Oral bio-modulation with probiotics during fixed orthodontic treatment: A scoping review of clinical and microbiological outcomes

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Abstract. Existing research has focused on individual probiotics with limited impetus placed on clinical outcomes; this has left a void on the broader landscape of probiotic-based interventions in orthodontics. To address this gap, the present scoping review was conducted to systematically map available clinical evidence on the use of probiotics during fixed orthodontic therapy, including probiotic strains and delivery systems, clinical and microbiological outcomes, and methodological and evidence gaps in the current literature. A scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. For this purpose, electronic databases were searched for clinical studies evaluating probiotic interventions in patients undergoing fixed orthodontic treatment. Animal and *in vitro* studies, case reports, case series, reviews and studies without comparative clinical or microbiological outcome data were excluded. Data regarding study characteristics, probiotic strains, delivery systems, intervention characteristics, clinical and microbiological outcomes, adverse effects, and methodological quality were charted and descriptively synthesized. As demonstrated by the findings of the present scoping review, probiotic interventions may provide benefits for selected microbiological, gingival, periodontal and patient-centered outcomes during fixed orthodontic treatment; however, the available evidence is heterogeneous and inconsistent across probiotic strains, delivery systems and outcome domains. In summary, the current evidence is insufficient to support definitive recommendations for routine clinical use. Further well-designed randomized controlled trials with standardized interventions and clinically relevant long-term outcomes are required.

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Introduction

The origins of oral microbiome research can be traced back to the 1670s, when Antonie van Leeuwenhoek first documented microorganisms in dental plaque (1-3). The oral microbiome, defined as the collective genome of microorganisms inhabiting the oral cavity, is recognized as the second most complex microbial community in the human body, surpassed only by the gut microbiome (1,4-8). Of note, ~700 prokaryotic species have been identified within this ecosystem. These microorganisms play a critical role in maintaining both oral and systemic health through intricate polymicrobial interactions and synergistic functions, while dysbiosis within this community is increasingly linked to the development of various oral diseases (6). Recently, the scientific understanding of the oral microbiota has expanded to include functional genomics, metabolic interactions, microbial succession patterns and host-microbe signaling. Orthodontic treatment often causes an alteration in the biofilm niches due to the unique mechanical alterations it introduces. It disrupts the ecological balance, which shifts the microbial consortia toward pathogenic microbiota. Evidence suggests that ecological perturbations during orthodontic therapy not only predisposes individuals to localized diseases, but may also modulate systemic inflammatory responses through microbial translocation and immunologic crosstalk, highlighting the importance of biologically informed strategies for microbial modulation (9-11). The goal of corrective orthodontics is improving occlusion, jaw associations, masticatory efficiency and overall facial aesthetics. However, the prolonged duration of treatment promotes biofilm accumulation, enhances plaque retention and leads to changes in the oral microbiome (12-14). Challenges in maintaining optimal oral hygiene, combined with shifts in the oral ecological environment, increase the risk of developing dental

caries, gingival and periodontal inflammation, white-spot lesions and halitosis (15,16). Furthermore, patient adherence to mechanical plaque-control measures often diminishes over time, and commonly prescribed antimicrobial agents, such as chlorhexidine may cause adverse effects, including tooth staining, taste disruptions and the potential development of antimicrobial resistance when used over longer periods of time (17). To counter this, a novel method has been adopted in dentistry for maintaining oral health using beneficial bacteria known as 'probiotics'. Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host, whether through dietary intake or supplementation. Probiotic bacterio-therapy is considered to exert its effects by competing with pathogenic oral bacteria for adhesion sites, nutrients and growth factors, while also modulating both local and systemic immune responses (18,19). Although a wide range of probiotic strains has been studied, those most frequently investigated for oral health applications belong to the genera *Lactobacillus*, *Bifidobacterium* and *Streptococcus*. Commonly evaluated strains include *Lactobacillus rhamnosus* GG, *Lactobacillus reuteri* ATCC 55739, *Bifidobacterium* DN-173010, (20) and *Streptococcus salivarius* strains K12 and M18 (21,22). Additionally, *Weissella cibaria* has been explored, though primarily for its role in reducing halitosis rather than broader oral health benefits (23).

The application of probiotics is grounded on the concept of oral bio-modulation: An ecological approach aimed at restoring microbial homeostasis rather than eradicating microorganisms. This aligns with contemporary paradigms emphasizing the ecological plaque hypothesis, precision oral health and microbiome-based therapeutics. Recent studies have examined the role of probiotics in maintaining oral health among orthodontic patients. Albardawel *et al* (24) reported that probiotic lozenges containing *Lactobacillus reuteri*, when used alongside good oral hygiene practices, were effective in reducing plaque accumulation and preventing early clinical signs of periodontal inflammation. Similarly, the studies by Alp and Baka (25), and Alforaidi *et al* (26) demonstrated the beneficial effects of probiotics in preventing decreases in salivary pH during orthodontic treatment. However, short-term probiotic use did not significantly alter the salivary *Streptococcus mutans* or Lactobacilli counts (25,26). Baghaei *et al* (27) observed that Lactogum probiotic lozenges helped reduce the incidence and severity of traumatic oral ulcers, although the generalizability of these findings was limited by a small sample size. Additionally, the administration of *Streptococcus salivarius* M18 was found to reduce halitosis in patients undergoing fixed orthodontic therapy, although it did not exert any measurable effect on plaque or gingival indices (28). Despite these encouraging findings, the heterogeneity in probiotic strains, dosages, delivery systems and treatment durations renders it difficult to draw definitive conclusions about their efficacy in orthodontic care. Moreover, studies vary widely in methodological rigor, sample sizes and outcome measures. Numerous trials had short follow-up periods that do not adequately reflect the long duration of orthodontic treatment (25-27). Existing reviews have narrowly focused on individual probiotic strains or limited clinical outcomes. This has left substantial gaps in knowledge regarding the broader landscape of probiotic-based interventions in orthodontics. To date, no comprehensive mapping exists that integrates clinical and microbiological, outcomes across all study designs.

To address this gap, the present scoping review was conducted to summarize the existing literature on probiotics in orthodontics. Biological mechanisms provide reasonable explanations for observed clinical effects. Mechanistic evidence from animal and *in vitro* studies however, were excluded from the present scoping review. Unlike systematic reviews that focus narrowly on answering a specific, well-defined question, scoping reviews aim to map the extent, range and nature of research activity which allows the inclusion of a wide variety of study types and outcomes, making it possible to chart key concepts, identify gaps in existing literature research, and clarify areas in which further primary research is needed. This is critical for an emerging field where interventions, strains and clinical contexts are still evolving. Therefore, the objective of the present scoping review was to systematically map the available evidence on the use of probiotics in orthodontic patients. The present scoping review focused on studies on patients undergoing fixed orthodontic treatment and evaluated a range of probiotic strains, delivery systems, intervention characteristics, clinical outcomes and microbiological outcomes reported in the past. The present scoping review also sought to identify any methodological limitations and evidence gaps that may guide future clinical research and the development of standardized probiotic protocols in orthodontic therapy. the objectives of the present scoping review were the following: i) Identify the types of probiotic strains and formulations evaluated in patients undergoing fixed orthodontic therapy; ii) describe the delivery systems dosage regimens, frequency and duration of probiotic administration; iii) summarize the clinical and microbiological outcomes assessed in orthodontic patients receiving probiotic interventions, including plaque levels, gingival inflammation, salivary parameters, microbial counts, halitosis, oral discomfort and enamel demineralization indicators; iv) describe the methodological characteristics and methodological quality of the available clinical studies; and v) identify evidence gaps and methodological limitations to inform future clinical research on probiotic use during fixed orthodontic treatment.

