applied sciences

MDPI

*Systematic Review*

# The Influence of Probiotics in Halitosis and Cariogenic Bacteria: A Systematic Review and Meta-Analysis

**Victoria Offenbächer [1], Roberto Lo Giudice [2,*], José Nart [3], Francisco Real-Voltas [1], María Arregui [1], Alice Rose Greethurst [1] and Cosimo Galletti [1]**

[1] School of Dentistry, Department of Integrated Dentistry, International University of Catalonia, Sant Cugat del Vallès, 08195 Barcelona, Spain; offenbaechervictoria@uic.es (V.O.); freal@uic.es (F.R.-V.); mariaarregui@uic.es (M.A.); alice.greethurst@uic.es (A.R.G.); cgalletti@uic.es (C.G.)
[2] Department of Human Pathology of Adults and Developmental Age, Messina University, 98100 Messina, Italy
[3] Department of Periodontology, International University of Catalonia, Sant Cugat del Vallès, 08195 Barcelona, Spain; josenart@uic.es
* Correspondence: roberto.logiudice@unime.it

**Abstract:** Background: The aim of this systematic review was to evaluate the therapeutic potential of probiotics in patients with halitosis and to assess whether probiotics can also be implemented as a preventative tool in oral health. Secondary objectives included the effect of probiotics on oral-health-related quality of life, as well as their safety. Materials and methods: An electronic literature search in Medline (PubMed), Scopus, Web of Science, and the Cochrane library was carried out for the identification and selection of relevant randomized controlled trials. Eligibility was based on inclusion criteria, which included RCTs published after 2013, and the outcome variables were volatile sulfur compound (VSC) levels, organoleptic scores, plaque, or saliva samples to assess cariogenic bacteria counts and/or pH levels. Results: Out of 192 identified records, 16 randomized controlled trials were included. Ten of those studied the effects of probiotics on halitosis and the other six analyzed the effect of probiotics on oral health parameters, such as cariogenic bacteria counts, pH levels, and salivary flow and quality. A total of 921 patients were evaluated. The risk of bias was assessed using the Cochrane risk-of-bias assessment tool version 2. Conclusions: Probiotics exhibit the potential for oral health management by reducing VSC levels, improving saliva quality, and enhancing oral-health-related quality of life. Combining probiotics with tongue scraping may sustain VSC reduction, while symbiotics show potential in reducing tongue coating. However, different bacterial strains have been used in the included studies; hence, the conclusions cannot be generalized, being one of the main limitations of this review. Future research should explore the probiotics' potential to persist in the oral cavity post-treatment and employ standardized methodologies for conclusive efficacy assessment.

**Keywords:** probiotics; halitosis; cariogenic bacteria; systematic review



**Citation:** Offenbächer, V.; Lo Giudice, R.; Nart, J.; Real-Voltas, F.; Arregui, M.; Greethurst, A.R.; Galletti, C. The Influence of Probiotics in Halitosis and Cariogenic Bacteria: A Systematic Review and Meta-Analysis. *Appl. Sci.* **2024**, *14*, 6639. https://doi.org/10.3390/app14156639

Academic Editor: Bruno Chrcanovic

Received: 10 July 2024
Revised: 25 July 2024
Accepted: 26 July 2024
Published: 30 July 2024



## 1. Introduction

One of the most prevalent oral pathologies is periodontal disease, counting approximately 750 million affected individuals globally [1]. Periodontal disease affects the supporting tissues of the teeth, also called the periodontium, including the gingiva, periodontal ligament, cementum, and alveolar bone, and can be defined as a multi-stage illness of inflammatory and infection-driven nature [2,3]. A dysbiosis of the subgingival microbiome is the main etiology of periodontal disease, caused by an excessive accumulation of dental plaque and beginning in the form of gingivitis, which is a reversible inflammation of the gingiva, presenting typical signs and symptoms of inflammation. However, if left untreated, it can progress into an irreversible condition known as periodontitis, which is the advanced stage of periodontal disease. Its clinical manifestations include deep, subgingival inflammation, accompanied by alveolar bone and connective tissue loss [3].

Smokers are at an increased risk of developing periodontal disease, demonstrating a likelihood of developing periodontal disease three times higher than non-smokers [2,4]. Diabetes mellitus has been shown to cause a similar effect; inflammatory mediators are found in higher concentrations in gingival crevicular fluids and saliva in diabetics with periodontal disease compared to healthy individuals with periodontal disease [4]. Other modifiable factors that have been linked to periodontal disease are hormonal changes in females, obesity, poor oral hygiene, and stress [2–4], whereas non-modifiable factors include age [4], gender, genetics, ethnicity, and socioeconomic status [2,3].

Diagnostic measurements of periodontal disease include specific clinical indexes, such as bleeding on probing (BOP), plaque index (PII), gingival index (GI), periodontal pocket depth (PPD), clinical attachment level (CAL), gingival recession (REC), and gingival crevicular fluid (GCF) volume [3]. In addition to the clinical indexes, an evaluation of outcomes reported by the patient (bleeding gums while brushing, halitosis, tooth sensitivity, etc.) is carried out, as well as a radiographic assessment. Combining the periodontal examination, the radiographic evaluation, and the patient's medical history, a clinical diagnosis of periodontal disease can be made. According to the American Academy of Periodontology (AAP), periodontitis can be classified into four stages and three grades. Meanwhile, the four stages (I, II, III, and IV) are based on severity, complexity, and extent, and the three grades (A, B, and C) are based on the disease progression and its rate (slow, moderate, and fast) [3,5].

Periodontal treatment involves the elimination of both supra- and subgingival plaque through Scaling and Root Planning (SRP). Adjunctive to SRP, surgical procedures such as resective or regenerative surgery can be performed. In addition, antibiotics are often administered as adjunctive therapy; however, antibiotics may cause undesired side effects or may even be contraindicated in certain situations. Furthermore, bacterial resistance to antibiotics due to their excessive clinical implementation is an increasing global problem, and there is a frequent recolonization of pathogenic bacteria once antibiotic therapy is finished [6]. Hence, therapeutic alternatives are being investigated, one of them being probiotics [3].

Probiotics are non-pathogenic live organisms with potential benefits for the host if taken in adequate amounts. Common probiotics are various species of the genera *Lactobacillus* and *Bifidobacterium*, *Bacillus coagulans*, *Streptococcus thermophilus*, *Enterococcus faecium*, and *Saccharomyces cerevisiae* [7]. They can be taken in two forms, either in fermented foods or as supplements in the form of powder, capsule, or tablet. For them to show a clinical effect, the probiotic microorganisms must be viable. The quantity of viable organisms determines the dosage of probiotic foods and supplements; clinical trials have shown that effective therapeutic results have been achieved with a daily intake ranging from 107 to 1011 live bacteria [7]. There are various mechanisms that could explain their positive effects on the human body, such as modifying the gut pH, decreasing the quantity of pathogenic bacteria in the gut, and competing for nutrients with pathogens, among others, and they have already been implemented in numerous gastrointestinal disorders [7], as well as in the clinical management of infections to the respiratory tract, urinary tract infections, bacterial vaginosis, and depression [8].

Even though recent randomized controlled trials, published in the past few years, have demonstrated clinical, microbiological, and inflammatory improvements of periodontal parameters after the administration of probiotics [9–13], conflicting outcomes exist in the literature, and non-surgical mechanical debridement (NSMD) remains the "gold standard" for managing periodontal disease [14,15]. Furthermore, there is no consensus on the optimal duration, dosage, and frequency of probiotic administration regarding the treatment of periodontal disease [13,14]. Probiotics may be applied as a non-invasive adjunct to periodontal therapy mainly to reduce inflammatory parameters [13], but to the authors' knowledge, current periodontal guidelines do not include probiotics as an adjunct to periodontal therapy. Nonetheless, probiotics have been shown to have a decreasing effect both on salivary *Streptococcus mutans* levels in adolescents [16], as well as on halitosis, also known as bad breath, though with insufficient evidence [17]. Keeping in mind that probiotics have been discarded as an adjunct to periodontal therapy, the research question arose whether probiotics exert a beneficial influence on halitosis and other oral health parameters, such as salivary *Streptococcus mutans* levels, oral immunity, and saliva quality. Moreover, there is a lack of evidence of the preventative potential of probiotics in relation to oral health. Hence, the aim of this systematic review is to evaluate the therapeutic potential of probiotics in patients with halitosis and to assess whether probiotics can also be implemented as a preventative tool in oral health.

## 2. Materials and Methods

### *2.1. Eligibility Criteria*

The research question "Do probiotics have a positive effect on oral health?" was formulated following the PICO model [18]:

- Population: individuals with halitosis and/or carious lesions/risk factors for caries formation
- Intervention: administration of probiotics
- Comparison: placebo/no administration
- Outcome: reducing halitosis parameters/improving oral health parameters
- Study design: randomized controlled trials (RCTs)

### *2.2. Search Strategy*

This systematic review's search strategy was based on the PRISMA 2020 statement [18] guidelines, and it is registered in PROSPERO under the following number: CRD42024529033.

