GRADUATION PROJECT

Degree in Dentistry

DO PROBIOTICS REDUCE THE RISK OF DENTAL CARIES IN ADULT?

PREVENTIVE DENTISTRY-DOCUMENTARY RESEARCH

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RESUMEN

Introducción: Los probióticos han sido propuestos como medida preventiva contra la caries dental, principalmente debido a su posible efecto sobre el microbiota oral; sin embargo, su eficacia en adultos no está clara. **Objetivos:** Este estudio tuvo como objetivo evaluar si el uso de probióticos puede reducir el riesgo o la incidencia de caries dental en la población adulta, al mismo tiempo que examina la evidencia actual y sus limitaciones. **Metodología:** Se realizó una investigación documental utilizando bases de datos científicas electrónicas y criterios de inclusión predefinidos para identificar estudios que evaluaran los efectos de los probióticos sobre parámetros relacionados con la caries en adultos. Los estudios seleccionados se analizaron según su diseño, población, intervenciones y resultados reportados, tanto microbiológicos como clínicos. **Resultados:** Los resultados sugieren que los probióticos pueden influir en factores implicados en el desarrollo de la caries, incluyendo bacterias cariogénicas, propiedades de la placa y parámetros salivales. Varios estudios informaron reducciones en niveles de *Streptococcus mutans* y cambios en la composición salival. Sin embargo, estos efectos fueron variables y no se observaron de manera consistente, y algunos no mostraron diferencias significativas en comparación con los grupos control. Algunos estudios también describieron cambios en lesiones de caries tempranas, especialmente en caries radicular, mientras que otros reportaron principalmente modificaciones microbiológicas o salivales. En general, la evidencia actual no permite establecer una conclusión clara sobre el impacto de los probióticos en la incidencia o progresión de la caries dental en adultos. **Conclusiones**: Los probióticos pueden contribuir a un enfoque preventivo en la salud oral, especialmente en la intervención temprana y la reducción del riesgo. Sin embargo, sus efectos siguen siendo inciertos y deben considerarse como un complemento a las medidas preventivas establecidas. Esto resalta la necesidad de interpretar su uso con cuidado en la práctica clínica.

PALABRAS CLAVE

Odontología, Probióticos, Caries dental, Prevención de Caries, Adultos

ABSTRACT

Introduction: Probiotics have been suggested as a preventive approach for dental caries, mainly due to their potential effect on the oral microbiota, but their effectiveness in adults remains unclear. **Objectives**: This study aimed to evaluate whether the use of probiotics can reduce the risk or incidence of dental caries in adult population, while also examining the current evidence and its limitations. **Methodology:** A documentary research was conducted using scientific electronic databases and predefined inclusion criteria to identify studies evaluating the effects of probiotics on caries-related parameters in adults. The selected studies were analyzed according to their design, population, interventions, and reported outcomes, both microbiological and clinical. **Results:** The findings suggest that probiotics may influence several factors involved in caries development, including cariogenic bacteria, plaque properties, and salivary parameters. Several studies reported reductions in *Streptococcus mutans* levels and changes in salivary composition. However, these effects were variable and not consistently observed across studies, with some reporting no significant differences compared to control groups. Some studies also described changes in early caries lesions, particularly root caries, while others mainly reported microbiological or salivary modifications. Overall, current evidence does not allow a clear conclusion regarding the impact of probiotics on the incidence or progression of dental caries in adults. **Conclusions:** Probiotics may contribute to a preventive approach to oral health, particularly in early intervention and risk reduction. However, their effects remain uncertain, and they should be considered as complementary to established preventive measures. This highlights the need for a cautious interpretation of their use in clinical practice.

KEYWORDS

Dentistry, Probiotics, Dental Caries, Caries Prevention, Adults

INDEX

1. INTRODUCTION 6

1.1 Importance and Prevention of Dental Caries Nowadays 6
1.1.1 Definition of Dental Caries 6
1.1.2 Prevalence of Dental Caries 6
1.1.3 Importance of Early Detection and Management 6

1.2 Mechanism and Etiology of Dental Caries 7
1.2.1 Evolution of the Caries Hypotheses 7
1.2.2 Main Contributing Factors 8
1.2.3 Demineralization and Remineralization 8
1.2.4 Cariogenic Bacteria 9