Data and methods

Study design. A review protocol was developed a priori, outlining the review objectives, eligibility criteria, information sources, study-selection procedures, data-charting domains and approach to synthesis. However, the protocol was not prospectively registered or made publicly available. The present scoping review was conducted in accordance with the methodological framework proposed by Arksey and O'Malley (28), further refined by Levac *et al* (29) and the Joanna Briggs Institute (JBI) (30) guidance for scoping reviews. The reporting adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines.

Eligibility criteria. The following inclusion criteria were used: Studies including participants who were healthy individuals of any age undergoing orthodontic treatment with fixed orthodontic appliances were eligible for inclusion. Studies

involving patients with craniofacial anomalies or syndromes of the head and neck region, systemic diseases, or concurrent antibiotic or antimicrobial therapy unrelated to orthodontic treatment were excluded.

Interventions. Studies evaluating probiotic interventions administered during fixed orthodontic treatment were eligible. Studies were required to provide an adequate description of the intervention, including the probiotic product or strain, route or delivery system, dosage or regimen, and duration of administration.

Comparators. Eligible comparisons included placebo, no probiotic intervention, standard oral-hygiene care, active comparators, or within-participant pre-intervention baseline measurements. Studies without any comparative clinical or microbiological outcome data were excluded.

Outcomes. Clinical outcomes included gingival inflammation and periodontal parameters (e.g., gingival index, bleeding indices), plaque-related outcomes (e.g., plaque index), enamel demineralization or white spot lesion indicators, halitosis, oral discomfort and other patient-reported outcomes. Microbiological outcomes included changes in salivary or plaque levels and composition of microorganisms, particularly cariogenic and potentially pathogenic species. Adverse effects and other intervention-related outcomes were also charted where reported. Plaque-related outcomes were included as secondary clinical outcomes as they were reported in several eligible studies. However, changes in plaque accumulation were interpreted descriptively and were not considered, in isolation, to establish a direct clinical oral-health benefit.

Study design. Randomized clinical trials, non-randomized comparative studies and prospective single-arm pre-post interventional studies involving patients undergoing fixed orthodontic treatment were eligible.

Exclusion criteria. Animal studies, *in vitro* studies, studies conducted exclusively outside the context of orthodontic treatment, case reports, case series, systematic reviews, meta-analyses, study protocols without clinical outcome data, and studies not reporting comparative clinical or microbiological outcome data were excluded.

Information sources and search strategy. A comprehensive literature search was conducted across the PubMed/MEDLINE, Scopus, Web of Science and the Cochrane Central Register of Controlled Trials (CENTRAL) databases. Additional sources of published and grey literature included Google Scholar, ClinicalTrials.gov., and dissertations where accessible was additionally searched to identify potentially relevant grey and supplementary literature. The search strategy combined free-text terms and controlled vocabulary, where applicable, representing two main concepts: Probiotics and orthodontic treatment. Search syntax was adapted according to the requirements of each database or information source.

Broad terms, such as prebiotics and clear aligners were included in selected initial searches to maximize sensitivity and avoid omitting potentially relevant mixed-intervention or orthodontic studies. However, studies evaluating prebiotics alone and studies conducted exclusively in patients treated with clear aligners or other removable appliances were excluded during screening because the eligibility criteria were restricted to probiotic interventions during fixed orthodontic treatment.

The initial literature search was conducted on February 1, 2025. Prior to the finalization of the review, the search was updated to identify recently published eligible studies (September 12, 2026). Following consolidation of the original and updated search results, 390 records were identified. Following deduplication and completion of the screening and eligibility-assessment process, 28 studies were included in the final evidence base. No date, language, participant-age, or publication-type restrictions were applied at the database-search stage. The complete database-specific search strategies, dates of searching, and limits or restrictions applied are provided in Table I.

Selection of sources of evidence. All search results were exported into reference management software (e.g., EndNote, Zotero). Duplicates were removed following which two authors (AK and SPD) independently screened titles and abstracts against the eligibility criteria, followed by full-text screening. Disagreements were resolved through discussion or consultation with a third author (NTH). A PRISMA-ScR flow diagram illustrating the study selection process is presented in Fig. 1.

Data charting process. A standardized data-charting form was developed a priori based on the review objectives and eligibility criteria. The form was pilot-tested on a subset of studies to assess its completeness, clarity, and suitability for capturing the characteristics and outcomes relevant to the review question. Minor refinements were made to the charting fields following pilot testing before commencement of full data charting. Two authors (AK and SPD) independently charted data from all included studies. Discrepancies were discussed and resolved by consensus, with consultation with a third author (NTH) when necessary. The following data items were charted: Author, year of publication, study title, study design, sample size, participant characteristics, orthodontic appliance type (formulation and strain of probiotic; delivery method, dosage, frequency and duration) comparator, outcomes assessed (clinical, microbiological, patient-reported), key findings/results, reported adverse effects, conclusion and reported funding sources or conflicts of interest.

Reporting guideline. The present scoping review was reported in accordance with the PRISMA-ScR guidelines.

Risk of bias assessment. The methodological quality of the included studies was assessed at the study level using design-appropriate risk-of-bias tools. Randomized controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool. For randomized crossover trials, potential bias arising from period and carryover effects was additionally considered. Non-randomized intervention studies were evaluated using the Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I) tool.

Synthesis of results. Given the heterogeneity in clinical study designs, probiotic strains, formulations, delivery systems, intervention regimens and outcome measures, the findings were synthesized descriptively and narratively. The evidence was organized according to probiotic strains and formulations, delivery systems and intervention characteristics,

Table I. Search strategies, dates of searching, and limits or restrictions applied for the purposes of the present scoping review.

Database/ information source	Search terms	Search date	Limits
PubMed/ MEDLINE	((Probiot) OR (Lactobacillus acidophilus) OR (Bifidobacterium bifidum) OR (Lactobacillus rhamnosus) OR (Streptococcus salivarius) OR (Lactobacillus plantarum) OR (Lactobacillus paracasei) OR (Lactobacillus reuteri) OR (Streptococcus uberis) OR (Streptococcus oralis) OR (Streptococcus rattus) OR (Bifidobacterium animalis OR Prebiot)) AND (fixed appliance OR orthodon OR fixed orthodontic OR bracket OR multibracket OR Clear Aligners)	February 1, 2025	None
Scopus	((Probiot) OR (Lactobacillus acidophilus) OR (Bifidobacterium bifidum) OR (Lactobacillus rhamnosus) OR (Streptococcus salivarius) OR (Lactobacillus plantarum) OR (Lactobacillus paracasei) OR (Lactobacillus reuteri) OR (Streptococcus uberis) OR (Streptococcus oralis) OR (Streptococcus rattus) OR (Bifidobacterium animalis OR Prebiot)) AND ('fixed appliance' OR orthodon OR 'fixed orthodontic' OR bracket OR multibracket OR 'Clear Aligner')	February 1, 2025	None
Web of Science Core Collection	TS=((probiotic* OR 'Lactobacillus acidophilus' OR 'Bifidobacterium bifidum' OR 'Lactobacillus rhamnosus' OR 'Streptococcus salivarius' OR 'Lactobacillus plantarum' OR 'Lactobacillus paracasei' OR 'Lactobacillus reuteri' OR 'Streptococcus uberis' OR 'Streptococcus oralis' OR 'Streptococcus rattus' OR 'Bifidobacterium animalis') AND (orthodont* OR 'fixed orthodontic*' OR 'fixed appliance*' OR 'orthodontic appliance*' OR 'fixed orthodontic appliance*' OR bracket* OR multibracket*))	February 1, 2025	None
Cochrane Central Register of Controlled Trials (CENTRAL)	((Probiot) OR (Lactobacillus acidophilus) OR (Bifidobacterium bifidum) OR (Lactobacillus rhamnosus) OR (Streptococcus salivarius) OR (Lactobacillus plantarum) OR (Lactobacillus paracasei) OR (Lactobacillus reuteri) OR (Streptococcus uberis) OR (Streptococcus oralis) OR (Streptococcus rattus) OR (Bifidobacterium animalis OR Prebiot)) AND (fixed appliance OR orthodon OR fixed orthodontic OR bracket OR multibracket OR Clear Aligners)	February 1, 2025	None
Google Scholar	('probiotic' OR 'probiotics' OR Lactobacillus OR Bifidobacterium) AND ('fixed orthodontic' OR 'fixed appliance' OR 'orthodontic appliance' OR orthodontic OR brackets)	February 1, 2025	None
ClinicalTrials.gov	Orthodontic probiotics	February 1, 2025	None
ProQuest Dissertations and Theses Global	((Probiot) OR (Lactobacillus acidophilus) OR (Bifidobacterium bifidum) OR (Lactobacillus rhamnosus) OR (Streptococcus salivarius) OR (Lactobacillus plantarum) OR (Lactobacillus paracasei) OR (Lactobacillus reuteri) OR (Streptococcus uberis) OR (Streptococcus oralis) OR (Streptococcus rattus) OR (Bifidobacterium animalis OR Prebiot)) AND ('fixed appliance' OR orthodon OR 'fixed orthodontic' OR bracket OR multibracket OR 'Clear Aligners')	February 1, 2025	Subject: Healthcare

