	0	0	-0.9100	.	-0.9100		.	.
Sbbif:Slreut	0	0	-1.5900	.	-1.5900		.	.
Sbbif:SLreutD	0	0	-0.2100	.	-0.2100		.	.
Sbbif:SLreutDA	0	0	-0.1400	.	-0.1400		.	.
Sbbif:SLreutU	0	0	2.4300	.	2.4300		.	.
Sbbif:SLsppBspp	0	0	-0.1700	.	-0.1700		.	.
Sbbif:Splac	0	0	-0.1100	.	-0.1100		.	.
Sbbif:SRP	1	1.00	-0.0900	-0.0900	.		.	.
Sbbif:SRPLacidBinfEfae	0	0	-0.8100	.	-0.8100		.	.
SBlacLacidBbifLrham:SBlactDN	0	0	0.3700	.	0.3700		.	.
SBlacLacidBbifLrham:SBlactis	0	0	0.2800	.	0.2800		.	.
SBlacLacidBbifLrham:SChx	0	0	0.8400	.	0.8400		.	.
SBlacLacidBbifLrham:SfaeCbutBmesLspo	0	0	0.4700	.	0.4700		.	.
SBlacLacidBbifLrham:SLacidLcasBbifLrhamLsal	0	0	0.4890	.	0.4890		.	.
SBlacLacidBbifLrham:SLacidLrhaBlongSboul	0	0	0.0600	.	0.0600		.	.
SBlacLacidBbifLrham:Slbrevis	0	0	0.6460	.	0.6460		.	.
SBlacLacidBbifLrham:SLbreviseplant	0	0	0.5500	.	0.5500		.	.
SBlacLacidBbifLrham:SLcas	0	0	-0.2500	.	-0.2500		.	.
SBlacLacidBbifLrham:Slreut	0	0	-0.9300	.	-0.9300		.	.
SBlacLacidBbifLrham:SLreutD	0	0	0.4500	.	0.4500		.	.
SBlacLacidBbifLrham:SLreutDA	0	0	0.5200	.	0.5200		.	.
SBlacLacidBbifLrham:SLreutU	0	0	3.0900	.	3.0900		.	.
SBlacLacidBbifLrham:SLsppBspp	0	0	0.4900	.	0.4900		.	.
SBlacLacidBbifLrham:Splac	1	1.00	0.5500	0.5500	.		.	.
SBlacLacidBbifLrham:SRP	0	0	0.5700	.	0.5700		.	.
SBlacLacidBbifLrham:SRPLacidBinfEfae	0	0	-0.1500	.	-0.1500		.	.
SBlactDN:SBlactis	0	0	-0.0900	.	-0.0900		.	.
SBlactDN:SChx	0	0	0.4700	.	0.4700		.	.
SBlactDN:SfaeCbutBmesLspo	0	0	0.1000	.	0.1000		.	.
SBlactDN:SLacidLcasBbifLrhamLsal	0	0	0.1190	.	0.1190		.	.
SBlactDN:SLacidLrhaBlongSboul	0	0	-0.3100	.	-0.3100		.	.
SBlactDN:Slbrevis	0	0	0.2760	.	0.2760		.	.
SBlactDN:SLbreviseplant	0	0	0.1800	.	0.1800		.	.
SBlactDN:SLcas	0	0	-0.6200	.	-0.6200		.	.
SBlactDN:Slreut	0	0	-1.3000	.	-1.3000		.	.
SBlactDN:SLreutD	0	0	0.0800	.	0.0800		.	.
SBlactDN:SLreutDA	0	0	0.1500	.	0.1500		.	.
SBlactDN:SLreutU	0	0	2.7200	.	2.7200		.	.
SBlactDN:SLsppBspp	0	0	0.1200	.	0.1200		.	.
SBlactDN:Splac	1	1.00	0.1800	0.1800	.		.	.
SBlactDN:SRP	0	0	0.2000	.	0.2000		.	.
SBlactDN:SRPLacidBinfEfae	0	0	-0.5200	.	-0.5200		.	.
SBlactis:SChx	0	0	0.5600	.	0.5600		.	.
SBlactis:SfaeCbutBmesLspo	0	0	0.1900	.	0.1900		.	.
SBlactis:SLacidLcasBbifLrhamLsal	0	0	0.2090	.	0.2090		.	.
SBlactis:SLacidLrhaBlongSboul	0	0	-0.2200	.	-0.2200		.	.
SBlactis:Slbrevis	0	0	0.3660	.	0.3660		.	.
SBlactis:SLbreviseplant	0	0	0.2700	.	0.2700		.	.
SBlactis:SLcas	0	0	-0.5300	.	-0.5300		.	.
SBlactis:Slreut	0	0	-1.2100	.	-1.2100		.	.
SBlactis:SLreutD	0	0	0.1700	.	0.1700		.	.
SBlactis:SLreutDA	0	0	0.2400	.	0.2400		.	.
SBlactis:SLreutU	0	0	2.8100	.	2.8100		.	.
SBlactis:SLsppBspp	0	0	0.2100	.	0.2100		.	.
SBlactis:Splac	1	1.00	0.2700	0.2700	.		.	.
SBlactis:SRP	0	0	0.2900	.	0.2900		.	.
SBlactis:SRPLacidBinfEfae	0	0	-0.4300	.	-0.4300		.	.