1.3 Prevention of dental caries 9
1.3.1 Concept and Levels of Prevention 9
1.3.2 Traditional Primary Prevention Methods 10

1.4 Probiotics: Biological Basis and Clinical Relevance in Dentistry 10
1.4.1 History and General Definition 10
1.4.2 Classification and Main Probiotic groups 10
1.4.3 Sources of Probiotics: Natural and Exogenous forms. 11
1.4.4 Common uses and mechanisms in general health 11
1.4.5 The oral microbiome and rational for probiotic use 12
1.4.6 Mechanism of action in the oral cavity 12
1.4.7 Probiotics most commonly studied in dentistry 13

2. OBJECTIVE 14

3. MATERIAL AND METHODS 15

3.1 Study Design 15

3.2 Inclusion and Exclusion criteria 15

3.3 Search strategy 17
3.3.1 Databases 17
3.3.2 Keywords and MeSH terms 17
3.3.3 Boolean operators 18
3.3.4 Study selection 18

4. RESULTS 19

4.1 Selection of the studies 19

4.2 Synthesis of the results 20

5. DISCUSION 28

5.1 Summary of the main findings 28

5.2 Interpretation of the results 28

5.3 Clinical relevance 29

5.4 Safety and limitations of probiotic use 30

5.5 Limitations of the included studies 30

5.6 Future perspectives and recommendations 31

6. CONCLUSIONS 33

7. SUSTAINABILITY 34

8. REFERENCES 35

1. INTRODUCTION

1.1 Importance and Prevention of Dental Caries Nowadays

1.1.1 Definition of Dental Caries

According to the World Health Organization (WHO), dental caries also known as tooth decay, is defined as "the localized destruction of dental hard tissues caused by acids produced when bacteria in dental plaque metabolize sugars."

It is considered as a chronic and non-communicable disease (NCD), characterized by a dynamic process of alternating cycles of demineralization and remineralization.

Dental caries can affect both deciduous and permanent teeth (1), and represents the main cause of tooth loss in the world (2).

From a clinical point of view, caries does not appear suddenly. Indeed, it develops over time due to an imbalance between protective and pathogenic factors within the oral environment. The host, diet, bacterial biofilm, and time interact, making dental caries a multifactorial disease (3).

1.1.2 Prevalence of Dental Caries

According to NIH tooth decay is the most common non communicable disease, as approximately 2.5 billion people are affected. As described, it touches both children and adults, but with a higher prevalence in permanent teeth: 2 billion adults with permanent teeth affected and 510 million children with primary teeth affected. Nearly 90% of adults between 20 to 64 years old, have experienced tooth decay, and this prevalence has remained stable over the past two decades (4,5).

In addition to age, socio-economic status influences the risk of caries, with higher rates observed in low- and middle-income countries which illustrates the differences in access to preventive care and oral health education (6).

1.1.3 Importance of Early Detection and Management

Dental caries remains a major public health concern because of its consequences. When left untreated, tooth decay can cause persistent pain, difficulty in eating or sleeping, affect speech

and self-esteem, and can lead to tooth extraction. These outcomes do not only affect individuals but also healthcare systems and society, given the cost of treatments and lost productivity (7).
Clinical research shows that early detection and timely management of carious lesions plays a crucial role in managing this disease. In its initial phase, tooth decay is a reversible lesion that can be reversed through remineralization and so the tooth can recover without a filling. Therefore, routine dental check-ups, risk assessments, and minimally invasive interventions are crucial to prevent more invasive treatment later.
By focusing on early stages rather than waiting for cavitation, dental care can shift from reactive to proactive — preserving natural tooth structure, reducing discomfort, and cutting long-term cost (8).

1.2 Mechanism and Etiology of Dental Caries

1.2.1 Evolution of the Caries Hypotheses

Throughout history, several theories about the origin and development of caries have emerged. Early concept, such as W.D. Miller's chemico- parasitic theory, described caries as a result of the chemical dissolution of enamel by acids when bacteria metabolized dietary sugars (9).
Later, two other major theories emerged to explain the role of the oral biofilm:
The « Specific Plaque hypothesis » by Loesche in 1976 suggest that only specific bacterial species, such as *Streptococcus mutans* and *Lactobacillus*, could directly be responsible for the caries initiation and development (10). In contrast, the « Non-Specific plaque Hypothesis » proposed by Theilade in 1986 suggested that the overall activity of the entire biofilm, rather than specific bacteria, was responsible for disease.
Finally, Marsh introduced in 1994 a new theory: the « Ecological Plaque Hypothesis », redefined in 2003 and 2008, which joint both previous theories. According to Marsh, dental caries arises from an ecological shift within the oral microbiota: frequent sugar exposure and low pH environments select for acidogenic and aciduric bacteria, disrupting the balance between commensal and pathogenic species. This hypothesis now serves as the most widely accepted model for understanding caries development (11,12).