clinical outcomes, microbiological outcomes, patient-reported outcomes and adverse effects, and methodological and evidence gaps. No quantitative meta-analysis was undertaken as the primary objective was to map the available evidence rather than estimate a pooled intervention effect. Risk-of-bias assessments for randomized and non-randomized studies are presented in Figs. 2 and 3, respectively.

Results

Study selection. Following the completion and reconciliation of the original and updated searches, 390 records were identified. Following the removal of 172 duplicate records, 218 unique records underwent title and abstract screening. Of these, 184 records were excluded, and 34 reports were retrieved and assessed for eligibility. In total, six reports were excluded at the full-text stage: Three were study protocols without completed clinical results, one was a pilot or preliminary study that did not meet the predefined eligibility criteria, and two involved participants with craniofacial anomalies and therefore did not meet the population eligibility criteria. Consequently, 28 studies were included in the final scoping review. The PRISMA-ScR flow diagram depicts the study selection process followed (Fig. 1).

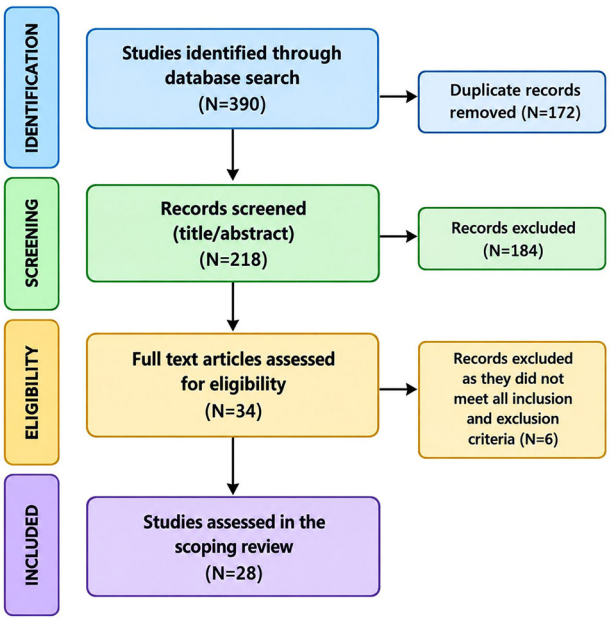

Figure 1. PRISMA-ScR flow diagram of the study selection process.

Characteristics of the included studies. The included studies comprised both randomized controlled trials and non-randomized clinical studies conducted in orthodontic patients undergoing fixed appliance therapy. Animal or *in vitro* studies were excluded. Sample sizes ranged from small single-center cohorts to moderate-sized parallel-arm clinical trials. The duration of probiotic administration varied widely, from short-term interventions of 2-4 weeks to longer follow-up periods extending up to several months. A broad range of probiotic strains was evaluated, most commonly species of *Lactobacillus*, *Bifidobacterium* and *Streptococcus*. Probiotics were delivered through multiple vehicles, including lozenges, chewable tablets, mouth rinses, gels, yogurts, and fermented milk products. Control groups typically received placebo formulations or standard oral hygiene instructions alone. The 28 included studies and the study characteristics are presented in Table II. The findings were organized by outcome domain and mapped at the study level in Table III.

Study-level mapping of clinical and microbiological outcomes. The effects of probiotic interventions varied substantially according to the outcome assessed, probiotic strain, delivery system, duration of administration, and study design. Accordingly, the evidence was mapped at the study level and organized into microbiological, gingival/plaque and periodontal, plaque acidogenicity and salivary, white spot lesion, halitosis, traumatic oral lesion, patient-centered and inflammatory/biochemical outcomes (Table III).

Microbiological outcomes. Although microbiological outcomes were the most frequently investigated, the findings were heterogeneous. Alp and Baka (25) reported significant reductions in salivary *Streptococcus mutans* and *Lactobacillus* levels following probiotic interventions. Baxi *et al* (31) reported significant reductions in plaque *Streptococcus mutans* with probiotic lozenges, sachets, and beverages. In the study by Singhal *et al* (32), probiotic yogurt significantly reduced salivary *Streptococcus mutans* (P=0.001), whereas the significant plaque *Streptococcus mutans* reduction was reported with Indian curd (P=0.026). Cildir *et al* (33) reported a significant reduction in salivary *Streptococcus mutans* following the use of probiotic yogurt, without a significant change in Lactobacilli. Rajaram *et al* (34) reported a significant reduction in plaque *Streptococcus mutans*, and Goyal *et al* (35) reported a significant reduction in subgingival *Porphyromonas gingivalis* with probiotic mouthwash.

By contrast, several studies did not demonstrate a significant probiotic-specific reduction in cariogenic or periodontal bacteria. Chen *et al* (36) observed non-significant reductions in *Streptococcus mutans* and *Lactobacillus*. Nisha *et al* (37) found no significant intergroup difference in plaque *Streptococcus mutans*. Alforaidi *et al* (26) found no significant changes in *Streptococcus mutans* or Lactobacilli despite a significant improvement in plaque acidogenicity. Dadgar *et al* (38) found no significant reduction in plaque *Streptococcus mutans* with *Lactobacillus plantarum* mouth rinse, whereas the fluoride comparator significantly reduced counts. Ebrahim *et al* (39) reported no significant probiotic effect on salivary or plaque *Streptococcus mutans* DNA. Among the newer studies, Chandrashekaraiah *et al* (40) observed a significant reduction in plaque *Streptococcus mutans* over 9 months, although the reduction was smaller than with fluoride or propolis; Jabbareh *et al* (41) reported lower cultivable bacterial counts with kefir in the longitudinal model (P=0.014), although the day-20 between-group difference was not significant (P=0.148); and Kusnoto *et al* (42) found decreases in *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* in all three toothpaste groups without significant treatment-by-group interactions.

Gingival, plaque and periodontal outcomes. Clinical periodontal outcomes were also variable. Albardawel *et al* (24) demonstrated a significantly lower plaque index, gingival index, papillary bleeding index, and probing-depth values in the probiotic group than in the control group at follow-up. Widyarman *et al* (43) reported improvements in oral hygiene and papillary bleeding indices, while Tahir *et al* (44) observed significantly less gingival bleeding but no significant difference in plaque scores with probiotic toothpaste. Shah *et al* (45) reported favorable changes in plaque and gingival indices with probiotic mouth rinse. Vasoglou *et al* (46) subsequently demonstrated significant treatment-by-time effects for the modified plaque index (P=0.01) and gingival index (P<0.001) in the fixed-appliance trial.