Two reviewers (V.O. and A.R.G.) carried out an independent electronic literature search for this systematic review, utilizing the databases Medline (PubMed), Scopus, Web of Science, and Cochrane, combining the following keywords by the Boolean operator "AND":

- Probiotics AND Halitosis
- Probiotics AND Prevention AND Oral Health

### *2.3. Data Management, Selection Process, and Data Collection Process*

To decide whether to include or exclude the pre-selected records, the articles were individually assessed by the two reviewers (V.O. and A.R.G.) based on their titles and abstracts. The reviewer (C.G.) was consulted in the event of any discrepancies between the two reviewers. Afterward, a full-text reading of articles considered suitable for the study was conducted, and a final inclusion/exclusion of articles was performed based on the following criteria:

### *2.4. Inclusion and Exclusion Criteria*

Inclusion Criteria

- Full text available
- Article available in English or Spanish
- Published in 2013 and onwards
- RCT performed on humans
- Adults
- Patients with halitosis
- Patients with carious lesions or presenting caries formation risk factors
- Administration of probiotics in any form
- Assessment of at least one of the following parameters: volatile sulfur compound levels, organoleptic scores, plaque, or saliva samples to assess cariogenic bacteria counts and/or pH levels

Exclusion Criteria

- In vitro studies
- Case report studies
- Case series studies
- Case–control studies
- Cross-sectional studies
- Clinical trial studies
- Performed on animals
- Periimplantitis
- Small sample sizes ($n < 20$)
- Children
- Pregnant patients
- Patients with intellectual disability
- Effect of probiotics on oral candida

Subsequently, from the included RCTs, the following variables were extracted and registered in a table: authors and year of publication, the aim of the study, study design, sample size, health status, type and dose of probiotic administered, treatment duration, other treatments (if applied), oral hygiene instructions (if applied), outcomes investigated, and key findings.

### 2.5. Risk of Bias Assessment

Assessment of the risk of bias was performed by two reviewers (V.O. and A.R.G.) in accordance with the ROB-2 tool [19] and from the RTCs selected for this review, the following domains were analyzed:

1. Bias arising from the randomization process.
2. Bias due to deviations from included interventions.
3. Bias due to missing outcome data.
4. Bias in measurement of the outcome.
5. Bias in the selection of the reported result.

The risk of bias was categorized as "low" risk (sufficient data, unlikely to modify the results), "some concerns" (insufficient information, raising doubts on the results), and "high" risk (possibility of serious adjustments of the results). Following that, if all the items were defined as low, the overall risk of bias was defined as "low" and if at least one of the domains was defined as "high" or "some concerns", all the domains were classified as "high" or "some concerns".

### 2.6. Statistical Analysis

The meta-analysis was carried out using the software Jamovi version 2.2.5 with the add-on MAJOR. A random-effects model was used. The mean difference (M) and the standard deviation (SD) were used to assess the variable probiotic with a 95% confidence interval (CI).

The variables volatile sulfur compound (VSC) levels and organoleptic scores were evaluated in the statistical analysis, using the mean values both for the baseline and at 4 weeks. For the evaluation of VSC levels, four studies were included [20–23], as they provided values measured both at baseline and at 4 weeks. The assessment of organoleptic scores involved three studies [21,22,24] that also stated values both at baseline and at 4 weeks. This allowed an analysis of more homogeneous values and avoided skewing the statistics.

## 3. Results

### 3.1. Study Selection

A total of 192 records were identified through a widespread electronic search of the databases PubMed and Web of Science, as shown in Figure 1 (the flow chart was created using the PRISMA Flow Diagram tool) [25]. After removing duplicates, 32 records were screened based on their titles and abstracts. Out of those 32 records, 21 were sought for retrieval. Two references could not be retrieved; hence, full-text screening was performed of 19 articles based on the inclusion criteria and 16 finally remained for this systematic review, with a total number of 921 patients being evaluated. All the present articles were RCTs.

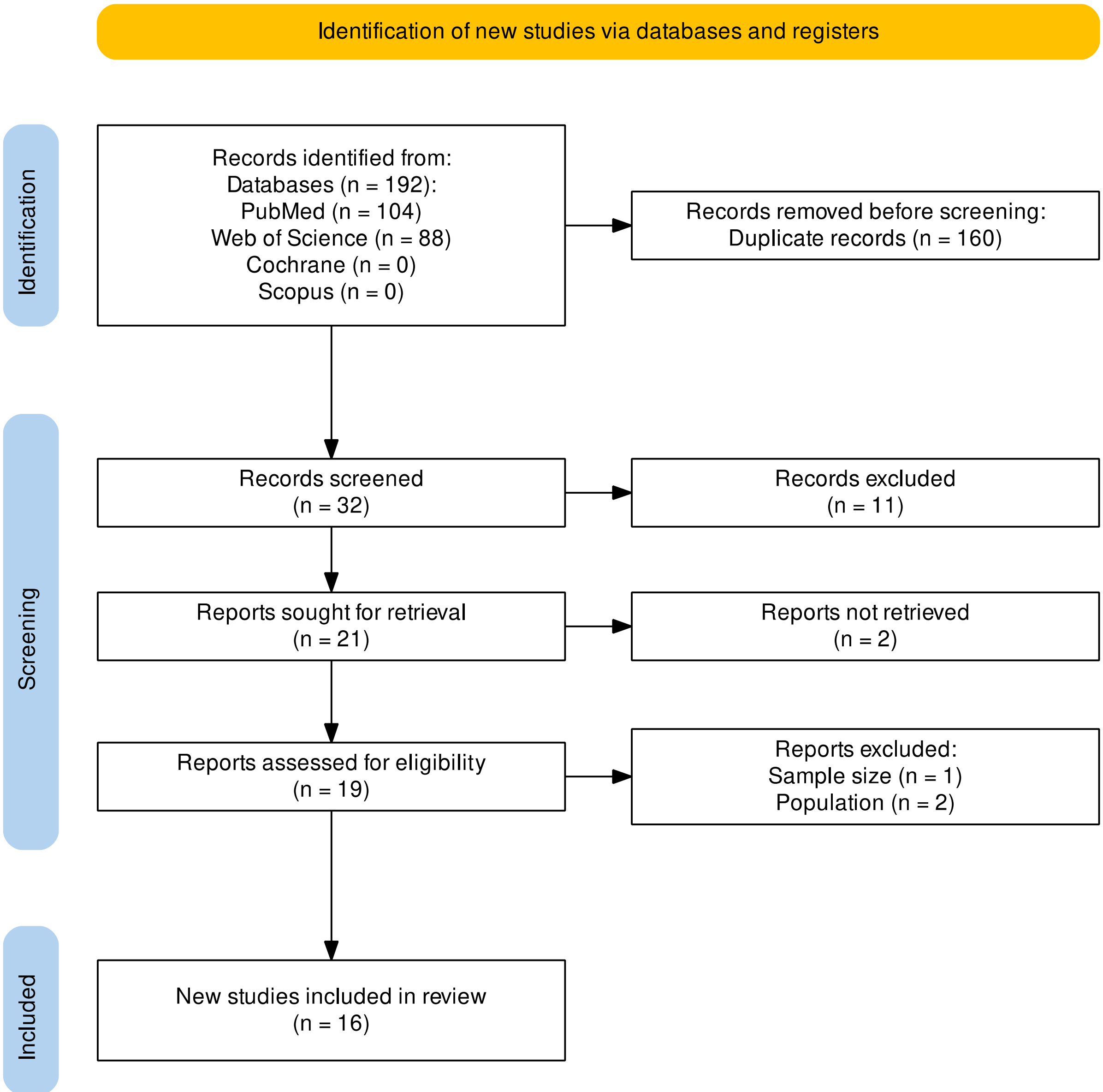


**Figure 1.** Flow chart.

### *3.2. Risk of Bias Assessment*

The risk of bias in the 16 randomized controlled trials was assessed using the Cochrane risk-of-bias assessment tool version 2 [19]; most studies included were classified as having a low risk of bias (n = 9). Seven studies were classified as having some concerns, mainly due to questions related to the randomization process. The results are reported in Figure 2.