1.2.2 Main Contributing Factors

Nowadays caries is characterized by the result of complex interactions between biological and environmental factors. According to the ecological model, four main factors contribute to the initiation and progression of the disease: host factors, diet, time and microbial composition.

Host factors regroup the tooth structure, with the composition and structure of both enamel and dentin, which influence how easily acids can penetrate the tooth. Saliva is also known to play an important protective role due to its buffer, antibacterial and remineralization capacity. For instance, when the salivary flow rate decreases, due to xerostomia, age, medications, the risk of caries increases significantly (13).

Beyond host susceptibility, external factors, such as diet, play a crucial role in the caries progress. Frequent sugar intake especially sucrose is the most significant risk factor. The metabolism of the sugar by the bacteria will create an acid production, which will cause the drop of the pH and so will lead to the demineralization. As caries is a chronic and progressive process time should also be considered as an important risk factor. It is required repeated acid attacks over time before irreversible demineralization occurs (14).

The microbial composition of dental plaque strongly determines its cariogenic potential. Specific bacteria such as *Streptococcus mutans* and *Lactobacillus* are considered key. Under conditions of frequent sugar intake, these bacteria become dominant, altering the balance of the oral microbiota, shifting the biofilm from a symbiotic to a dysbiotic state, leading to a demineralization (11).

1.2.3 Demineralization and Remineralization

The development of dental caries can be understood as a dynamic balance between demineralization and remineralization. Each sugar intake leads to a rapid drop of pH in the dental plaque as illustrated by the Stephan Curve. When the pH falls below a critical threshold (approximately 5,5), enamel demineralization begins.

Over time, the pH gradually returns to neutral thanks to the natural protective factors such as fluoride or the buffering capacity of saliva, which also provides calcium and phosphate ions necessary for remineralization**.**

However, if these acid phases occur frequently enough or last long enough, enamel demineralization will dominate over the remineralization and can lead to the accumulation of enamel damage.

The duration and frequency of these acidic episodes are key determinants in the development and progression of carious lesions.

1.2.4 Cariogenic Bacteria

Specific bacteria play a central role in the development of dental caries. Even if hundreds of microbial species live in the oral cavity, a few of them are considered cariogenic because of their capacity to produce acids, adhere to teeth and survive in low pH. They are said to be opportunistic.

Streptococcus mutans is considered as the primary actor of enamel caries. It adheres strongly to the tooth surface, forming biofilms and metabolizing sugars into acid. Its acidogenic and aciduric properties allow it to dominate the microbial community when exposed to frequent sugar intake, pulling the oral microbial balance in a dysbiotic state that favors demineralization (15).

Lactobacillus species are known to be less involved in the initiation of the tooth decay but more in the progression of the disease. They act in acidic environment and enhance the demineralization of already touched enamel. Their presence shows deep carious lesions rather than early enamel changes (16,17).

Together, these bacteria and other cariogenic species contribute to a shift in the oral microbiota toward a more cariogenic state.

1.3 Prevention of dental caries

1.3.1 Concept and Levels of Prevention

Prevention, defined as “any measure that would reduce the probability of occurrence of a condition or disease, or interrupt or slow its progression,” plays a central role in the management of dental caries.

Three levels of prevention are commonly described: primary prevention, which aims to prevent the onset of disease; secondary prevention, which focuses on early detection and management; and tertiary prevention, which involves limiting the consequences of established disease.

In the case of dental caries, prevention is mainly a matter of primary prevention. Its objective is to anticipate the onset of the disease, to reverse its early progress, or to stop the pathological process before secondary treatments, such as fillings, become necessary (18).

1.3.2 Traditional Primary Prevention Methods

Several preventive strategies have been developed to reduce the risk of dental caries. These include dietary control, oral hygiene practices, fluoride use, topical antimicrobials, and the application of pit and fissure sealants. Among these, regular toothbrushing with fluoridated toothpaste remains the cornerstone of caries prevention.