Conversely, Benic *et al* (47) found no significant treatment effect of *Streptococcus salivarius* M18 on either the plaque or gingival index. Kohar *et al* (18) observed numerical improvements in plaque, interdental hygiene and papillary bleeding indices following probiotic lozenges or drinks, although the between-group differences were not statistically significant. Kusnoto *et al* (42) reported no change in the orthodontic plaque index and no probiotic-specific benefit. Thus, favorable periodontal effects were observed in several studies, but were not reproduced consistently across interventions.

Plaque acidogenicity and salivary parameters. The effects on functional salivary and plaque parameters

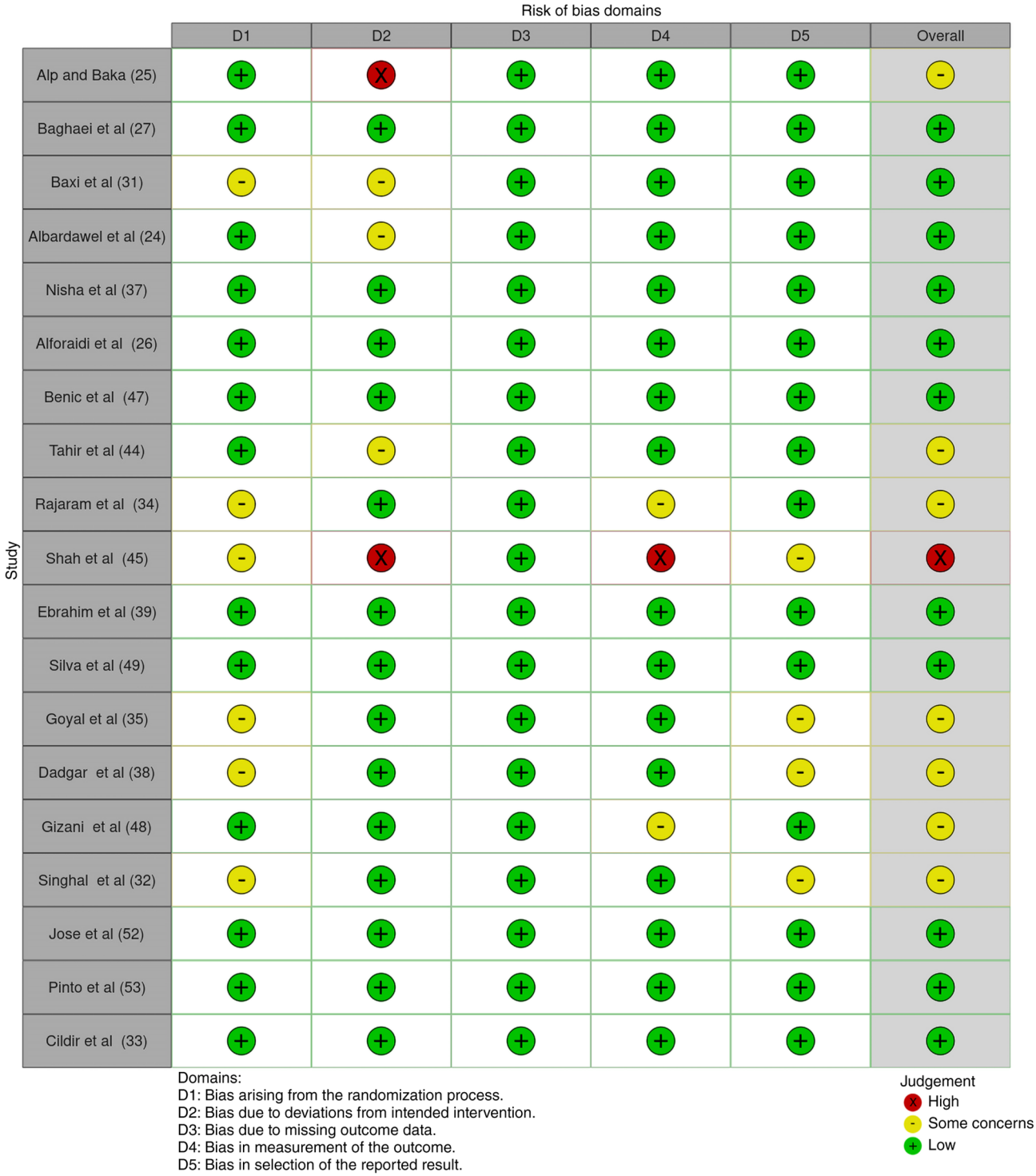

Figure 2. Risk-of-bias assessment of randomized controlled trials using the Cochrane Risk of Bias 2 (RoB 2) tool.

appeared outcome-specific. Alp and Baka (25) reported an improvement in salivary buffering capacity with probiotic toothpaste, while salivary flow rate was not significantly altered. Alforaidi *et al* (26) demonstrated significant reduction in plaque acidogenicity following 3 weeks of *Lactobacillus reuteri* administration, despite the absence of significant changes in the counts of cariogenic bacteria. This finding indicates that changes in plaque metabolic activity may occur without a corresponding measurable reduction in bacterial count.

White spot lesions. Evidence regarding prevention of enamel demineralization was limited. In the study by Gizani *et al* (48), which directly evaluated white spot lesion development over a mean intervention period of ~17 months, reported new white spot lesions in 20 of 42 participants receiving *L. reuteri* compared with 17 of 43 receiving placebo, with no significant difference between groups. The corresponding risk ratio was ~1.21, providing no evidence of a protective probiotic effect on white spot lesion development during fixed orthodontic treatment (48).

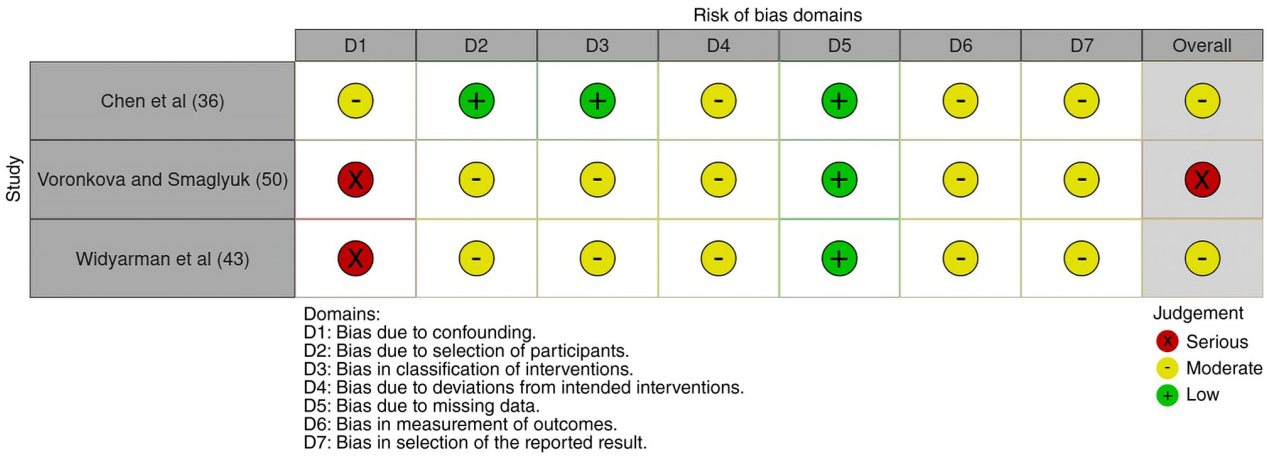

Figure 3. Risk-of-bias assessment of non-randomized intervention studies using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool.