SChx:SfaeCbutBmesLspo	0	0	-0.3700	.	-0.3700		.	.
SChx:SLacidLcasBbifLrhamLsal	0	0	-0.3510	.	-0.3510		.	.
SChx:SLacidLrhaBlongSboul	0	0	-0.7800	.	-0.7800		.	.

SChx:Slbrevis	0	0	-0.1940		-0.1940			
SChx:SLbreviseplant	0	0	-0.2900		-0.2900			
SChx:SLcas	0	0	-1.0900		-1.0900			
SChx:Slreut	0	0	-1.7700		-1.7700			
SChx:SLreutD	0	0	-0.3900		-0.3900			
SChx:SLreutDA	0	0	-0.3200		-0.3200			
SChx:SLreutU	0	0	2.2500		2.2500			
SChx:SLsppBspp	0	0	-0.3500		-0.3500			
SChx:Splac	0	0	-0.2900		-0.2900			
SChx:SRP	1	1.00	-0.2700	-0.2700				
SChx:SRPLacidBinfEfae	0	0	-0.9900		-0.9900			
SfaeCbutBmesLspo:SLacidLcasBbifLrhamLsal	0	0	0.0190		0.0190			
SfaeCbutBmesLspo:SLacidLrhaBlongSboul	0	0	-0.4100		-0.4100			
SfaeCbutBmesLspo:Slbrevis	0	0	0.1760		0.1760			
SfaeCbutBmesLspo:SLbreviseplant	0	0	0.0800		0.0800			
SfaeCbutBmesLspo:SLcas	0	0	-0.7200		-0.7200			
SfaeCbutBmesLspo:Slreut	0	0	-1.4000		-1.4000			
SfaeCbutBmesLspo:SLreutD	0	0	-0.0200		-0.0200			
SfaeCbutBmesLspo:SLreutDA	0	0	0.0500		0.0500			
SfaeCbutBmesLspo:SLreutU	0	0	2.6200		2.6200			
SfaeCbutBmesLspo:SLsppBspp	0	0	0.0200		0.0200			
SfaeCbutBmesLspo:Splac	0	0	0.0800		0.0800			
SfaeCbutBmesLspo:SRP	2	1.00	0.1000	0.1000				
SfaeCbutBmesLspo:SRPLacidBinfEfae	0	0	-0.6200		-0.6200			
SLacidLcasBbifLrhamLsal:SLacidLrhaBlongSboul	0	0	-0.4290		-0.4290			
SLacidLcasBbifLrhamLsal:Slbrevis	0	0	0.1570		0.1570			
SLacidLcasBbifLrhamLsal:SLbreviseplant	0	0	0.0610		0.0610			
SLacidLcasBbifLrhamLsal:SLcas	0	0	-0.7390		-0.7390			
SLacidLcasBbifLrhamLsal:Slreut	0	0	-1.4190		-1.4190			
SLacidLcasBbifLrhamLsal:SLreutD	0	0	-0.0390		-0.0390			
SLacidLcasBbifLrhamLsal:SLreutDA	0	0	0.0310		0.0310			
SLacidLcasBbifLrhamLsal:SLreutU	0	0	2.6010		2.6010			
SLacidLcasBbifLrhamLsal:SLsppBspp	0	0	0.0010		0.0010			
SLacidLcasBbifLrhamLsal:Splac	0	0	0.0610		0.0610			
SLacidLcasBbifLrhamLsal:SRP	1	1.00	0.0810	0.0810				
SLacidLcasBbifLrhamLsal:SRPLacidBinfEfae	0	0	-0.6390		-0.6390			
SLacidLrhaBlongSboul:Slbrevis	0	0	0.5860		0.5860			
SLacidLrhaBlongSboul:SLbreviseplant	0	0	0.4900		0.4900			
SLacidLrhaBlongSboul:SLcas	0	0	-0.3100		-0.3100			
SLacidLrhaBlongSboul:Slreut	0	0	-0.9900		-0.9900			
SLacidLrhaBlongSboul:SLreutD	0	0	0.3900		0.3900			
SLacidLrhaBlongSboul:SLreutDA	0	0	0.4600		0.4600			
SLacidLrhaBlongSboul:SLreutU	0	0	3.0300		3.0300			
SLacidLrhaBlongSboul:SLsppBspp	0	0	0.4300		0.4300			
SLacidLrhaBlongSboul:Splac	1	1.00	0.4900	0.4900				
SLacidLrhaBlongSboul:SRP	0	0	0.5100		0.5100			
SLacidLrhaBlongSboul:SRPLacidBinfEfae	0	0	-0.2100		-0.2100			
Slbrevis:SLbreviseplant	0	0	-0.0960		-0.0960			
Slbrevis:SLcas	0	0	-0.8960		-0.8960			
Slbrevis:Slreut	0	0	-1.5760		-1.5760			
Slbrevis:SLreutD	0	0	-0.1960		-0.1960			
Slbrevis:SLreutDA	0	0	-0.1260		-0.1260			
Slbrevis:SLreutU	0	0	2.4440		2.4440			
Slbrevis:SLsppBspp	0	0	-0.1560		-0.1560			
Slbrevis:Splac	1	1.00	-0.0960	-0.0960				
Slbrevis:SRP	0	0	-0.0760		-0.0760			
Slbrevis:SRPLacidBinfEfae	0	0	-0.7960		-0.7960			
SLbreviseplant:SLcas	0	0	-0.8000		-0.8000			
SLbreviseplant:Slreut	0	0	-1.4800		-1.4800			
SLbreviseplant:SLreutD	0	0	-0.1000		-0.1000			
SLbreviseplant:SLreutDA	0	0	-0.0300		-0.0300			
SLbreviseplant:SLreutU	0	0	2.5400		2.5400			
SLbreviseplant:SLsppBspp	0	0	-0.0600		-0.0600			
SLbreviseplant:Splac	1	1.00	-0.0000	0.0000				