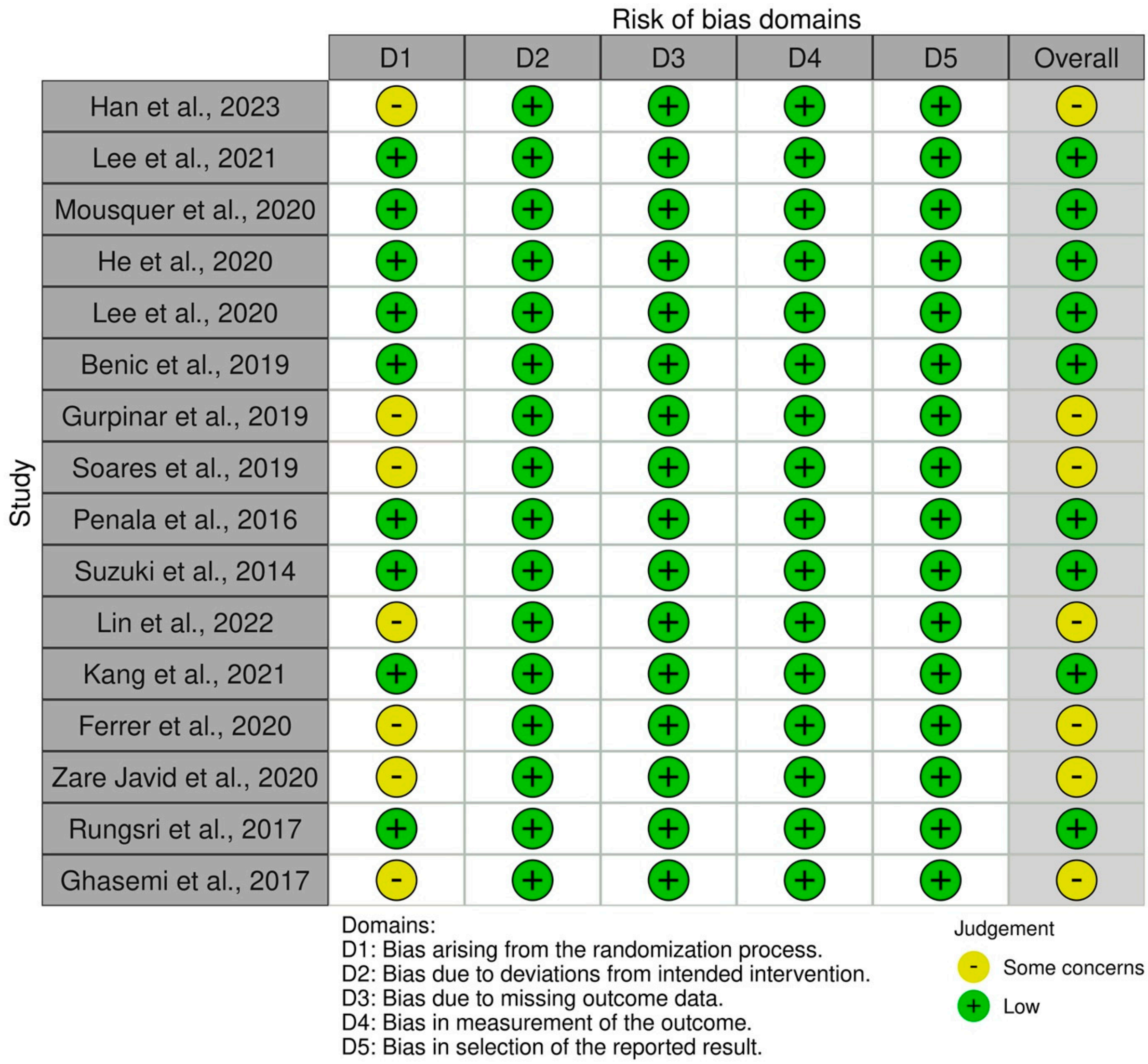


**Figure 2.** Risk of bias assessment.

### *3.3. Study Characteristics*

All the clinical trials included systemically healthy subjects. He et al. also accepted subjects with gingivitis or mild periodontitis [21]; Soares et al. investigated subjects presenting periodontitis stage III and IV, grade B and C [26]; and Penala et al. performed their study on subjects with chronic periodontitis [24].

The following probiotics were administered: *L. salivarius* [24,26–29], *S. salivarius* [21,30], *L. paracasei* [27], *L. plantarum* [27], *W. cibaria* [20,22,31,32], *S. dentisani* [33], *B. lactis* [23,34], *L. rhamnosus* [35], *L. acidophilus* [26,36], *B. bifidum* [36], *S. thermophilus* [23], *L. bulgaricus* [23], and *L. reuteri* [24,26].

Treatment duration ranged from 10 days [29] to 2 weeks [28,34], 3 weeks [36], 1 month [21,23,24,27,30,33,35], 2 months [20,22,31,32], and 3 months [26].

Most of the studies did not perform any other treatments, except for five studies. Mousquer et al. administered probiotics in combination with inulin, a prebiotic, to study their effect on halitosis and tongue coating [29]. Benic et al. investigated the effect of oral probiotics on oral hygiene indices and halitosis in patients wearing fixed orthodontic appliances [30]. Gurpinar et al. instructed some of their subjects to use a tongue scraper [23]. In both the study carried out by Soares et al. and by Penala et al., periodontal therapy was performed on all the participants at baseline [24,26].

In most of the studies [21–24,28,29,32,33], the patients received oral hygiene instructions that mainly encompassed to refrain from other commercial probiotic products and antimicrobial mouth rinses, to maintain their usual oral hygiene and dietary habits, to use toothbrush and toothpaste provided by the investigator, and to abstain from consuming food or beverages, as well as to avoid any oral hygiene practices on the morning of each visit [32].

The outcomes investigated varied depending on the aim of the study; 10 [20–24,26,28–30,32] out of the 16 included RCTs investigated the effect of probiotics on oral halitosis and recorded parameters such as volatile sulfur compound (VSC) levels [20–23,26,28–30], bad breath improvement (BBI) scores [20,22], organoleptic scores (OLS) [21,22,24,26,28,29], tongue coating scores (TCS) [21,28,29], quality of life (QOL) [20,29,32], plaque index (PI) [21,24,26,28,30], gingival index (GI) [30] and modified GI (MGI) [24], probing depth (PD) [21,24,26,28] and probing depth reduction (PDR) [24], bleeding index (BI) [21,24] and gingival BI (GBI) [26], bleeding on probing (BOP) [21,26,28], clinical attachment levels (CALs) [24,26] and clinical attachment gain (CAG) [24], plaque samples [30], metagenomic analysis [30], Winkel scores [23], Wood's light scores [23], and N-benzoyl-DL-arginine-naphthylamide (BANA) scores [24]. In Table 1, a detailed description of these 10 studies investigating the effect of probiotics on oral halitosis is demonstrated, including authors and year of publication, study design, sample size, health status, probiotic and its form of administration, treatment duration, whether the participants received any other treatment, whether they were given oral hygiene instructions, outcomes investigated, and the study's key findings.

The other six studies assessed the clinical efficacy of probiotics on oral health, more precisely. Lin et al. studied the effect of post- and probiotics on oral health parameters such as oral microbiota and oral pathogens, immunological (IgA levels), and plaque levels [27]; Kang et al. assessed whether there is caries activity after the ingestion of probiotics [31]; Ferrer et al. investigated oral health parameters such as plaque accumulation and saliva quality after the administration of probiotics [33]; Zare Javid et al. evaluated whether probiotic yogurt has an effect on initial stages of caries [34]; Rungsri et al. examined the effect of fermented milk containing probiotics on oral microbiota [35]; and Ghasemi et al. investigated whether probiotic yogurt can reduce salivary *S. mutans* levels [36]. Table 2 presents an individual description of these six studies, stating authors and year of publication, study design, the aim of the study, sample size, health status, a probiotic and its form of administration, treatment duration, outcomes investigated, and the study's key findings.