Despite the effectiveness of these conventional measures, dental caries continues to be highly prevalent worldwide. This highlights the need for complementary preventive approaches that could enhance current strategies and better address the multifactorial nature of the disease (19,20).

1.4 Probiotics: Biological Basis and Clinical Relevance in Dentistry

1.4.1 History and General Definition

The term “probiotics” has a Greek etymology coming from the prefix “pro” meaning “for” and the world “bios” meaning “life” (“for life”). It was introduced in the 20th century to describe beneficial microorganisms, in contrast to antibiotics. Early observations by Elie Metchnikoff suggested that the consumption of fermented foods could have positive effects on health, linking certain bacteria to increased longevity (21).

Over time, studies were performed and the scientists moved beyond the traditional use of fermented foods and began isolating specific bacteria strains to better understand their effect on health.

Nowadays, probiotics are defined as *“*live microorganisms which, when administered in adequate amounts, confer a health benefit on the host”- this definition was established by WHO and FAO (Food and Agriculture Organization of the United Nations) in 2001 and redefined by ISAPP (International Scientific Association for Probiotics and Prebiotics) in 2014 (22).

1.4.2 Classification and Main Probiotic groups

Probiotics are considered as an heterogenous group of microorganisms classified according to various factors: their taxonomy, biological origin, site and mechanism of action. The most used

classification is taxonomy which is a way to identify microorganisms according to their genus, species and strain, as probiotics are strain specific (22).

The most frequently studied probiotics belong to the genera *Lactobacillus, Bifidobacterium*, and *Streptococcus. Lactobacillus* species, such as *Lactobacillus rhamnosus* and *Lactobacillus reuteri* (23), have been widely investigated for their potential to influence cariogenic bacteria and modify the oral environment. *Bifidobacteriu*m species have also been studied for their role in maintaining microbial balance and reducing the growth of pathogenic microorganisms.

In addition, certain oral commensal species, particularly *Streptococcus salivarius* (including strains such as K12 and M18), have been explored for their ability to interact with the oral microbiota and inhibit cariogenic bacteria (24).

This classification highlights that probiotic effects are not generalizable, as they depend on the specific strains used, which may explain the variability observed in clinical studies.

1.4.3 Sources of Probiotics: Natural and Exogenous forms.

The term source refers to the origin of probiotic microorganisms. Two main sources are known: Natural and Exogenous sources.

Natural sources include probiotics found in fermented foods traditionally consumed such as dairy: yogurt, cheese; vegetables: pickles; drinks: kombucha and soy-based foods (25). Some probiotics are also commensal organisms, meaning they are naturally part of the human microbiota, such as gut or the oral cavity.

On the other hand, some probiotics come from exogenous sources. They are added intentionally through industrial processes or drugs such as dietary supplements (capsules, powders…), Oral-care products (gums, toothpastes, mouthrinses…) (26) or functional foods. These products contain selected and standardized bacterial strains to ensure their survival, effective dosage, and specific health benefits. They are designed to deliver probiotics directly to target sites such as the intestine or the oral cavity (27).

1.4.4 Common uses and mechanisms in general health

Probiotics are used in many areas of medicine because of their beneficial effects on the general health. Their most common use is in the digestive field, where they help prevent and reduce antibiotic-associated diarrhea, irritable bowel syndrome and constipation. They are also known

to support the immune system, lowering the risk of respiratory and intestinal infections (20), cardiovascular system and have been used in dermatology and allergy prevention (28).

Their multiple uses can be explained by different biological actions. Probiotics block and compete against pathogens from adhering to mucosal surfaces, produce antimicrobial substances (bacteriocins, organic acids), restore the balance of the microbiota, stimulate the immune system and increase the strength of the epithelial barrier, preventing the entry of harmful microorganisms (22).

These same actions may occur in the oral cavity, opening new perspectives for oral health applications.

1.4.5 The oral microbiome and rational for probiotic use

The oral microbiome represents a complex and dynamic community of microorganisms located in the mouth. It includes fungi, viruses and more than 700 bacterial species distributed in different locations: tongue, mucosa, saliva, tooth surfaces (29).