SLbreviseplant:SRP	0	0	0.0200		0.0200			
SLbreviseplant:SRPLacidBinfEfae	0	0	-0.7000		-0.7000			
SLcas:Slreut	0	0	-0.6800		-0.6800			
SLcas:SLreutD	0	0	0.7000		0.7000			
SLcas:SLreutDA	0	0	0.7700		0.7700			
SLcas:SLreutU	0	0	3.3400		3.3400			
SLcas:SLsppBspp	0	0	0.7400		0.7400			
SLcas:Splac	0	0	0.8000		0.8000			
SLcas:SRP	1	1.00	0.8200	0.8200				
SLcas:SRPLacidBinfEfae	0	0	0.1000		0.1000			
Slreut:SLreutD	0	0	1.3800		1.3800			
Slreut:SLreutDA	0	0	1.4500		1.4500			
Slreut:SLreutU	0	0	4.0200		4.0200			
Slreut:SLsppBspp	0	0	1.4200		1.4200			
Slreut:Splac	1	1.00	1.4800	1.4800				
Slreut:SRP	0	0	1.5000		1.5000			
Slreut:SRPLacidBinfEfae	0	0	0.7800		0.7800			
SLreutD:SLreutDA	0	0	0.0700		0.0700			
SLreutD:SLreutU	0	0	2.6400		2.6400			
SLreutD:SLsppBspp	0	0	0.0400		0.0400			
SLreutD:Splac	1	1.00	0.1000	0.1000				
SLreutD:SRP	0	0	0.1200		0.1200			
SLreutD:SRPLacidBinfEfae	0	0	-0.6000		-0.6000			
SLreutDA:SLreutU	0	0	2.5700		2.5700			
SLreutDA:SLsppBspp	0	0	-0.0300		-0.0300			
SLreutDA:Splac	1	1.00	0.0300	0.0300				
SLreutDA:SRP	1	1.00	0.0500	0.0500				
SLreutDA:SRPLacidBinfEfae	0	0	-0.6700		-0.6700			
SLreutU:SLsppBspp	0	0	-2.6000		-2.6000			
SLreutU:Splac	0	0	-2.5400		-2.5400			
SLreutU:SRP	1	1.00	-2.5200	-2.5200				
SLreutU:SRPLacidBinfEfae	0	0	-3.2400		-3.2400			
SLsppBspp:Splac	2	1.00	0.0600	0.0600				
SLsppBspp:SRP	0	0	0.0800		0.0800			
SLsppBspp:SRPLacidBinfEfae	0	0	-0.6400		-0.6400			
SRP:Splac	0	0	-0.0200		-0.0200			
SRPLacidBinfEfae:Splac	0	0	0.7000		0.7000			
SRP:SRPLacidBinfEfae	1	1.00	-0.7200	-0.7200				

Legend:
 comparison - Treatment comparison
 k   - Number of studies providing direct evidence
 prop   - Direct evidence proportion
 nma   - Estimated treatment effect (MD) in network meta-analysis
 direct   - Estimated treatment effect (MD) derived from direct evidence
 indir.   - Estimated treatment effect (MD) derived from indirect evidence
 Diff   - Difference between direct and indirect treatment estimates
 z   - z-value of test for disagreement (direct versus indirect)
 p-value   - p-value of test for disagreement (direct versus indirect)

PPD (long-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

```
Random effects model:

                comparison k prop     nma  direct  indir. Diff z p-value
      SLreutDA:Slreutincrem 0    0  0.7159       .  0.7159    . .       .
      SLreutDA:SLreutsingle 0    0  0.5759       .  0.5759    . .       .
            SLreutDA:SLrham 0    0  0.6959       .  0.6959    . .       .
             SLreutDA:Splac 3 1.00  0.7959  0.7959       .    . .       .
     SLreutDA:SSoraluberrat 0    0  0.8959       .  0.8959    . .       .
  Slreutincrem:SLreutsingle 1 1.00 -0.1400 -0.1400       .    . .       .
        Slreutincrem:SLrham 0    0 -0.0200       . -0.0200    . .       .
         Slreutincrem:Splac 1 1.00  0.0800  0.0800       .    . .       .
 Slreutincrem:SSoraluberrat 0    0  0.1800       .  0.1800    . .       .
        SLreutsingle:SLrham 0    0  0.1200       .  0.1200    . .       .
         SLreutsingle:Splac 1 1.00  0.2200  0.2200       .    . .       .
 SLreutsingle:SSoraluberrat 0    0  0.3200       .  0.3200    . .       .
              SLrham:Splac 1 1.00  0.1000  0.1000       .    . .       .
       SLrham:SSoraluberrat 0    0  0.2000       .  0.2000    . .       .