**Table 1.** Characteristics of the included studies about halitosis.

| Authors, Year | Study Design | Sample Size | Health Status | Probiotic (Administration) | Treatment Duration | Other Treatments | Oral Hygiene Instructions | Outcomes Investigated | Key Findings |
|---|---|---|---|---|---|---|---|---|---|
| Han et al., 2023 [20] | RCT, double-blind, placebo-controlled | n = 91 | Healthy | *W. cibaria* (1 tablet/night) | 2 months | None | Not mentioned | VSC levels (Oral Chroma), BBI scores, *W. cibaria*, psychosocial health | Probiotic administration may be considered an adjunctive treatment of halitosis. |
| Lee et al., 2021 [32] | RCT, double-blind, placebo- controlled, pretest-posttest | n = 62 | Healthy | *W. cibaria* (1 tablet/night) | 2 months | None | Yes | Subjective halitosis, subjective oral health status, psychosocial health | Probiotic administration can help reduce subjective halitosis and improved OHQoL. |
| Mousquer et al., 2020 [29] | RCT, double-blind, placebo-controlled, parallel, phase II | n = 44 | Healthy | *L. salivarius* (1 gum every 12 hours) | 10 days | Inulin (prebiotic) | Yes | OLT, VSC levels (Halimeter), tongue coating index, QOL | Treatment with probiotics combined or not with inulin can reduce halitosis. However, there was no significant difference between the groups. |
| He et al., 2020 [21] | RCT, double-blind, placebo-controlled | n = 28 | Healthy, gingivitis or mild periodontitis | *S. salivarius* (2 lozenges/day) | 1 month (2-week follow-up) | None | Yes | OLT score, VSC levels (Halimeter), tongue coating, PI, PD, BI, BOP | The use of probiotics alone did not influence halitosis with tongue coating cause when the tongue coating was not removed beforehand. |
| Lee et al., 2020 [22] | RCT, double-blind, placebo-controlled | n = 68 | Healthy | *W. cibaria* (1 tablet/night) | 2 months | None | Yes | OLT, VSC levels (Oral Chroma), BBI scores, *W. cibaria* | Oral ingestion of probiotics can help to reduce halitosis. |
| Benic et al., 2019 [30] | Prospective RCT, triple-blind, two-arm parallel group, placebo-controlled | n = 64 | Healthy | *S. salivarius* (2 lozenges/day) | 1 month (3-month follow-up) | Fixed orthodontic appliances | Not mentioned | PI, GI, VSC levels (Halimeter), plaque samples, metagenomic analysis | The use of oral probiotics resulted in a reduction of halitosis in individuals with orthodontic braces; however, it did neither decrease their PIs nor GIs. |
| Gurpinar et al., 2020 [23] | Prospective, multicenter, controlled RCT | n = 100 | Healthy | *B. lactis*, *S. thermophilus*, *L. bulgaricus* (probiotic product) | 1 month (1-month follow-up) | Tongue scraping | Yes | VSC levels (Halimeter), Winkel scores, Wood's light scores | Tongue scraping in combination with probiotics can maintain its effect in halitosis therapy, even after cessation of the treatment. |
| Soares et al., 2019 [26] | RCT, double-blind, placebo-controlled | n = 60 | Periodontitis stage III and IV, grade B and C | *L. reuteri*, *L. salivarius*, *L. acidophilus* (diluted with water) | 3 months (follow-up at 30, 60 and 90 days) | Periodontal therapy | Only if necessary | PPD, CAL, BOP, PI, GBI, VSC levels (TTS), OLS | Oral administration of probiotics reduced periodontal parameters and halitosis. |

**Table 1.** *Cont.*

| Authors, Year | Study Design | Sample Size | Health Status | Probiotic (Administration) | Treatment Duration | Other Treatments | Oral Hygiene Instructions | Outcomes Investigated | Key Findings |
|---|---|---|---|---|---|---|---|---|---|
| Penala et al., 2015 [24] | RCT, double-blind, placebo-controlled, parallel design | n = 29 | Systemically healthy with chronic periodontitis | *L. salivarius*, *L. reuteri* (mouthwash and subgingival delivery of PB solution) | 1 month (3-month follow-up) | Full-mouth SRP (at baseline) | Yes | PD, CAL, PI, MGI, BI, ORG, PDR, CAG, BANA scores | The adjunctive use of probiotics offers clinical benefits in terms of PDR in moderate pockets and in halitosis. |
| Suzuki et al., 2014 [28] | RCT, double-blind, crossover, placebo-controlled | n = 23 | Healthy | *L. salivarius* (3 tablets/day) | 2 weeks | None | Yes | OLT scores, VSC levels, PPD, BOP, PI, TCS, bacterial quantitative analysis | Daily consumption of tablets containing probiotic lactobacilli can help control halitosis. |

Abbreviations: BANA = N-benzoyl-DL-arginine-napthylamide, BBI = Bad Breath Improvement, BI = Bleeding Index, BOP = Bleeding on Probing, CAG = Clinical Attachment Gain, CAL = Clinical Attachment Level, GBI = Gingival Bleeding Index, MGI = Modified Gingival Index, OHQoL = Oral-Health-Related Quality of Life, OLS = Organoleptic Score, OLT = Organoleptic Test, ORG = Organoleptic Score, PD = Probing Depth, PDR = Plaque Reduction, PI = Plaque Index, PPD = Probing Pocket Depth, QOL = Quality of Life, TCS = Tongue Coating Score, TTS = Tanita device, VSC = Volatile Sulfur Compounds.

**Table 2.** Characteristics of the included studies about oral health.

| Authors, Year | Study Design | Aim of Study | Sample Size | Health Status | Probiotic (Administration) | Treatment Duration | Outcomes Investigated | Key Findings |
|---|---|---|---|---|---|---|---|---|
| Lin et al., 2022 [27] | RCT, single-blind, placebo-controlled | To test the effect of postbiotic and heat-killed probiotic lozenges on oral health. | n = 75 | Healthy | *L. salivarius*, *L. paracasei*, *L. plantarum* (3 lozenges/day) | 1 month | Oral microbiota, IgA levels, oral pathogens, plaque, and oral health questionnaire | Lozenges containing postbiotics or heat-killed probiotics may effectively enhance oral immunity, inhibit the growth of oral pathogens, and increase the quantity of beneficial oral microbiota. |
| Kang et al., 2021 [31] | RCT, double-blind, placebo- controlled | To assess whether there is caries activity after the ingestion of *W. cibaria*. | n = 68 | Healthy | *W. cibaria* (1 tablet/night) | 2 months | Acidogenic potential of dental plaque (Cariview kit) | Oral probiotics are safe to consume since the Cariview test showed that there was no risk for caries activity. |

**Table 2.** *Cont.*

| Authors, Year | Study Design | Aim of Study | Sample Size | Health Status | Probiotic (Administration) | Treatment Duration | Outcomes Investigated | Key Findings |
|---|---|---|---|---|---|---|---|---|
| Ferrer et al., 2020 [33] | RCT, double-blind, placebo-controlled, parallel | To evaluate the clinical efficacy of *S. dentisani*. | n = 50 | Healthy | *S. dentisani* (buccoadhesive gel, applied with splints every 48 h) | 1 month (follow-up on day 15, 30, 45 post-treatment) | Plaque samples, saliva samples, odontogram, DMFT index, PI, GI and salivary flow, lactic acid, pH, electrolytes | The topic application of probiotics appears to improve oral health, such as plaque accumulation, saliva quality and salivary flow. |
| Zare Javid et al., 2019 [34] | RCT, double-blind, parallel | To investigate the effect of consumption of probiotic yogurt on salivary *S. mutans* and lactobacilli in students with initial stages of caries. | n = 66 | Healthy | *B. lactis* (yoghurt, 300 g/day) | 2 weeks | Saliva samples (isolating *S. mutans* and lactobacilli) | It is suggested that short-term consumption of probiotic yogurt may prevent the progression of dental caries through reducing the population of cariogenic bacteria in saliva. |
| Rungsri et al., 2017 [35] | Prospective RCT, double-blind | To evaluate whether short-term consumption of fermented milk containing *L. rhamnosus* affects levels of oral microbiota and whether it can colonize the human mouth. | n = 43 | Healthy | *L. rhamnosus* (fermented milk, 100 mL/day) | 1 month (1-month follow-up) | DMFT, PI, GI, saliva samples (*S. mutans* and lactobacilli) | The daily consumption of fermented milk containing probiotics may have beneficial effects on oral health by reducing salivary levels of cariogenic bacteria. |
| Ghasemi et al., 2017 [36] | RCT | To investigate the effects of probiotic yogurts on reducing salivary *S. mutans* levels. | n = 50 | Healthy | *L. acidophilus*, *B. bifidum* (yoghurt, 200 g/night) | 3 weeks (1-day, two-week, 1-month follow-up) | Saliva samples (*S. mutans*) | Probiotic yoghurt is an effecting method to reduce salivary *S. mutans* counts. |

DMFT = Decayed, Missing due to caries, Filled Teeth.

### 3.4. Limitations

Due to the extensive selection criteria, 16 articles were included in this systematic review and meta-analysis, which can be considered a small number of articles; hence, this represents a limitation of this study. Furthermore, different probiotic strains were studied in different studies, which undermines a possible generalization of the results.

### 3.5. Meta-Analysis Results

The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data. Figures 3 and 4 show the forest plot and funnel plot of the four included studies assessing VSC levels at baseline and at 4 weeks, respectively, and Figures 5 and 6 depict the three included studies evaluating organoleptic scores at baseline and at 4 weeks, respectively.