Halitosis. Benic *et al* (47) evaluated *Streptococcus salivarius* M18 for orthodontic-associated halitosis and demonstrated a significant treatment-by-time effect for volatile sulfur compounds, despite no significant effects on plaque or gingival indices. Vasoglou *et al* (46) also reported significant treatment-by-time effects for hydrogen sulfide (P=0.03) and total volatile sulfur compounds (P=0.03); the findings for methyl mercaptan were mixed, and no significant treatment-by-time interaction was reported for dimethyl sulfide. These findings suggest that effects on halitosis-related outcomes may occur independently of changes in conventional plaque or gingival indices.

Traumatic oral lesions and patient-centered outcomes. Probiotics also exhibited potential effects on orthodontic-associated traumatic oral lesions. Baghaei *et al* (27) reported significantly fewer traumatic ulcers and lower pain scores with probiotic lozenges than with placebo. Silva *et al* (49) reported fewer days with traumatic lesions with *Lactobacillus brevis* CD2 (2.5±1.0 vs. 4.9±3.0 days; P=0.018) and lower pain scores (P=0.039), while OHIP-14 did not exhibit a significant between-group difference. These findings suggest a possible benefit for soft-tissue morbidity, although evidence remains based on a limited number of studies and relatively small samples.

Inflammatory and biochemical outcomes. Biochemical and inflammatory outcomes were reported in a smaller number of studies. Voronkova and Smaglyuk (50) reported favorable changes in oral-fluid biochemical markers, including reductions in malondialdehyde, elastase, and urease with increases in catalase, lysozyme and the antioxidant-prooxidant index (API). Chandrashekaraiah *et al* (40) reported a significant reduction in salivary 8-hydroxy-2'-deoxyguanosine over nine months in the probiotic group, although the reduction was smaller than with the active fluoride and propolis comparators. Erdemir *et al* (51) reported increased gingival crevicular fluid IL-10 and decreased TNF-α after probiotic use; the TNF-α T1/T0 ratio was significantly lower than in the control group (P=0.002).

Patient-centered outcomes and adverse effects. Patient-reported outcomes and tolerability were infrequently assessed. Nisha *et al* (37) found no significant differences in taste, burning, or staining outcomes, and Chandrashekaraiah *et al* (40) reported no significant intergroup differences in taste, burning, or overall satisfaction. Silva *et al* (49) reported lower pain with L. brevis CD2 but no significant between-group effect on OHIP-14. Where adverse events were reported, no severe probiotic-related adverse events were identified; however, adverse-event reporting was not uniform across studies.

Study-level evidence mapping of clinical and microbiological outcomes. Study-level evidence mapping demonstrated considerable heterogeneity in the direction of probiotic-associated effects across the included studies and outcome domains (Table II). Amongst the 28 studies included in the present scoping review, microbiological changes were evaluated most frequently. However, the findings were inconsistent across microorganisms and time points studied. An improvement was noted in the gingival, plaque and periodontal outcome for certain clinical indices. These findings were also heterogeneous. With regard to plaque acidogenicity, traumatic oral lesions and halitosis related outcomes the findings were consistent and favorable. Evidence for other clinical parameters such as white spot lesions and patient-centered outcomes was either limited or inconclusive. Inflammatory and biochemical outcomes were favorable but the findings were heterogeneous (Table III).

Risk of bias across the included studies. Risk-of-bias assessments demonstrated variation in methodological quality across the included studies. Of the 24 randomized studies assessed using the Cochrane RoB 2 tool, 11 were judged to be at low overall risk of bias, 12 raised some concerns, and one was judged to be at high risk of bias. Concerns most commonly related to insufficient reporting of the randomization or allocation-concealment process, limitations in blinding for interventions with distinguishable delivery modalities, and potential selective reporting. Among the four non-randomized studies assessed using ROBINS-I, two were judged to have moderate overall risk of bias and two serious overall risk of bias, with concerns arising principally from confounding, participant selection, and the non-randomized allocation of interventions (Figs. 2 and 3).

Table II. Characteristics of the 28 included studies.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
1	Alp and Baka, 2018	Turkey	RCT	45; 12-17 years	Fixed orthodontic appliances	Kefir, 100 ml twice daily; separate toothpaste arm using GD toothpaste containing bacteriocin extracted from lactic acid bacteria, twice daily	6 weeks	Control	Salivary flow, buffering capacity, *S. mutans, Lactobacillus*	Significantly lower salivary *S. mutans* levels in both intervention groups vs. control at six weeks. No significant between-group differences in lactobacilli, salivary buffering capacity or flow rate. Buffering capacity improved within the toothpaste group only.	NR	Some concerns	(25)
2	Baghaei *et al*, 2024	Iran	Double-masked RCT	64; 3 lost; >12 years	Fixed orthodontic appliances	Lactogum probiotic lozenge, once daily	28 days	Placebo lozenge	Oral ulcers, ulcer number, pain VAS	Fewer ulcers and lower pain with probiotics; P<0.001	NR	Low	(27)
3	Baxi *et al*, 2023	India	RCT	160 final; 14-29 years	Fixed appliance mechano-therapy/ orthodontic braces	Probiotic lozenge, sachet and beverage	NR	No-probiotic control	Plaque *S. mutans* colony count	Significant reduction in *S. mutans* with probiotic preparations; lozenge showed greatest reduction	NR	Low	(31)
4	Chen *et al*, 2022	Taiwan	Prospective non-randomized intervention	33; 12-30 years	Fixed orthodontic appliances	Biofermin tablets; Lacto-bacteria 3 mg + Glycobacteria 2 mg; 3 tablets x3/day	1 month	Self-control	Salivary *S. mutans* and Lactobacilli	Slight reduction, but not statistically significant	None reported	Moderate	(36)
5	Albardawel *et al*, 2024	Syria	Two-arm parallel RCT; single-blind	50 (25/group); 18-25 years	Fixed metal appliances; non-extraction treatment	Prodentis® probiotic tablets	6 months	Control	PI, GI, PBI, PD	Significantly lower PI, GI, PBI and PD in probiotic group	NR	Low	(24)
6	Nisha *et al*, 2023	India	Randomized triple-blind trial	90; 12-35 years	Fixed orthodontic appliances/ brackets	*S. boulardii* probiotic mouthwash	30 days	Aloe vera and 0.2% amine-fluoride mouthwash	Plaque *S. mutans* by qPCR; acceptability	No significant between-group difference; significant intragroup reductions	Sensory effects (taste, burning, staining) assessed; no major safety signal reported	Low	(37)