        SSoraluberrat:Splac 1 1.00 -0.1000 -0.1000       .    . .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (MD) in network meta-analysis
 direct     - Estimated treatment effect (MD) derived from direct evidence
 indir.     - Estimated treatment effect (MD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

CAL (short-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
LspoSfaeCbutBmes:Sbbif	0	0	0.0700	.	0.0700	.	.	.
LspoSfaeCbutBmes:SBlacLacidBbifLrham	0	0	0.3100	.	0.3100	.	.	.
LspoSfaeCbutBmes:SBlactDN	0	0	0.5700	.	0.5700	.	.	.
LspoSfaeCbutBmes:SBlactis	0	0	0.4200	.	0.4200	.	.	.
LspoSfaeCbutBmes:SChx	0	0	0.3800	.	0.3800	.	.	.
LspoSfaeCbutBmes:SfaeCbutBmesLspo	0	0	0.1300	.	0.1300	.	.	.
LspoSfaeCbutBmes:SLacidLcasBbifLrhamLsal	0	0	0.3790	.	0.3790	.	.	.
LspoSfaeCbutBmes:SLacidLrhaBlongSboul	0	0	-0.3200	.	-0.3200	.	.	.
LspoSfaeCbutBmes:Slbrevis	0	0	1.0910	.	1.0910	.	.	.
LspoSfaeCbutBmes:SLbreviseplant	0	0	0.8300	.	0.8300	.	.	.
LspoSfaeCbutBmes:SLcas	0	0	-0.1300	.	-0.1300	.	.	.
LspoSfaeCbutBmes:Slreut	0	0	0.1500	.	0.1500	.	.	.
LspoSfaeCbutBmes:SLreutD	0	0	0.3600	.	0.3600	.	.	.
LspoSfaeCbutBmes:SLreutDA	0	0	0.4900	.	0.4900	.	.	.
LspoSfaeCbutBmes:SLreutU	0	0	0.1100	.	0.1100	.	.	.
LspoSfaeCbutBmes:SLsppBspp	0	0	0.4500	.	0.4500	.	.	.
LspoSfaeCbutBmes:Splac	1	1.00	0.7300	0.7300	.	.	.	.
LspoSfaeCbutBmes:SRP	0	0	0.4600	.	0.4600	.	.	.
Sbbif:SBlacLacidBbifLrham	0	0	0.2400	.	0.2400	.	.	.
Sbbif:SBlactDN	0	0	0.5000	.	0.5000	.	.	.
Sbbif:SBlactis	0	0	0.3500	.	0.3500	.	.	.
Sbbif:SChx	1	1.00	0.3100	0.3100	.	.	.	.
Sbbif:SfaeCbutBmesLspo	0	0	0.0600	.	0.0600	.	.	.
Sbbif:SLacidLcasBbifLrhamLsal	0	0	0.3090	.	0.3090	.	.	.
Sbbif:SLacidLrhaBlongSboul	0	0	-0.3900	.	-0.3900	.	.	.
Sbbif:Slbrevis	0	0	1.0210	.	1.0210	.	.	.
Sbbif:SLbreviseplant	0	0	0.7600	.	0.7600	.	.	.
Sbbif:SLcas	0	0	-0.2000	.	-0.2000	.	.	.
Sbbif:Slreut	0	0	0.0800	.	0.0800	.	.	.
Sbbif:SLreutD	0	0	0.2900	.	0.2900	.	.	.
Sbbif:SLreutDA	0	0	0.4200	.	0.4200	.	.	.
Sbbif:SLreutU	0	0	0.0400	.	0.0400	.	.	.
Sbbif:SLsppBspp	0	0	0.3800	.	0.3800	.	.	.
Sbbif:Splac	0	0	0.6600	.	0.6600	.	.	.
Sbbif:SRP	1	1.00	0.3900	0.3900	.	.	.	.
SBlacLacidBbifLrham:SBlactDN	0	0	0.2600	.	0.2600	.	.	.
SBlacLacidBbifLrham:SBlactis	0	0	0.1100	.	0.1100	.	.	.
SBlacLacidBbifLrham:SChx	0	0	0.0700	.	0.0700	.	.	.
SBlacLacidBbifLrham:SfaeCbutBmesLspo	0	0	-0.1800	.	-0.1800	.	.	.
SBlacLacidBbifLrham:SLacidLcasBbifLrhamLsal	0	0	0.0690	.	0.0690	.	.	.
SBlacLacidBbifLrham:SLacidLrhaBlongSboul	0	0	-0.6300	.	-0.6300	.	.	.
SBlacLacidBbifLrham:Slbrevis	0	0	0.7810	.	0.7810	.	.	.
SBlacLacidBbifLrham:SLbreviseplant	0	0	0.5200	.	0.5200	.	.	.
SBlacLacidBbifLrham:SLcas	0	0	-0.4400	.	-0.4400	.	.	.
SBlacLacidBbifLrham:Slreut	0	0	-0.1600	.	-0.1600	.	.	.
SBlacLacidBbifLrham:SLreutD	0	0	0.0500	.	0.0500	.	.	.
SBlacLacidBbifLrham:SLreutDA	0	0	0.1800	.	0.1800	.	.	.
SBlacLacidBbifLrham:SLreutU	0	0	-0.2000	.	-0.2000	.	.	.
SBlacLacidBbifLrham:SLsppBspp	0	0	0.1400	.	0.1400	.	.	.
SBlacLacidBbifLrham:Splac	1	1.00	0.4200	0.4200	.	.	.	.