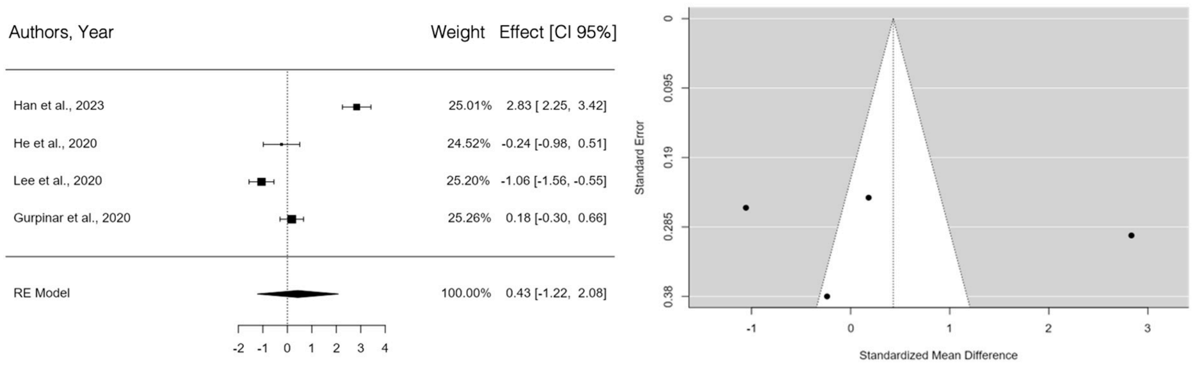


**Figure 3.** Forest plot and funnel plot of the effectiveness of probiotics on halitosis in comparison with the placebo group. Values of VSC levels at baseline.

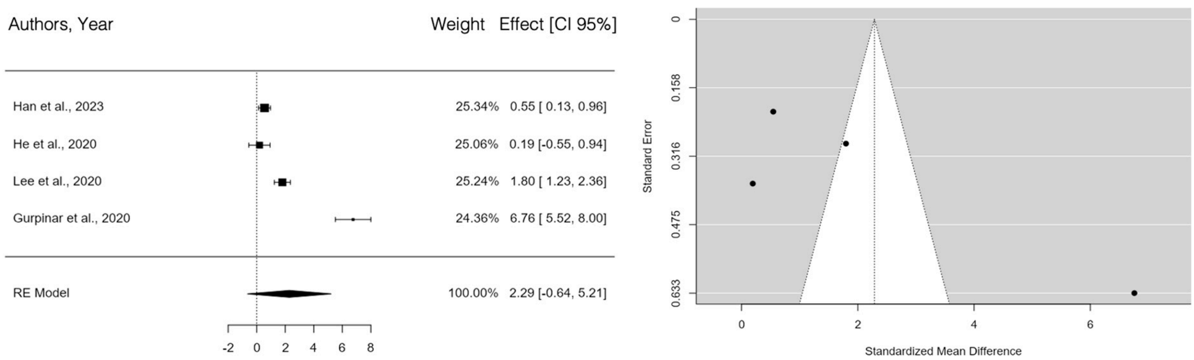


**Figure 4.** Forest plot and funnel plot of the effectiveness of probiotics on halitosis in comparison with the placebo group. Values of VSC levels at 4 weeks.

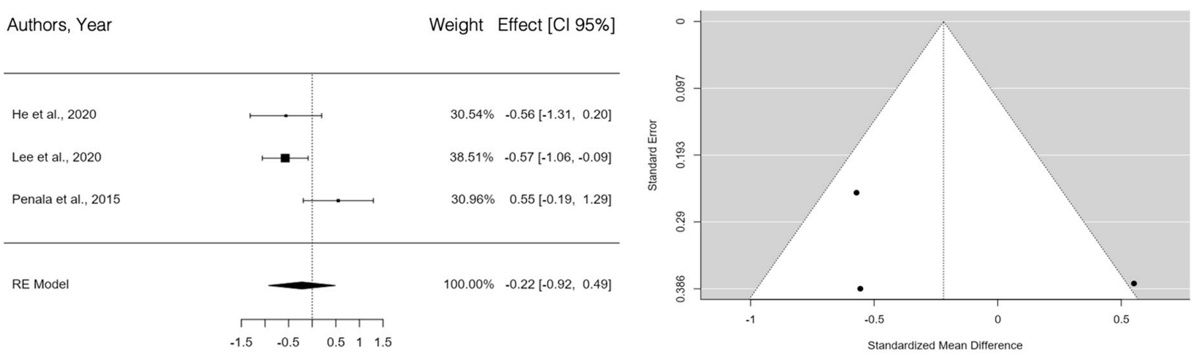


**Figure 5.** Forest plot and funnel plot of the effectiveness of probiotics on halitosis in comparison with the placebo group. Values of organoleptic scores at baseline.

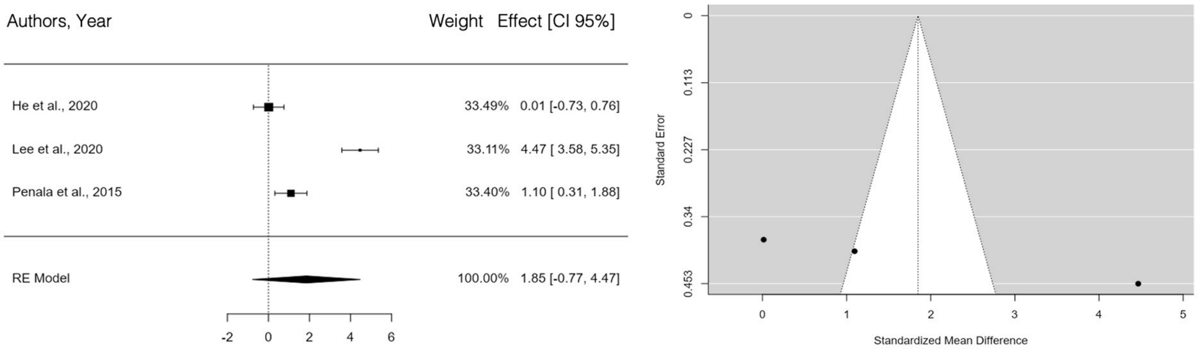


**Figure 6.** Forest plot and funnel plot of the effectiveness of probiotics on halitosis in comparison with the placebo group. Values of organoleptic scores at 4 weeks.

## 4. Discussion

### *4.1. Probiotics as a Treatment Option for Halitosis*

This systematic review studied probiotics as another treatment option for halitosis, based on the evaluation of existing randomized clinical trials (RCTs). Each of the incorporated studies noted a decrease in halitosis parameters, leading to the conclusion that probiotics can effectively mitigate halitosis.

The oral probiotics *W. cibaria*, *L. salivarius*, *S. salivarius*, *B. lactis*, *S. thermophilus*, *L. bulgaricus*, and *L. reuteri* all demonstrated the ability to decrease VSC levels.

In the study conducted by Han et al., tablets containing *W. cibaria* led to a significant decrease in overall VSCs and the combined levels of hydrogen sulfide and methyl mercaptan by week 8, which could be because of the increase in the presence of *W. cibaria* in the oral cavity. The authors explain that *W. cibaria* produces higher levels of hydrogen peroxide, a potent antibacterial substance, able to modify the composition of bacteria in the oral cavity and hence impeding the growth of *F. nucleatum*, resulting in a significant reduction in the proportion of *F. nucleatum* in the oral cavity, hence leading to the elimination of harmful bacteria and, consequently, preventing the production of VSCs. Moreover, the authors state that future research is necessary to evaluate whether *W. cibaria* has a significant inhibitory effect on bacteria producing VSCs by also measuring the bacterial quantity, something that was not performed in their study [20].

This is coherent with the findings of a study carried out by Lee et al., in which they found out that the oral consumption of *W. cibaria* resulted in lower VSC levels compared to levels observed after taking the placebo [22].

Mousquer et al. were able to show a decrease in halitosis measured by a Halimeter after the administration of *L. salivarius* for 10 days in the form of gum. *L. salivarius* can alter the oral environment by influencing both pH and oxidation–reduction potential. This undermines the stability of pathogens through its antimicrobial properties, reduces the invasion of resident pathogenic bacteria, and stimulates protective immune responses, consequently, effectively hindering the release of VSCs [29].

Soares et al. and Suzuki et al. observed a similar VSC-decreasing potential of lactobacilli, namely, *L. reuteri* and *L. salivarius* [26,28]. Suzuki et al. detected a significant reduction in methyl mercaptan, a compound closely associated with oral malodor originating from periodontal disease, upon the administration of *L. salivarius* [28].

*S. salivarius* also seems to be able to reduce VSC levels, as He et al. and Benic et al. found out in their clinical trials [21,30]. In the trial carried out by He et al., a notable decrease in VSCs was observed while participants were undergoing administration of the probiotic *S. salivarius*; nonetheless, this reduction was not sustained after the course concluded. Along these lines, the study did not recommend relying solely on probiotics as an approach to address persistent tongue-coating halitosis [21]. Benic et al. examined the impact of *S. salivarius* on oral hygiene indices and halitosis in individuals with orthodontic braces and performed a 3-month follow-up. The authors observed that even though the VSC scores showed a notable decrease in both the probiotic and placebo-control groups after the 1-month intervention, during the 3-month intervention-free follow-up, the VSC levels in the placebo group reverted to a value similar to the baseline, whereas in the probiotic group, the VSC levels continued to decrease further from the baseline. The authors state though that the clinical significance of the VSC reduction observed in this study (from 201 $\pm$ 71 ppb to 180 $\pm$ 47 ppb) remains uncertain, as the established threshold for the clinical diagnosis of halitosis is typically considered between 150 and 160 ppb [30].