Table II. Continued.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
7	Alforaidi *et al*, 2021	Sweden	Randomized double-blind placebo-controlled trial	28; 1 dropout; NR	Fixed orthodontic appliances	*L. reuteri* DSM 17938 + ATCC PTA 5289; 5 drops twice daily	3 weeks	Placebo drops	Plaque acidogenicity, *L. reuteri*, *S. mutans*, lactobacilli, salivary parameters	Significant improvement in plaque pH/AUC; no significant salivary bacterial differences	NR	Low	(26)
8	Benic *et al*, 2019	New Zealand	Randomized triple-blind placebo-controlled trial	64; NR	Fixed orthodontic braces	*S. salivarius* BLIS M18; 2 lozenges/day	1 month + 3-month follow-up	Placebo	PI, GI, VSC/halitosis, dental biofilm microbial composition assessed by 16S rRNA sequencing	No significant PI/GI effect; VSC decreased during follow-up	NR	Low	(47)
9	Widyarman *et al*, 2022	Indonesia	Prospective single-arm pre-post interventional study	20; 18-23 years	Fixed orthodontic appliances	*L. reuteri* Prodentis lozenges	14 days	Pre-intervention baseline; within-participant comparison; no separate control/placebo group	OHIS, PBI, salivary microbiome	Oral-health indices improved; no significant alpha-diversity change	NR	Moderate	(43)
10	Tahir *et al*, 2025	Pakistan	Prospective open-label RCT	44; 18-50 years	Fixed orthodontic braces	Probiotic toothpaste containing *L. paracasei* Dental-Lac	4 weeks	Regular toothpaste	PI, gingival bleeding index	Significantly lower gingival score; plaque difference NS	No significant adverse events or side effects reported	Some concerns	(44)
11	Rajaram *et al*, 2023	India	Randomized parallel-arm trial	30; 19-32 years	Fixed orthodontic brackets	Probiotic-impregnated resin composite containing *L. rhamnosus* GG	2 months	Conventional resin composite	Plaque *S. mutans*	Significant reduction in experimental group	NR	Some concerns	(34)
12	Shah *et al*, 2019	India	RCT	30 initially; NR	Fixed orthodontic appliances	Probiotic mouthwash prepared from Sporlac sachets dissolved in distilled water (reported concentration:	NR	Chlorhexidine and no-mouthwash controls	PI, GI, *S. mutans*	Numerical reductions in plaque index, gingival index and salivary *S. mutans* counts were reported; inconsistencies between the narrative	NR	High	(45)

Table II. Continued.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
						$2x10^8$ CFU/g); used twice daily after brushing for 28 days				and statistical tables prevent a clear conclusion regarding comparative benefit.			
13	Ebrahim *et al*, 2022	Canada	Double-blind placebo-controlled RCT	60; 2 withdrawals; 11-18 years	Fixed orthodontic appliances (≥6 mo at enrolment)	Lorodent® probiotic lozenge containing *S. salivarius* K12 + 5 *Lactobacillus* spp.	28 days + 28-day follow-up	Placebo	PI, composite PI, *S. mutans* DNA, adverse events	No significant difference in PI or *S. mutans* DNA	Safety/ adverse events monitored; treatment-related adverse events not clearly quantified	Low	(39)
14	Silva *et al*, 2021	Brazil	Randomized double-blind placebo-controlled trial	20; 14-57 years	Fixed orthodontic appliance (early treatment)	*L. brevis* CD2; 12 billion CFU/day	21 days	Placebo	Traumatic oral lesions, pain, OHIP-14	Fewer lesion days and lower pain; OHIP-14 difference NS	One participant reported mild diarrhea	Low	(49)
15	Goyal *et al*, 2019	India	RCT	30 initially; 15-35 years	Fixed orthodontic appliances	Probiotic mouth-wash containing *L. reuteri*, *L. rhamnosus*, *B. longum*, B. *bifidum* + prebiotics	6 months	Brushing only; amine-fluoride mouthwash	Subgingival *P. gingivalis*	Significant reduction in *P. gingivalis* with probiotic mouthwash	None reported	Some concerns	(35)
16	Dadgar *et al*, 2021	Iran	Randomized placebo-controlled trial	38; 12-20 years	Fixed orthodontic appliances/ brackets	*L. plantarum* mouth rinse	2 weeks	0.05% sodium fluoride; placebo	Plaque *S. mutans* CFU	Probiotic reduction NS; fluoride significantly reduced *S. mutans*	None reported	Some concerns	(38)
17	Gizani *et al*, 2016	Greece	Randomized double-blind placebo-controlled trial	85; Mean 15.9 years	Fixed appliances on ≥8 maxillary anterior teeth	*L. reuteri* DSM 17938 + ATCC PTA 5289; 10^8 CFU/ strain/lozenge	Mean 17 months	Placebo	White-spot lesions; salivary *S. mutans*/ *Lactobacillus*; oral hygiene	No significant difference in WSL development	No adverse events reported; 8 participants disliked lozenge taste	Some concerns	(48)
18	Singhal *et al*, 2019	India	Randomized double-blind placebo-controlled trial	30; 3 lost; 8-15 years	Fixed interceptive orthodontic appliance	Probiotic yoghurt (L. acidophilus + Bifidobacteria) and Indian curd	2 weeks	Ultra-heated yoghurt	Salivary/ plaque *S. mutans*	Probiotic yoghurt significantly reduced salivary and plaque *S. mutans*	None reported	Some concerns	(32)

Table II. Continued.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
19	Jose *et al*, 2013	India	Double-blind RCT	60; 14-29 years	Fixed orthodontic brackets	Probiotic curd, 200 ml/day; probiotic tooth-paste twice daily	30 days	No-probiotic control	Plaque *S. mutans* by PCR	Significant *S. mutans* reduction in probiotic groups	None reported	Low	(52)
20	Pinto *et al*, 2014	Brazil	Double-blind randomized placebo-controlled crossover trial	30; 4 dropouts; 10-30 y (median 15)	Fixed orthodontic appliances	Yogurt containing *B. animalis* subsp. lactis DN-173010; 200 g/day	2 weeks/ intervention + 4-week washout	Control yogurt	Salivary/ plaque *S. mutans*, Lactobacilli, total micro-organisms	No significant *S. mutans*/ *Lactobacillus* reduction; total microbial count decreased	None reported	Low	(53)
21	Voronkova and Smaglyuk, 2018	Ukraine	Prospective controlled non-randomized clinical study	45; 18-24 years	Bracket system	Probiotic mucosal gel, twice daily	2 months	Bracket therapy alone; non-orthodontic control	MDA, elastase, urease, lysozyme, catalase, API, dysbiosis	Reduced MDA/ elastase/urease and increased catalase/ lysozyme/API	NR	Serious	(50)
22	Cildir *et al*, 2009	Turkey	Double-blind randomized crossover trial	26 enrolled; 24 completed; 12-16 years; 12-16 years	Fixed orthodontic appliances	*B. animalis* subsp. lactis DN-173010 probiotic yoghurt, 200 g/day ($2x10^8$ CFU/g)	2 weeks per intervention period; 6-week washout	Identical/ non-probiotic control yoghurt	Salivary *S. mutans* and Lactobacilli	Significant reduction in salivary *S. mutans* after probiotic yoghurt ($P<0.05$); proportion with high counts fell from 63 to 21%. No significant change in Lactobacilli.	None reported	Low	(33)
23	Kohar *et al*, 2015	Indonesia	Randomized clinical trial	30 (10/group); 18-25 years	Fixed orthodontic appliances	BioGaia® *L. reuteri* Prodentis lozenge: ≥200 million live organisms, 1/day; Yakult® *L. casei* Shirota: 65 ml/day, ≥6.5 million viable cells	14 days	SRP + plaque-control instruction	PII, HYG, PBI	PII decreased: control 1.19→1.03; *L. reuteri* 1.22→0.91; *L. casei* 1.01→0.76. PBI: 0.82→0.58, 1.01→0.67 and 0.49→0.43, respectively. Between-group differences NS: PII P=0.173, HYG P=0.196, PBI P=0.053	NR	Some concerns	(18)
24	Chandra-shekaraiah *et al*, 2025	India	Prospective parallel-group triple-blind RCT	90 (30/group); 12-35 years	Fixed orthodontic appliances	Probiotic mouthwash containing *L. reuteri* + *S. salivarius* K12; twice daily	9 months	10% propolis mouthwash; 0.05% sodium fluoride mouthwash	Plaque *S. mutans* (qPCR), salivary 8-OHdG, Ct values,	Probiotic significantly reduced *S. mutans* and 8-OHdG over time, but reductions were smaller than with	Well tolerated; no significant differences in taste/	Some concerns	(40)