SBlacLacidBbifLrham:SRP	0	0	0.1500	.	0.1500	.	.	.
SBlactDN:SBlactis	0	0	-0.1500	.	-0.1500	.	.	.
SBlactDN:SChx	0	0	-0.1900	.	-0.1900	.	.	.
SBlactDN:SfaeCbutBmesLspo	0	0	-0.4400	.	-0.4400	.	.	.
SBlactDN:SLacidLcasBbifLrhamLsal	0	0	-0.1910	.	-0.1910	.	.	.
SBlactDN:SLacidLrhaBlongSboul	0	0	-0.8900	.	-0.8900	.	.	.
SBlactDN:Slbrevis	0	0	0.5210	.	0.5210	.	.	.
SBlactDN:SLbreviseplant	0	0	0.2600	.	0.2600	.	.	.
SBlactDN:SLcas	0	0	-0.7000	.	-0.7000	.	.	.
SBlactDN:Slreut	0	0	-0.4200	.	-0.4200	.	.	.
SBlactDN:SLreutD	0	0	-0.2100	.	-0.2100	.	.	.
SBlactDN:SLreutDA	0	0	-0.0800	.	-0.0800	.	.	.
SBlactDN:SLreutU	0	0	-0.4600	.	-0.4600	.	.	.
SBlactDN:SLsppBspp	0	0	-0.1200	.	-0.1200	.	.	.
SBlactDN:Splac	1	1.00	0.1600	0.1600	.	.	.	.
SBlactDN:SRP	0	0	-0.1100	.	-0.1100	.	.	.
SBlactis:SChx	0	0	-0.0400	.	-0.0400	.	.	.
SBlactis:SfaeCbutBmesLspo	0	0	-0.2900	.	-0.2900	.	.	.
SBlactis:SLacidLcasBbifLrhamLsal	0	0	-0.0410	.	-0.0410	.	.	.
SBlactis:SLacidLrhaBlongSboul	0	0	-0.7400	.	-0.7400	.	.	.
SBlactis:Slbrevis	0	0	0.6710	.	0.6710	.	.	.
SBlactis:SLbreviseplant	0	0	0.4100	.	0.4100	.	.	.
SBlactis:SLcas	0	0	-0.5500	.	-0.5500	.	.	.
SBlactis:Slreut	0	0	-0.2700	.	-0.2700	.	.	.
SBlactis:SLreutD	0	0	-0.0600	.	-0.0600	.	.	.
SBlactis:SLreutDA	0	0	0.0700	.	0.0700	.	.	.
SBlactis:SLreutU	0	0	-0.3100	.	-0.3100	.	.	.
SBlactis:SLsppBspp	0	0	0.0300	.	0.0300	.	.	.
SBlactis:Splac	1	1.00	0.3100	0.3100	.	.	.	.
SBlactis:SRP	0	0	0.0400	.	0.0400	.	.	.
SChx:SfaeCbutBmesLspo	0	0	-0.2500	.	-0.2500	.	.	.
SChx:SLacidLcasBbifLrhamLsal	0	0	-0.0010	.	-0.0010	.	.	.
SChx:SLacidLrhaBlongSboul	0	0	-0.7000	.	-0.7000	.	.	.
SChx:Slbrevis	0	0	0.7110	.	0.7110	.	.	.
SChx:SLbreviseplant	0	0	0.4500	.	0.4500	.	.	.
SChx:SLcas	0	0	-0.5100	.	-0.5100	.	.	.
SChx:Slreut	0	0	-0.2300	.	-0.2300	.	.	.
SChx:SLreutD	0	0	-0.0200	.	-0.0200	.	.	.

```
                                SChx:SLreutDA 0    0  0.1100       .  0.1100    . .       .
                                 SChx:SLreutU 0    0 -0.2700       . -0.2700    . .       .
                                SChx:SLsppBspp 0    0  0.0700       .  0.0700    . .       .
                                   SChx:Splac 0    0  0.3500       .  0.3500    . .       .
                                     SChx:SRP 1 1.00  0.0800  0.0800       .    . .       .
    SfaeCbutBmesLspo:SLacidLcasBbifLrhamLsal 0    0  0.2490       .  0.2490    . .       .
       SfaeCbutBmesLspo:SLacidLrhaBlongSboul 0    0 -0.4500       . -0.4500    . .       .
                  SfaeCbutBmesLspo:SLbrevis 0    0  0.9610       .  0.9610    . .       .
         SfaeCbutBmesLspo:SLbreviseplant 0    0  0.7000       .  0.7000    . .       .
                   SfaeCbutBmesLspo:SLcas 0    0 -0.2600       . -0.2600    . .       .
                  SfaeCbutBmesLspo:SLreut 0    0  0.0200       .  0.0200    . .       .
                 SfaeCbutBmesLspo:SLreutD 0    0  0.2300       .  0.2300    . .       .
                SfaeCbutBmesLspo:SLreutDA 0    0  0.3600       .  0.3600    . .       .
                 SfaeCbutBmesLspo:SLreutU 0    0 -0.0200       . -0.0200    . .       .
               SfaeCbutBmesLspo:SLsppBspp 0    0  0.3200       .  0.3200    . .       .
                   SfaeCbutBmesLspo:Splac 0    0  0.6000       .  0.6000    . .       .
                     SfaeCbutBmesLspo:SRP 2 1.00  0.3300  0.3300       .    . .       .