Gurpinar et al. were able to show that tongue scraping in combination with oral probiotics allows for lasting effects in terms of VSC levels even after cessation of probiotic intake. Post-treatment measurements, after the discontinuation of the intervention, exhibited statistical differences favoring the probiotic group [23].

Concerning the organoleptic test (OLT), not all the included studies investigated it, as it lacks objectivity. The included clinical trials that did examine it, all observed a decrease in organoleptic scores after probiotic therapy [21,22,24,26,28,29].

Nonetheless, Soares et al. and Penala et al. were the only ones who found improvements that differed significantly among the study groups [24,26]. This could be due to a small sample size [29], no prior removal of tongue coating [21], but also due to the subjectivity of this evaluation method, which decreases its statistical power in the identification of differences [29].

Tongue coating was analyzed in four of the included clinical trials [21,23,28,29]. The dorsum of the tongue is coated with papillae, and within the crevices of these papillae, a build-up of bacteria, dead epithelial cells, and food particles occurs. This accumulation of plaque on the tongue can lead to halitosis. A plaque with a thickness of 0.1–0.2 mm can reduce oxygen levels, thus creating an anaerobic environment conducive to bacterial colonization [23].

Mousquer et al. investigated the effect of probiotic administration together with the prebiotic inulin on halitosis and tongue coating. Prebiotics, with inulin being one of the most used ones, are indigestible fibers present in foods like onions, cereals, and bananas and can be consumed along with probiotics, forming a combination known as symbiotics. This combination stimulates the growth and function of microbial flora by suppressing the proliferation of harmful pathogens and supporting the immune defense. Mousquer et al. found that within each treatment group, all three groups exhibited a significant decrease in the coating index after the treatment. While there was no significant difference in the reduction among the treatments, patients treated with the probiotic *L. salivarius* and inulin showed a trend towards a lower coating index compared to those treated with *L. salivarius* alone. But this difference was not statistically significant compared to the placebo group [29].

He et al. observed that the application of *S. salivarius* did not produce a noteworthy impact on halitosis accompanied by tongue coating when the tongue coating was not pre-treated either physically or chemically. This suggests that the removal of tongue coating is necessary before employing *S. salivarius* for effective results [21].

This is coherent with the results of the study carried out by Gurpinar et al., in which they concluded that the "effect of tongue scraping with a probiotic continued even after the cessation of the treatment" [23].

Conversely, Suzuki et al. were able to show significant improvements in tongue coating scores in the probiotic group compared to the placebo group, even though the authors did not perform any removal of tongue coating before probiotic administration. This may be because the study carried out by Suzuki et al. was a crossover randomized controlled trial, which gave rise to the period effect. The investigators performed a washout period of 2 weeks but stated that extended washout periods might be necessary to assess alterations in the tongue coating scores [28].

Bad breath improvement (BBI) scores were measured in the studies carried out by Han et al. and Lee et al. Both studies noted no significant differences at week 4; however, by week 8 of the intervention, the placebo group displayed an increase in BBI scores, whereas the probiotics group exhibited a reduction in BBI scores. BBI scores are evaluated by a self-estimation of bad breath using a scale of 1 to 5, with a higher score indicating worsening of symptoms after intake [20,22].

Regarding periodontal parameters, He et al. determined that there were no statistically significant differences observed in the average probing depth (PD), bleeding index (BI), and plaque index (PI) between and within the two groups when comparing baseline measurements to those taken on day 14, before and after treatment [21]. Similarly, Benic et al. analyzed the variables PI and GI and observed that both scores were not significantly influenced by the probiotic administration [30]. In contrast, Soares et al. observed an improvement in periodontal parameters, namely, probing pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BOP), PI, and GI [26]. This is coherent with the findings of the study carried out by Penala et al. in which they observed that the probiotic group showed significant improvement in the parameters PI, modified gingival index (MGI), and BI at 3 months compared with the control group [24]. Furthermore, Suzuki et al. discovered that the average PPD significantly improved during the probiotic period compared to the placebo period, and intra-period comparison revealed a significant improvement in the number of BOP sites from day 0 to day 14 in the probiotic period, whereas no such improvement was observed in the placebo period [28]. The contradicting findings between these studies could be explained by the different probiotic strains the authors used; He et al. and Benic et al. administered the probiotic *S. salivarius*, whereas Soares et al. and Penala et al. administered the strains *L. reuteri* and *L. salivarius* [21,24,26,30]. Suzuki et al. also administered *L. salivarius* [28]. Furthermore, the study conditions vary between the different clinical trials. Benic et al., for instance, performed their study on patients wearing orthodontic braces [30], whereas Soares et al. and Penala et al. realized periodontal therapy (scaling and root planning, SRP) on their patients [24,26]. Given this heterogeneity among these studies might explain the incongruity of the results.

### *4.2. Probiotics as a Preventative Tool in Oral Health*

Preventive strategies for dental caries primarily revolve around managing risk factors, with probiotic administration emerging as a promising tool within these preventive measures.

Lin et al. for example found out that postbiotic or heat-killed probiotic lozenges, namely, *Lactobacillus* salivarius, *L. paracasei*, and *L. plantarum*, reduced the number of *S. mutans* in the oral cavity [27]. This is coherent with the findings of a study carried out by Zare Javid et al., which indicated that the intake of probiotic yogurt containing *Bifidobacterium* lactis led to a significant decrease of *S. mutans* present in saliva [34]. Moreover, Rungsri et al. observed a notable reduction in salivary *S. mutans* levels and overall bacterial counts after *L. rhamnosus* administration. They also detected that *L. rhamnosus* remained present in the probiotic group for up to 4 weeks after the cessation of treatment, suggesting its ability to adhere to the oral mucosa [35]. Additionally, Ghasemi et al. assessed the impact of probiotics on diminishing *S. mutans* levels in saliva and potential caries prevention and instructed their participants to consume probiotic yogurt daily for 3 weeks, containing *L. acidophilus* and *Bifidobacterium bifidum*. This intervention resulted in a significant reduction in salivary *S. mutans* counts, with the most substantial decrease observed in the second week after the conclusion of the intervention [36,37].

A study carried out by Kang et al. aimed to determine if there is a potential for caries development when consuming a tablet containing *W. cibaria* over an 8-week period. To assess dental caries activities, the Cariview score, a predictor of caries incidence based on the acid production rate of oral bacteria, was used for comparison. After the ingestion of tablets for 8 weeks, both groups exhibited a significant decrease in Cariview scores. But there was no statistically significant difference observed between the two groups. Despite this lack of a significant difference, the findings indicated that the consumption of *W. cibaria* eradicated the potential for dental caries development arising from acid production in the oral flora, which can be attributed to the colonization and presence of *W. cibaria* in dental plaque and the oral cavity, actively suppressing acid production [31,38].

Furthermore, Ferrer et al. collected plaque and saliva samples and administered *S. dentisani* to evaluate its clinical efficacy. Their findings are abundant and in favor of probiotic administration as a means of decreasing risk factors for dental caries. Their results show, among others, that *S. dentisani* can colonize in dental plaque, the administration of the probiotic *S. dentisani* leads to a shift in microbial composition aligning with a healthier microbiota, marked by a reduction in microorganisms typically linked to dental caries, and the salivary flow increased significantly in the probiotic group compared to the placebo group. Increased salivary flow is linked to enhanced buffering capacity, the rinsing away of undesirable components, a favorable shift in the remineralization/demineralization ratio, heightened antimicrobial activity, and improved immune function, all being factors creating an environment less conducive to the formation of cariogenic biofilms. Additionally, pH levels did not exhibit a significant difference between the groups receiving probiotics and placebos, which may be attributed to an overall enhancement in this parameter observed in both groups during the study, potentially influenced by effective and regular toothbrushing practices upon trial initiation. The authors conclude that *S. dentisani* seems to enhance various clinical aspects related to oral health, including the reduction in plaque accumulation and improvement in saliva quality and salivary flow [33,39,40].

### 4.3. The Effect of Probiotic Administration on Oral-Health-Related Quality of Life

Regarding psychosocial health and oral-health-related quality of life, Han et al. observed an improvement in the following parameters: depression, oral-health-related quality of life, and subjective oral health status. But the authors note that these findings should be interpreted carefully, because they used subjective measurement tools [20].