Table II. Continued.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
									patient-reported acceptability	fluoride and propolis; patient-reported outcomes did not differ significantly	burning/ overall satisfaction		
25	Vasoglou *et al*, 2026	Greece	Triple-blind randomized placebo-controlled parallel trial (fixed-appliance trial only)	60 randomized; 59 analyzed; 12-18 years	Fixed-appliance trial/ orthodontic brackets	*L. salivarius* Oral S1 probiotic lozenge; 1/day at bedtime after toothbrushing	1 month + 2-month post-intervention follow-up	Identical placebo lozenge	PI-M, GI, H2S, CH3SH, (CH3)2S, total VSC	Significant treatment x time effects for PI-M, GI, H2S and total VSC; benefits diminished after probiotic discontinuation	NR	Some concerns	(46)
26	Jabbareh *et al*, 2025	Iran	Single-blind randomized clinical trial	30 (15/group); >15 years; mean age 20.70±4.96 years	Fixed orthodontic appliances; elastomeric rings sampled	Kefir drink, 100 ml every 12 h	20 days	0.2% chlorhexidine mouthwash	Cultivable oral bacterial counts from orthodontic elastomeric rings	Both groups showed significant bacterial reduction over time. GEE showed lower bacterial counts with kefir vs. CHX (coefficient -316,511.1; 95% CI-568,839.2 to -64,183.1; P=0.014), although the between-group difference at 20 days was not significant (P=0.148).	NR	Some concerns	(41)
27	Kusnoto *et al*, 2025	Indonesia	Double-blind three-arm randomized controlled clinical trial	24 (8/group); 18-23 years	Fixed orthodontic appliances	*L. paracasei* probiotic toothpaste; twice-daily brushing	1 month	CPC toothpaste; amyloglucosidase-glucose oxidase enzyme toothpaste	Salivary *P. gingivalis* and *A. actinomycetemcomitans* by qPCR; Orthodontic Plaque Index (OPI)	*P. gingivalis* and *A. actinomycetemcomitans* decreased in all three groups. No significant treatment x group interaction for *P. gingivalis* (P=0.367) or *A. actinomycetemcomitans* (P=0.298). OPI remained unchanged.	NR	Some concerns	(42)

Table II. Continued.

Study no.	Authors, year of publication	Country[a]	Design	Sample sizeage	Orthodontic appliance	Probiotic intervention	Duration	Comparator	Outcomes	Main findings	Adverse events	RoB	(Refs.)
28	Erdemir *et al*, 2025	Turkey	Prospective case-control study	60 fixed-orthodontic patients (30 probiotic, 30 control); NR	Fixed orthodontic appliances	Motiflor AS chewable probiotic tablet, once daily for 15 days	15 days; assessment at baseline and day 21	Routine orthodontic treatment without probiotic	Gingival crevicular fluid IL-10 and TNF-α measured by ELISA	IL-10 increased and TNF-α decreased in the probiotic group. The TNF-α T1/T0 ratio was significantly lower in the probiotic group than control (P=0.002).	NR	Serious	(51)

[a]Country reflects the study setting reported in the article/source material, not journal publication country. NR, not reported in the uploaded source material; RCT, randomized controlled trial; VAS, visual analogue scale; PI, plaque index; GI, gingival index; PBI papilla bleeding index; PD, probing depth; VSC, Volatile Sulphur Compounds; OHIS Simplified Oral Hygiene Index; PBI, Papillary Bleeding Index.

Discussion

The present scoping review mapped and synthesized the existing clinical evidence on the use of probiotics for oral health maintenance during orthodontic treatment. Orthodontic appliances are known to increase plaque retention and thereby alter the oral microbial ecosystem, predisposing patients to gingival inflammation, enamel demineralization, and shifts in cariogenic and periodontopathogenic bacterial levels. Probiotic interventions have been explored as adjunctive strategies aimed at modulating the oral microbiome and improving clinical outcomes during orthodontic care.

Principal findings. Across the included studies, probiotics demonstrated variable and outcome-specific effects on oral health parameters during orthodontic treatment. Several randomized controlled trials reported reductions in salivary or plaque *Streptococcus mutans* levels following probiotic administration, particularly when probiotics were delivered as lozenges, curd, yogurt, or toothpaste formulations (25,31-34,52). By contrast, other trials reported no statistically significant differences between probiotic and control groups despite observing intragroup reductions over time (26,36-39,40,53). These varied findings highlight that probiotic efficacy in orthodontic patients is not uniform and may depend on multiple interrelated factors.

With respect to clinical periodontal outcomes, improvements in gingival indices, bleeding scores, or overall periodontal health were observed in several studies, particularly those employing longer intervention durations and tablet- or lozenge-based probiotic delivery (24,43-46). However, changes in plaque indices were less consistent, with multiple studies reporting no significant intergroup differences (18,39,42,47). Evidence supporting the prevention of enamel demineralization or white spot lesion development was limited, with one long-term randomized trial demonstrating no significant protective effect of *Lactobacillus reuteri* lozenges on white spot lesion incidence (48).

Influence of probiotic strains and delivery systems. The included studies evaluated a broad spectrum of probiotic strains, predominantly belonging to *Lactobacillus*, *Bifidobacterium* and *Streptococcus* species. Strain-specific effects were evident across trials. Preparations containing *Lactobacillus reuteri* were associated with improvements in plaque acidogenicity and halitosis-related outcomes but showed inconsistent effects on cariogenic bacterial counts and enamel outcomes (24,26,43,46,48). *Lactobacillus brevis* CD2 demonstrated beneficial effects in reducing traumatic oral lesions and pain during early orthodontic treatment, suggesting a potential role beyond plaque control (49).

The modes of probiotic delivery included lozenges, tablets, mouth rinses, toothpastes, gels and fermented dairy products. Favorable, as well as null or mixed findings were noted across these delivery systems, precluding firm conclusions regarding the superiority of any particular delivery modality. Dairy-based vehicles such as yogurt and curd also showed heterogeneous findings, with some studies reporting reductions in cariogenic microorganisms and others demonstrating no probiotic-specific benefit (30,31,52,53). These inconsistencies

Table III. Outcome-specific evidence for probiotic use during orthodontic treatment.

Outcome domain	Contributing studies	Key study-level findings	Direction of evidence (n)	Total
Microbiological	Alp and Baka (25); Baxi (31); Chen (36); Nisha (37); Alforaidi (26); Widyarman (43); Rajaram (34); Shah (45); Ebrahim (39); Goyal (35); Dadgar (38); Gizani (48); Singhal (32); Jose (52); Pinto (53); Cildir (33); Chandrashekaraiah (40); Jabbareh (41); Kusnoto (42)	Effects on *S. mutans*, Lactobacilli, periodontal pathogens and microbiome measures were inconsistent. Several studies reported significant microbial reductions, whereas others showed no probiotic-specific effect or discordant findings across organisms or time points.	Favorable: 6; NS: 8; Mixed: 5	19
Gingival, plaque and periodontal	Albardawel (24); Benic (47); Widyarman (43); Tahir (44); Shah (45); Ebrahim (39); Kohar (18); Vasoglou (46); Kusnoto (42)	Improvements were reported in PI, GI, PBI, bleeding and/or periodontal measures in some trials. Other studies showed no significant effects or improvements restricted to selected indices.	Favorable: 4; NS: 3; Mixed: 2	9
Plaque acidogenicity and salivary outcomes	Alp and Baka (25); Alforaidi (26)	Both studies reported favorable effects on acidogenicity or buffering-related outcomes. However, individual salivary measures were not uniformly altered, so the evidence is favorable but outcome-specific.	Favorable: 2; NS: 0; Mixed: 0	2
White spot lesions	Gizani (48)	No significant reduction in the development of new white spot lesions was demonstrated.	Favorable: 0; NS: 1; Mixed: 0	1
Halitosis and volatile sulphur compounds	Benic (47); Vasoglou (46)	Both studies reported favorable effects on halitosis or volatile sulphur compound outcomes. Vasoglou *et al* reported significant effects for H2S and total volatile sulphur compounds.	Favorable: 2; NS: 0; Mixed: 0	2
Traumatic oral lesions	Baghaei (27); Silva (49)	Probiotic use was associated with fewer or shorter-duration traumatic lesions and reduced pain.	Favorable: 2; NS: 0; Mixed: 0	2
Patient-centred outcomes	Baghaei (27); Nisha (37); Silva (49); Chandrashekaraiah (40)	Pain improved in Baghaei *et al* Acceptability and OHIP-related findings were generally non-significant, resulting in heterogeneous patient-reported evidence overall.	Favorable: 1; NS: 2; Mixed: 1	4
Inflammatory and biochemical outcomes	Voronkova and Smaglyuk (50); Chandrashekaraiah (40); Erdemir (51)	Favourable changes were reported in inflammatory or oxidative biomarkers in two studies. Chandra-shekaraiah *et al* showed mixed comparative findings.	Favorable: 2; NS: 0; Mixed: 1	3