SLacidLcasBbifLrhamLsal:SLacidLrhaBlongSboul 0    0 -0.6990       . -0.6990    . .       .
          SLacidLcasBbifLrhamLsal:SLbrevis 0    0  0.7120       .  0.7120    . .       .
      SLacidLcasBbifLrhamLsal:SLbreviseplant 0    0  0.4510       .  0.4510    . .       .
               SLacidLcasBbifLrhamLsal:SLcas 0    0 -0.5090       . -0.5090    . .       .
              SLacidLcasBbifLrhamLsal:SLreut 0    0 -0.2290       . -0.2290    . .       .
             SLacidLcasBbifLrhamLsal:SLreutD 0    0 -0.0190       . -0.0190    . .       .
            SLacidLcasBbifLrhamLsal:SLreutDA 0    0  0.1110       .  0.1110    . .       .
             SLacidLcasBbifLrhamLsal:SLreutU 0    0 -0.2690       . -0.2690    . .       .
           SLacidLcasBbifLrhamLsal:SLsppBspp 0    0  0.0710       .  0.0710    . .       .
              SLacidLcasBbifLrhamLsal:Splac 0    0  0.3510       .  0.3510    . .       .
                SLacidLcasBbifLrhamLsal:SRP 1 1.00  0.0810  0.0810       .    . .       .
              SLacidLrhaBlongSboul:SLbrevis 0    0  1.4110       .  1.4110    . .       .
         SLacidLrhaBlongSboul:SLbreviseplant 0    0  1.1500       .  1.1500    . .       .
                  SLacidLrhaBlongSboul:SLcas 0    0  0.1900       .  0.1900    . .       .
                 SLacidLrhaBlongSboul:SLreut 0    0  0.4700       .  0.4700    . .       .
                SLacidLrhaBlongSboul:SLreutD 0    0  0.6800       .  0.6800    . .       .
               SLacidLrhaBlongSboul:SLreutDA 0    0  0.8100       .  0.8100    . .       .
                SLacidLrhaBlongSboul:SLreutU 0    0  0.4300       .  0.4300    . .       .
              SLacidLrhaBlongSboul:SLsppBspp 0    0  0.7700       .  0.7700    . .       .
                  SLacidLrhaBlongSboul:Splac 1 1.00  1.0500  1.0500       .    . .       .
                    SLacidLrhaBlongSboul:SRP 0    0  0.7800       .  0.7800    . .       .
                     Slbrevis:SLbreviseplant 0    0 -0.2610       . -0.2610    . .       .
                              Slbrevis:SLcas 0    0 -1.2210       . -1.2210    . .       .
                             Slbrevis:SLreut 0    0 -0.9410       . -0.9410    . .       .
                            Slbrevis:SLreutD 0    0 -0.7310       . -0.7310    . .       .
                           Slbrevis:SLreutDA 0    0 -0.6010       . -0.6010    . .       .
                            Slbrevis:SLreutU 0    0 -0.9810       . -0.9810    . .       .
                          Slbrevis:SLsppBspp 0    0 -0.6410       . -0.6410    . .       .
                             Slbrevis:Splac 1 1.00 -0.3610 -0.3610       .    . .       .
                               Slbrevis:SRP 0    0 -0.6310       . -0.6310    . .       .
                        SLbreviseplant:SLcas 0    0 -0.9600       . -0.9600    . .       .
                       SLbreviseplant:SLreut 0    0 -0.6800       . -0.6800    . .       .
                      SLbreviseplant:SLreutD 0    0 -0.4700       . -0.4700    . .       .
                     SLbreviseplant:SLreutDA 0    0 -0.3400       . -0.3400    . .       .
                      SLbreviseplant:SLreutU 0    0 -0.7200       . -0.7200    . .       .
                    SLbreviseplant:SLsppBspp 0    0 -0.3800       . -0.3800    . .       .
                        SLbreviseplant:Splac 1 1.00 -0.1000 -0.1000       .    . .       .
                          SLbreviseplant:SRP 0    0 -0.3700       . -0.3700    . .       .
                               SLcas:SLreut 0    0  0.2800       .  0.2800    . .       .
                              SLcas:SLreutD 0    0  0.4900       .  0.4900    . .       .
                             SLcas:SLreutDA 0    0  0.6200       .  0.6200    . .       .
                              SLcas:SLreutU 0    0  0.2400       .  0.2400    . .       .
                            SLcas:SLsppBspp 0    0  0.5800       .  0.5800    . .       .
                               SLcas:Splac 0    0  0.8600       .  0.8600    . .       .
                                 SLcas:SRP 1 1.00  0.5900  0.5900       .    . .       .
                             Slreut:SLreutD 0    0  0.2100       .  0.2100    . .       .
                            Slreut:SLreutDA 0    0  0.3400       .  0.3400    . .       .
                             Slreut:SLreutU 0    0 -0.0400       . -0.0400    . .       .
                           Slreut:SLsppBspp 0    0  0.3000       .  0.3000    . .       .
                               Slreut:Splac 1 1.00  0.5800  0.5800       .    . .       .
                                 Slreut:SRP 0    0  0.3100       .  0.3100    . .       .
                            SLreutD:SLreutDA 0    0  0.1300       .  0.1300    . .       .
                             SLreutD:SLreutU 0    0 -0.2500       . -0.2500    . .       .
                           SLreutD:SLsppBspp 0    0  0.0900       .  0.0900    . .       .