Lee et al. conducted their study on college students presenting halitosis, with a focus on psychosocial variables, including subjective halitosis, subjective oral health status, depression, self-esteem, and oral-health-related quality of life. Their main findings were significant differences in subjective halitosis and oral-health-related quality of life; hence, the improvement in oral-health-related quality of life seems to be linked to a significant reduction in subjective halitosis. On the other hand, Lee et al. observed no significant differences in the subjective oral health status. This could be explained by an overall acceptable subjective oral health status of the college students to begin with. Therefore, in this research, the oral probiotic lacked a significant impact on subjective oral-health status; however, the authors also state that a comprehensive assessment of gum bleeding and gum status through objective measures is essential to accurately determine the oral health status. Moreover, the authors recognized that a reduction in subjective halitosis does not directly reduce depression. This may be because of the circumstance that among college students, depression is not merely influenced by halitosis, but rather by a combination of other factors, such as social support, stress, and personal perception. In addition, Lee et al. noted that after probiotic administration, there were no significant differences in self-esteem either, probably because of the same reasons as hypothesized in relation to depression. This study specifically targeted college students; consequently, its findings should not be presumed to apply to the broader general population [32,41–43].

Moreover, Mousquer et al. also assessed oral-health-related quality of life and observed an improvement in patients treated with the probiotic *L. salivarius* in combination with the prebiotic inulin [29].

### 4.4. Safety and Tolerability of Probiotic Administration

Considering the clinical safety of probiotics, no serious side effects were reported in any of the included RCTs. Ferrer et al. mentioned mild reactions potentially related to the probiotic administration, including dyspepsia and abdominal pain [33], and Lee et al. registered xerostomia and mild diarrhea; however, they discarded these symptoms to be related to the probiotic intake [22]. Generally, probiotics seem to be well tolerated, suggesting being considered safe for clinical application [44].

As for the clinical relevance of this study, probiotics have shown the capability to be considered a treatment option for halitosis, offering an alternative to methods like mouthwashes and tongue scrapers, as well as to antibiotics. This approach may reduce the reliance on antibiotics and help mitigate the risk of developing antibiotic resistance.

## 5. Conclusions

In general, probiotics exhibit potential as a safe and effective option for managing oral health, as they effectively reduce VSC levels, organoleptic scores, and cariogenic bacteria counts, as well as improving saliva quality and salivary flow. To sustain the reduction in VSC levels, tongue scraping in addition to probiotic intake can be recommended. Furthermore, the combination of prebiotics with probiotics (symbiotics) has been shown to decrease tongue coating. Moreover, probiotic administration seems to positively influence oral-health-related quality of life. Nevertheless, different bacterial strains have been used in the included studies; hence, the conclusions cannot be generalized, being one of the main limitations of this review. Additionally, further research on the probiotics' potential to persist in the oral cavity after cessation of treatment, as well as studies with prolonged follow-ups with standardized methodologies, is essential to establish their efficacy conclusively.

The research highlights the significant potential of probiotics in managing oral health, particularly in reducing VSC levels, improving saliva quality, and enhancing oral-health-related quality of life. This suggests that probiotics could be a viable, non-invasive adjunct to traditional oral health treatments. However, a key limitation of the study is the variation in bacterial strains used across different studies, which prevents the generalization of the findings. Additionally, there is a need for further research to explore the long-term persistence of probiotics in the oral cavity post-treatment and to employ standardized methodologies to conclusively determine their efficacy.

### *Future Expectations*

Future research with larger sample sizes, prolonged follow-up periods, and a more standardized mode of probiotic administration is advised, as those were limitations observed in the included studies. Furthermore, it would be interesting to develop a concept on how to provide access to probiotics to the general population, both from an economic as well as an educational standpoint.

**Author Contributions:** Conceptualization, F.R.-V.; methodology, M.A.; investigation, A.R.G.; data curation, C.G.; writing—original draft preparation, V.O.; writing—review and editing, R.L.G.; supervision, J.N.; project administration, C.G. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet* **2017**, *390*, 1211–1259. [CrossRef] [PubMed]
2. Könönen, E.; Gursoy, M.; Gursoy, U. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. *J. Clin. Med.* **2019**, *8*, 1135. [CrossRef] [PubMed]
3. Gheisary, Z.; Mahmood, R.; Shivanantham, A.H.; Liu, J.; Lieffers, J.R.L.; Papagerakis, P.; Papagerakis, S. The Clinical, Microbiological, and Immunological Effects of Probiotic Supplementation on Prevention and Treatment of Periodontal Diseases: A Systematic Review and Meta-Analysis. *Nutrients* **2022**, *14*, 1036. [CrossRef] [PubMed]

4. Nazir, M.A. Prevalence of periodontal disease, its association with systemic diseases and prevention. *Int. J. Health Sci.* **2017**, *11*, 72–80.
5. Tonetti, M.S.; Greenwell, H.; Kornman, K.S. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *J. Clin. Periodontol.* **2018**, *45*, S149–S161. [CrossRef] [PubMed]
6. Villafuerte, K.; Martinez, C.; Nobre, A.; Maia, L.; Tirapelli, C. What are microbiological effects of the adjunctive use of probiotics in the treatment of periodontal diseases? A systematic review. *Benef. Microbes* **2021**, *12*, 1–13. [CrossRef] [PubMed]
7. Palai, S.; Derecho, C.; Kesh, S.; Egbuna, C.; Onyeike, P. Prebiotics, Probiotics, Synbiotics and Its Importance in the Management of Diseases. In *Functional Foods and Nutraceuticals*; Springer: Cham, Switzerland, 2020; pp. 173–196.
8. Rondanelli, M.; Faliva, M.A.; Perna, S.; Giacosa, A.; Peroni, G.; Castellazzi, A.M. Using probiotics in clinical practice: Where are we now? A review of existing meta-analyses. *Gut Microbes* **2017**, *8*, 521–543. [CrossRef] [PubMed]
9. Zener, H.Ö.; Kuru, L.; Kadir, T.; Kuru, B. Bifidobacterium animalis subsp. lactis as adjunct to non-surgical periodontal treatment in periodontitis: A randomized controlled clinical trial. *Clin. Oral Investig.* **2023**, *27*, 1965–1972.
10. Ranjith, A.; Bin Nazimudeen, N.; Baiju, K.V. Probiotic mouthwash as an adjunct to mechanical therapy in the treatment of stage II periodontitis: A randomized controlled clinical trial. *Int. J. Dent. Hyg.* **2022**, *20*, 415–421. [CrossRef] [PubMed]
11. Minić, I.; Pejčić, A.; Bradić-Vasić, M. Effect of the local probiotics in the therapy of periodontitis A randomized prospective study. *Int. J. Dent. Hyg.* **2022**, *20*, 401–407. [CrossRef] [PubMed]
12. Ramos, T.C.d.S.; Boas, M.L.V.; Nunes, C.M.M.; Ferreira, C.L.; Pannuti, C.M.; Santamaria, M.P.; Jardini, M.A.N. Effect of systemic antibiotic and probiotic therapies as adjuvant treatments of subgingival instrumentation for periodontitis: A randomized controlled clinical study. *J. Appl. Oral Sci.* **2022**, *30*, e20210583. [CrossRef] [PubMed]
13. Patyna, M.; Ehlers, V.; Bahlmann, B.; Kasaj, A. Effects of adjunctive light-activated disinfection and probiotics on clinical and microbiological parameters in periodontal treatment: A randomized, controlled, clinical pilot study. *Clin. Oral Investig.* **2021**, *25*, 3967–3975. [CrossRef] [PubMed]
14. Alhamoudi, N.; Abduljabbar, T.; Vohra, F.; Javed, F. Influence of mechanical debridement with adjunct probiotic therapy on clinical status and salivary cortisol levels in patients with periodontal inflammation. *Eur. Rev. Med. Pharmacol. Sci.* **2023**, *27*, 8360–8370. [CrossRef] [PubMed]
15. Sanz, M.; Herrera, D.; Kebschull, M.; Chapple, I.; Jepsen, S.; Berglundh, T.; Sculean, A.; Tonetti, M.S.; On behalf of the EFP Workshop Participants and Methodological Consultants. Treatment of stage I–III periodontitis—The EFP S3 level clinical practice guideline. *J. Clin. Periodontol.* **2020**, *47*, 4–60. [CrossRef] [PubMed]
16. Ccedilaglar, E.; Kavaloglu Cildir, S.; Ergeneli, S.; Sandalli, N.; Twetman, S. Salivary mutans streptococci and lactobacilli levels after ingestion of the probiotic bacteriumLactobacillus reuteriATCC 55730 by straws or tablets. *Acta Odontol. Scand.* **2006**, *64*, 314–318. [CrossRef] [PubMed]
17. Huang, N.; Li, J.; Qiao, X.; Wu, Y.; Liu, Y.; Wu, C.; Li, L. Efficacy of probiotics in the management of halitosis: A systematic review and meta-analysis. *BMJ Open* **2022**, *12*, e060753. [CrossRef] [PubMed]
18. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **2021**, *372*, n71. [CrossRef] [PubMed]
19. Sterne, J.A.C.; Savović, J.; Page, M.J.; Elbers, R.G.; Blencowe, N.S.; Boutron, I.; Cates, C.J.; Cheng, H.Y.; Corbett, M.S.; Eldridge, S.M.; et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* **2019**, *366*, l4898. [CrossRef] [PubMed]
20. Han, H.-S.; Yum, H.; Cho, Y.-D.; Kim, S. Improvement of halitosis by probiotic bacterium Weissella cibaria CMU: A randomized controlled trial. *Front. Microbiol.* **2023**, *14*, 1108762. [CrossRef] [PubMed]
21. He, L.; Yang, H.; Chen, Z.; Ouyang, X. The Effect of Streptococcus salivarius K12 on Halitosis: A Double-Blind, Randomized, Placebo-Controlled Trial. *Probiotics Antimicrob. Proteins* **2020**, *12*, 1321–1329. [CrossRef] [PubMed]
22. Lee, D.; Lee, S.; Kim, M.; Nam, S.; Kang, M. Reduction of Halitosis by a Tablet Containing Weissella cibaria CMU: A Randomized, Double-Blind, Placebo-Controlled Study. *J. Med. Food* **2020**, *23*, 649–657. [CrossRef] [PubMed]
23. Gurpinar, B.; Yildirim, G.; Kumral, T.L.; Akgun, M.F.; Sari, H.; Tutar, B.; Uyar, Y. A simple method to reduce halitosis; tongue scraping with probiotics. *J. Breath Res.* **2019**, *14*, 016008. [CrossRef] [PubMed]
24. Penala, S.; Kalakonda, B.; Pathakota, K.R.; Jayakumar, A.; Koppolu, P.; Lakshmi, B.V.; Pandey, R.; Mishra, A. Efficacy of local use of probiotics as an adjunct to scaling and root planing in chronic periodontitis and halitosis: A randomized controlled trial. *J. Res. Pharm. Pract.* **2016**, *5*, 86–93. [CrossRef] [PubMed]
25. Haddaway, N.R.; Page, M.J.; Pritchard, C.C.; McGuinness, L.A. PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. *Campbell Syst. Rev.* **2022**, *18*, e1230. [CrossRef] [PubMed]
26. Soares, L.G.; de Carvalho, E.B.; Tinoco, E.M.B. Clinical effect of Lactobacillus on the treatment of severe periodontitis and halitosis: A double-blinded, placebo-controlled, randomized clinical trial. *Am. J. Dent.* **2019**, *32*, 9–13. [PubMed]
27. Lin, C.-W.; Chen, Y.-T.; Ho, H.-H.; Kuo, Y.-W.; Lin, W.-Y.; Chen, J.-F.; Lin, J.-H.; Liu, C.-R.; Lin, C.-H.; Yeh, Y.-T.; et al. Impact of the food grade heat-killed probiotic and postbiotic oral lozenges in oral hygiene. *Aging* **2022**, *14*, 2221–2238. [CrossRef] [PubMed]
28. Suzuki, N.; Yoneda, M.; Tanabe, K.; Fujimoto, A.; Iha, K.; Seno, K.; Yamada, K.; Iwamoto, T.; Masuo, Y.; Hirofuji, T. *Lactobacillus salivarius* WB21--containing tablets for the treatment of oral malodor: A double-blind, randomized, placebo-controlled crossover trial. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2014**, *117*, 462–470. [CrossRef] [PubMed]