Interpretation: Favorable indicates a probiotic-associated benefit; NS indicates no statistically significant probiotic-specific difference; Mixed indicates discordant or outcome-specific findings within a study or across studies. The present scoping review included 28 unique studies. Studies could contribute to more than one outcome domain; therefore, domain-specific totals are not mutually exclusive and should not be summed to obtain the total number of included studies. GI, gingival index; H2S, hydrogen sulfide; NS, no statistically significant probiotic-specific difference; OHIP, Oral Health Impact Profile; PBI, papillary bleeding index; PI, plaque index; VSC, volatile sulphur compounds.

underscore the absence of standardized formulations, dosing regimens, and durations of administration of probiotics.

Methodological quality and risk of bias. The methodological quality of the included studies varied considerably. Several randomized controlled trials were judged to be at low overall risk of bias (24,26,27,31,37,39,47,46,49,50), whereas other randomized studies raised some concerns or were judged to be at high risk of bias. The four non-randomized studies had a moderate or serious overall risk of bias (36,43,50,51). Heterogeneity in outcome measures, ranging from microbiological assays to clinical indices and patient-reported outcomes, further limited direct comparison across studies. Notably, studies utilizing objective microbiological assessments, including culture-based methods and quantitative PCR, provided more reproducible outcomes than those relying solely on clinical indices. However, even among microbiologically focused trials, variability in sampling sites, detection methods, and reporting metrics contributed to inconsistent findings.

Notably, studies utilizing objective microbiological assessments, including culture-based methods and quantitative PCR, provided more reproducible outcomes than those relying solely on clinical indices. However, even among microbiologically focused trials, variability in sampling sites, detection methods and reporting metrics contributed to inconsistent findings.

Clinical implications. From a clinical perspective, no severe probiotic-related adverse events were identified among studies that reported adverse events; however, adverse-event reporting was inconsistent. Probiotic interventions may provide adjunctive benefits for selected outcomes, such as reduction of cariogenic bacteria, improvement in gingival health, or mitigation of traumatic oral lesions. Nevertheless, probiotics should not be considered as substitutes for established preventive strategies, including mechanical plaque control and fluoride use, and regular professional check-up.

Plaque-related outcomes require interpretation with caution in the context of probiotic-based interventions. Several included studies assessed plaque index or other measures of plaque accumulation; however, the direction and magnitude of findings lacked consistency. Moreover, reduced plaque accumulation does not necessarily translate directly into improved gingival health or reduced caries risk, particularly when plaque composition and cariogenic activity are not simultaneously assessed. Accordingly, plaque-related outcomes were included in the present scoping review as secondary clinical measures and were interpreted alongside gingival, periodontal, enamel and microbiological outcomes rather than as standalone clinical efficacy indicators.

The variability in findings may be related to differences in probiotic strains, formulations, dosage, treatment duration, orthodontic appliance type, comparator interventions, and outcome-assessment methods. Consequently, the evidence should be interpreted by outcome domain rather than as a single overall treatment effect (Table III). Given the diversity of evidence, clinicians should exercise caution when recommending probiotic products during orthodontic treatment.

Future perspectives. Future studies using clearly defined clinical and microbiological endpoints, standardized sampling protocols, longer follow-up periods, and adequately powered randomized controlled designs are warranted. The optimization of probiotic use demands standardization of study protocols, including characterization of probiotic strains, viable dose, administration frequency, treatment duration, and delivery systems. Integration of microbiome sequencing with clinical, immunological, and metabolic measures may provide a more comprehensive understanding of how probiotic interventions influence the oral ecosystem during orthodontic treatment.

Personalized approaches represent another area of future research, as baseline microbial composition and host-related factors may influence the response to probiotic interventions. However, such approaches require validation in well-designed clinical studies before they can be translated into routine orthodontic practice.

Limitations of the scoping review. Considerable heterogeneity was observed across the included studies in terms of probiotic strains, formulations, delivery systems, dosages, intervention durations, comparators, follow-up periods and outcome measures. This limited direct comparison between studies and precluded meaningful quantitative pooling of the findings. In addition, the evidence base included studies with variable methodological quality and risk of bias, which should be considered when interpreting favorable findings. Several outcome domains were represented by only a small number of studies, particularly white spot lesion development, halitosis, traumatic oral lesions, patient-reported outcomes, and inflammatory or biochemical markers, limiting the strength of conclusions that can be drawn for these outcomes.

The present scoping review was restricted to clinical studies on patients undergoing fixed orthodontic treatment; consequently, the findings cannot be extrapolated to patients treated with clear aligners or other orthodontic appliances. In addition, heterogeneity in microbiological sampling sites, laboratory techniques, and reporting metrics limited comparison of microbiological outcomes across studies. Reporting of adverse-effects was also inconsistent, preventing definitive conclusions regarding comparative tolerability across probiotic formulations.

In conclusion, probiotic interventions have demonstrated favorable findings for selected microbiological, gingival, periodontal, and patient-centered outcomes during fixed orthodontic treatment; however, these findings were not consistently observed across studies or outcome domains. Some studies reported reductions in cariogenic and periodontal microorganisms and improvements in gingival parameters, while others demonstrated no significant probiotic-associated benefit. Evidence regarding the prevention of white spot lesions remains limited and with no clear beneficial effects.

Considerable heterogeneity was observed in probiotic strains, formulations, delivery systems, intervention duration, outcome measures, follow-up periods, and methodological quality. Consequently, the current evidence is insufficient to support definitive recommendations regarding the routine clinical use of probiotics as an adjunct during fixed orthodontic treatment. Well-designed, adequately powered randomized controlled trials using standardized probiotic preparations, clinically relevant outcome measures, and longer follow-up

periods are required to determine whether probiotic interventions provide consistent and clinically meaningful benefits and to clarify the strains, formulations, delivery systems, and treatment durations most appropriate for further clinical evaluation.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

AK was involved in the conceptualization of the study, in the study methodology, and in the writing and preparation of the original draft of the manuscript. SPD was involved in the study methodology, in data validation, and in the preparation of the original draft of the manuscript. NTH was involved in the design of the study, in the drafting of the manuscript and in the processing of the figures. GM was involved in data acquisition, analysis and supervised the study. All the authors were also involved in the reviewing and editing of the manuscript. All authors have read and approved the final manuscript. AK and SPD confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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