                               SLreutD:Splac 1 1.00  0.3700  0.3700       .    . .       .
                                 SLreutD:SRP 0    0  0.1000       .  0.1000    . .       .
                            SLreutDA:SLreutU 0    0 -0.3800       . -0.3800    . .       .
                          SLreutDA:SLsppBspp 0    0 -0.0400       . -0.0400    . .       .
                              SLreutDA:Splac 1 1.00  0.2400  0.2400       .    . .       .
                                SLreutDA:SRP 1 1.00 -0.0300 -0.0300       .    . .       .
                           SLreutU:SLsppBspp 0    0  0.3400       .  0.3400    . .       .
                               SLreutU:Splac 0    0  0.6200       .  0.6200    . .       .
                                 SLreutU:SRP 1 1.00  0.3500  0.3500       .    . .       .
                             SLsppBspp:Splac 2 1.00  0.2800  0.2800       .    . .       .
                               SLsppBspp:SRP 0    0  0.0100       .  0.0100    . .       .
                                   SRP:Splac 0    0  0.2700       .  0.2700    . .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (MD) in network meta-analysis
 direct     - Estimated treatment effect (MD) derived from direct evidence
 indir.     - Estimated treatment effect (MD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

CAL (long-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
SLreutDA:Slreutincrem	0	0	-0.4100	.	-0.4100	.	.	.
SLreutDA:SLreutsingle	0	0	-0.3000	.	-0.3000	.	.	.
SLreutDA:SLrham	0	0	0.0200	.	0.0200	.	.	.
SLreutDA:Splac	1	1.00	0.0200	0.0200	.	.	.	.
SLreutDA:SSoraluberrat	0	0	0.0700	.	0.0700	.	.	.
Slreutincrem:SLreutsingle	1	1.00	0.1100	0.1100	.	.	.	.
Slreutincrem:SLrham	0	0	0.4300	.	0.4300	.	.	.
Slreutincrem:Splac	1	1.00	0.4300	0.4300	.	.	.	.
Slreutincrem:SSoraluberrat	0	0	0.4800	.	0.4800	.	.	.
SLreutsingle:SLrham	0	0	0.3200	.	0.3200	.	.	.
SLreutsingle:Splac	1	1.00	0.3200	0.3200	.	.	.	.
SLreutsingle:SSoraluberrat	0	0	0.3700	.	0.3700	.	.	.
SLrham:Splac	1	1.00	0.0000	0.0000	.	.	.	.
SLrham:SSoraluberrat	0	0	0.0500	.	0.0500	.	.	.
SSoraluberrat:Splac	1	1.00	-0.0500	-0.0500	.	.	.	.

Legend:
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Diff - Difference between direct and indirect treatment estimates
z - z-value of test for disagreement (direct versus indirect)
p-value - p-value of test for disagreement (direct versus indirect)

BOP (short-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
SBlacLacidBbifLrham:SBlactDN	0	0	-9.9100	.	-9.9100	.	.	.
SBlacLacidBbifLrham:SBlactis	0	0	1.5029	.	1.5029	.	.	.
SBlacLacidBbifLrham:SLacidLcasBbifLrhamLsal	0	0	27.2350	.	27.2350	.	.	.
SBlacLacidBbifLrham:SLbreviseplant	0	0	7.8900	.	7.8900	.	.	.
SBlacLacidBbifLrham:Slreut	0	0	-25.4900	.	-25.4900	.	.	.
SBlacLacidBbifLrham:SLreutAA	0	0	-27.6100	.	-27.6100	.	.	.
SBlacLacidBbifLrham:SLreutD	0	0	-7.8700	.	-7.8700	.	.	.
SBlacLacidBbifLrham:SLreutDA	0	0	1.1500	.	1.1500	.	.	.
SBlacLacidBbifLrham:SLsppBspp	0	0	5.0203	.	5.0203	.	.	.
SBlacLacidBbifLrham:Splac	1	1.00	5.3900	5.3900	.	.	.	.
SBlacLacidBbifLrham:SRP	0	0	26.9000	.	26.9000	.	.	.
SBlactDN:SBlactis	0	0	11.4129	.	11.4129	.	.	.
SBlactDN:SLacidLcasBbifLrhamLsal	0	0	37.1450	.	37.1450	.	.	.
SBlactDN:SLbreviseplant	0	0	17.8000	.	17.8000	.	.	.
SBlactDN:Slreut	0	0	-15.5800	.	-15.5800	.	.	.
SBlactDN:SLreutAA	0	0	-17.7000	.	-17.7000	.	.	.
SBlactDN:SLreutD	0	0	2.0400	.	2.0400	.	.	.
SBlactDN:SLreutDA	0	0	11.0600	.	11.0600	.	.	.
SBlactDN:SLsppBspp	0	0	14.9303	.	14.9303	.	.	.
SBlactDN:Splac	1	1.00	15.3000	15.3000	.	.	.	.
SBlactDN:SRP	0	0	36.8100	.	36.8100	.	.	.
SBlactis:SLacidLcasBbifLrhamLsal	0	0	25.7321	.	25.7321	.	.	.
SBlactis:SLbreviseplant	0	0	6.3871	.	6.3871	.	.	.
SBlactis:Slreut	0	0	-26.9929	.	-26.9929	.	.	.
SBlactis:SLreutAA	0	0	-29.1129	.	-29.1129	.	.	.