29. Mousquer, C.R.; Della Bona, A.; Milani, D.C.; Callegari-Jacques, S.M.; Ishikawa, K.; Mayer, M.P.A.; Rösing, C.K.; Fornari, F. Are *Lactobacillus salivarius* G60 and inulin more efficacious to treat patients with oral halitosis and tongue coating than the probiotic alone and placebo? A randomized clinical trial. *J. Periodontol.* **2020**, *91*, 775–783. [CrossRef]
30. Benic, G.Z.; Farella, M.; Morgan, X.C.; Viswam, J.; Heng, N.C.; Cannon, R.D.; Mei, L. Oral probiotics reduce halitosis in patients wearing orthodontic braces: A randomized, triple-blind, placebo-controlled trial. *J. Breath Res.* **2019**, *13*, 036010. [CrossRef] [PubMed]
31. Kang, M.; Lee, D.; Kim, M.; Lee, S.; Nam, S. A Randomized, Double-Blind, Placebo-Controlled Trial to Assess the Acidogenic Potential of Dental Biofilms through a Tablet Containing *Weissella cibaria* CMU. *Int. J. Environ. Res. Public Health* **2021**, *18*, 4674. [CrossRef] [PubMed]
32. Lee, D.; Kim, M.; Nam, S.; Kang, M.; Lee, S. Effects of Oral Probiotics on Subjective Halitosis, Oral Health, and Psychosocial Health of College Students: A Randomized, Double-Blind, Placebo-Controlled Study. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1143. [CrossRef] [PubMed]
33. Ferrer, M.D.; López-López, A.; Nicolescu, T.; Perez-Vilaplana, S.; Boix-Amorós, A.; Dzidic, M.; Garcia, S.; Artacho, A.; Llena, C.; Mira, A. Topic Application of the Probiotic Streptococcus dentisani Improves Clinical and Microbiological Parameters Associated with Oral Health. *Front. Cell. Infect. Microbiol.* **2020**, *10*, 465. [CrossRef] [PubMed]
34. Zare Javid, A.; Amerian, E.; Basir, L.; Ekrami, A.; Haghighizadeh, M.H.; Maghsoumi-Norouzabad, L. Effects of the Consumption of Probiotic Yogurt Containing Bifidobacterium lactis Bb12 on the Levels of Streptococcus mutans and Lactobacilli in Saliva of Students with Initial Stages of Dental Caries: A Double-Blind Randomized Controlled Trial. *Caries Res.* **2020**, *54*, 68–74. [CrossRef] [PubMed]
35. Rungsri, P.; Akkarachaneeyakorn, N.; Wongsuwanlert, M.; Piwat, S.; Nantarakchaikul, P.; Teanpaisan, R. Effect of fermented milk containing Lactobacillus rhamnosus SD11 on oral microbiota of healthy volunteers: A randomized clinical trial. *J. Dairy Sci.* **2017**, *100*, 7780–7787. [CrossRef] [PubMed]
36. Ghasemi, E.; Mazaheri, R.; Tahmourespour, A. Effect of Probiotic Yogurt and Xylitol-Containing Chewing Gums on Salivary S Mutans Count. *J. Clin. Pediatr. Dent.* **2017**, *41*, 257–263. [CrossRef] [PubMed]
37. Wu, J.; Cannon, R.D.; Ji, P.; Farella, M.; Mei, L. Halitosis: Prevalence, risk factors, sources, measurement and treatment—A review of the literature. *Aust. Dent. J.* **2020**, *65*, 4–11. [CrossRef] [PubMed]
38. Apatzidou, A.D.; Bakirtzoglou, E.; Vouros, I.; Karagiannis, V.; Papa, A.; Konstantinidis, A. Association between oral malodour and periodontal disease-related parameters in the general population. *Acta Odontol. Scand.* **2013**, *71*, 189–195. [CrossRef] [PubMed]
39. Scully, C.; Greenman, J. Halitosis (breath odor). *Periodontol. 2000* **2008**, *48*, 66–75. [CrossRef] [PubMed]
40. Miyazaki, H.; Sakao, S.; Katoh, Y.; Takehara, T. Correlation between volatile sulphur compounds and certain oral health measurements in the general population. *J. Periodontol.* **1995**, *66*, 679–684. [CrossRef] [PubMed]
41. Lo Giudice, R.; Militi, A.; Nicita, F.; Bruno, G.; Tamà, C.; Lo Giudice, F.; Puleio, F.; Calapai, F.; Mannucci, C. Correlation between oral hygiene and IL-6 in children. *Dent. J.* **2020**, *8*, 91. [CrossRef] [PubMed]
42. Sparabombe, S.; Monterubbianesi, R.; Tosco, V.; Orilisi, G.; Hosein, A.; Ferrante, L.; Putignano, A.; Orsini, G. Efficacy of an All-Natural Polyherbal Mouthwash in Patients with Periodontitis: A Single-Blind Randomized Controlled Trial. *Front. Physiol.* **2019**, *10*, 632. [CrossRef] [PubMed]
43. Monterubbianesi, R.; Sparabombe, S.; Tosco, V.; Profili, F.; Mascitti, M.; Hosein, A.; Putignano, A.; Orsini, G. Can desensitizing toothpastes also have an effect on gingival inflammation? A double-blind, three-treatment crossover clinical trial. *Int. J. Environ. Res. Public Health* **2020**, *17*, 8927. [CrossRef] [PubMed]
44. Amato, M.; Di Spirito, F.; D'ambrosio, F.; Boccia, G.; Moccia, G.; De Caro, F. Probiotics in periodontal and peri-implant health management: Biofilm control, dysbiosis reversal, and host modulation. *Microorganisms* **2022**, *10*, 2289. [CrossRef] [PubMed]