SBlactis:SLreutD	0	0	-9.3729	.	-9.3729	.	.	.
SBlactis:SLreutDA	0	0	-0.3529	.	-0.3529	.	.	.
SBlactis:SLsppBspp	0	0	3.5174	.	3.5174	.	.	.
SBlactis:Splac	2	1.00	3.8871	3.8871	.	.	.	.
SBlactis:SRP	0	0	25.3971	.	25.3971	.	.	.
SLacidLcasBbifLrhamLsal:SLbreviseplant	0	0	-19.3450	.	-19.3450	.	.	.
SLacidLcasBbifLrhamLsal:Slreut	0	0	-52.7250	.	-52.7250	.	.	.
SLacidLcasBbifLrhamLsal:SLreutAA	0	0	-54.8450	.	-54.8450	.	.	.
SLacidLcasBbifLrhamLsal:SLreutD	0	0	-35.1050	.	-35.1050	.	.	.
SLacidLcasBbifLrhamLsal:SLreutDA	0	0	-26.0850	.	-26.0850	.	.	.
SLacidLcasBbifLrhamLsal:SLsppBspp	0	0	-22.2147	.	-22.2147	.	.	.
SLacidLcasBbifLrhamLsal:Splac	0	0	-21.8450	.	-21.8450	.	.	.
SLacidLcasBbifLrhamLsal:SRP	1	1.00	-0.3350	-0.3350	.	.	.	.
SLbreviseplant:Slreut	0	0	-33.3800	.	-33.3800	.	.	.
SLbreviseplant:SLreutAA	0	0	-35.5000	.	-35.5000	.	.	.
SLbreviseplant:SLreutD	0	0	-15.7600	.	-15.7600	.	.	.
SLbreviseplant:SLreutDA	0	0	-6.7400	.	-6.7400	.	.	.
SLbreviseplant:SLsppBspp	0	0	-2.8697	.	-2.8697	.	.	.
SLbreviseplant:Splac	1	1.00	-2.5000	-2.5000	.	.	.	.
SLbreviseplant:SRP	0	0	19.0100	.	19.0100	.	.	.
Slreut:SLreutAA	0	0	-2.1200	.	-2.1200	.	.	.
Slreut:SLreutD	0	0	17.6200	.	17.6200	.	.	.
Slreut:SLreutDA	0	0	26.6400	.	26.6400	.	.	.
Slreut:SLsppBspp	0	0	30.5103	.	30.5103	.	.	.
Slreut:Splac	1	1.00	30.8800	30.8800	.	.	.	.
Slreut:SRP	0	0	52.3900	.	52.3900	.	.	.
SLreutAA:SLreutD	0	0	19.7400	.	19.7400	.	.	.
SLreutAA:SLreutDA	0	0	28.7600	.	28.7600	.	.	.
SLreutAA:SLsppBspp	0	0	32.6303	.	32.6303	.	.	.
SLreutAA:Splac	1	1.00	33.0000	33.0000	.	.	.	.
SLreutAA:SRP	0	0	54.5100	.	54.5100	.	.	.
SLreutD:SLreutDA	0	0	9.0200	.	9.0200	.	.	.
SLreutD:SLsppBspp	0	0	12.8903	.	12.8903	.	.	.
SLreutD:Splac	1	1.00	13.2600	13.2600	.	.	.	.
SLreutD:SRP	0	0	34.7700	.	34.7700	.	.	.
SLreutDA:SLsppBspp	0	0	3.8703	.	3.8703	.	.	.
SLreutDA:Splac	1	1.00	4.2400	4.2400	.	.	.	.
SLreutDA:SRP	1	1.00	25.7500	25.7500	.	.	.	.
SLsppBspp:Splac	2	1.00	0.3697	0.3697	.	.	.	.
SLsppBspp:SRP	0	0	21.8797	.	21.8797	.	.	.
SRP:Splac	0	0	-21.5100	.	-21.5100	.	.	.

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BOP (long-term studies)
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
SLreutDA:Slreutincrem	0	0	-15.2657	.	-15.2657	.	.	.
SLreutDA:SLreutsingle	0	0	-11.9457	.	-11.9457	.	.	.
SLreutDA:SLrham	0	0	4.6443	.	4.6443	.	.	.
SLreutDA:Splac	2	1.00	8.0443	8.0443	.	.	.	.
SLreutDA:SSoraluberrat	0	0	3.0243	.	3.0243	.	.	.
Slreutincrem:SLreutsingle	1	1.00	3.3200	3.3200	.	.	.	.
Slreutincrem:SLrham	0	0	19.9100	.	19.9100	.	.	.
Slreutincrem:Splac	1	1.00	23.3100	23.3100	.	.	.	.
Slreutincrem:SSoraluberrat	0	0	18.2900	.	18.2900	.	.	.
SLreutsingle:SLrham	0	0	16.5900	.	16.5900	.	.	.
SLreutsingle:Splac	1	1.00	19.9900	19.9900	.	.	.	.
SLreutsingle:SSoraluberrat	0	0	14.9700	.	14.9700	.	.	.
SLrham:Splac	1	1.00	3.4000	3.4000	.	.	.	.
SLrham:SSoraluberrat	0	0	-1.6200	.	-1.6200	.	.	.
SSoraluberrat:Splac	1	1.00	5.0200	5.0200	.	.	.	.

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