In healthy conditions, these microorganisms live in harmony and form a stable and protective ecosystem, known as a state of microbial balance or symbiosis. This symbiosis is considered essential for oral health. When it is disturbed by factors like poor oral hygiene, excessive sugar intake, antibiotic use or xerostomia, the microbiota can shift into a dysbiotic state. This imbalance leads to the growth of pathogenic species like *Streptococcus mutans* , leading to oral diseases and to dental caries (30).

Probiotics can have a role and help restoring microbial balance, by inhibiting pathogenic bacteria and promoting beneficial species. They can also support local immunity, improve salivary defenses, and help maintain a neutral pH (26).Through these mechanisms, probiotics offer a biological and preventive approach to oral care, acting directly on the causes of imbalance rather than only on the symptoms, and contributing to long-term oral health.

1.4.6 Mechanism of action in the oral cavity

In the oral cavity, probiotics act locally through several specific mechanisms that differ from those observed in the gut. Once introduced, they can attach to oral surfaces and interfere with biofilm formation, reducing the adhesion and growth of cariogenic bacteria such as *Streptococcus mutans* and periodontopathogens like *Porphyromonas gingivalis*. By modifying the biofilm structure, probiotics help create an environment less favorable to disease (31).

They can also influence salivary properties, stimulate salivary flow and increase buffering capacity, which helps maintain a neutral pH and favors enamel remineralization. In addition, probiotics interact directly with oral epithelial and immune cells, regulating inflammatory mediators and strengthening mucosal defenses.

Through these local actions, probiotics help stabilize the oral ecosystem, reduce the presence of harmful microorganisms, and protect hard and soft tissues. These mechanisms explain their potential benefits in preventing dental caries, gingivitis, and halitosis, supporting their use as a biological and preventive approach in modern dentistry (32).

1.4.7 Probiotics most commonly studied in dentistry

Several probiotic strains have been investigated for their potential benefits in oral health. Among them, species of the genera *Lactobacillus***,** *Bifidobacterium***,** and *Streptococcus* are the most widely studied.

Lactobacillus reuteri is one of the best-documented strains in dentistry. It can adhere to oral tissues, inhibit *Streptococcus mutans*, and reduce gingival inflammation (23). Clinical studies have shown that it may lower plaque accumulation and bleeding on probing. *Lactobacillus rhamnosus* and *Lactobacillus casei* have also demonstrated anti-cariogenic properties by decreasing the number of cariogenic bacteria and modulating the oral microbiota. *Bifidobacterium bifidum* and *Bifidobacterium animalis* have been studied mainly for their role in reducing the risk of dental caries and balancing the oral flora (33).

In addition, some commensal oral species such as *Streptococcus salivarius* strains *K12* and *M18* have attracted attention for their ability to produce bacteriocins that inhibit *S. mutans* and other pathogens involved in halitosis and periodontal disease (34). Together, these findings highlight that probiotic effects are strain-specific, and their success depends on their ability to survive, adhere, and interact within the oral ecosystem (22)— making these microorganisms promising agents in preventive and therapeutic dentistry.

2. OBJECTIVE

Primary objective:

To evaluate**,** whether the use of probiotics can reduce the risk or incidence of dental caries in adults.

Secondary objective:

To analyze the current evidence and limitations of clinical studies assessing probiotics in caries prevention among adult populations.

3. MATERIAL AND METHODS

3.1 Study Design

This preventive thesis was conduct as documentary research, structured around a previously and clearly defined PICO question.

PICO stands for:

P- Population: adults, defined as men and women over 18 years old.

Although adults are the population of interest, this criterion was not included in the search strategy. Many studies involve mixed-age populations, and using an age filter could exclude relevant articles that still provide extractable adult data. For this reason, age restrictions were applied only during the screening phase and not during the initial database search.

I-intervention: referring to the administration of probiotics.

C-comparison: comparison with a placebo or with adults not receiving any probiotic.

O-outcomes: assessing the effects of probiotics on dental caries, demineralization and risks factors.

Based on these elements, the research question emerged: In adults, does the regular use of probiotics compared with placebo or no probiotic use reduce the risk or incidence of dental caries?

3.2 Inclusion and Exclusion criteria

To gather pertinent, relevant and quality information a selection of articles was done, following systematic criteria.

Inclusion criteria	Exclusion criteria
Articles written in English	Articles written in languages other than English Articles for which full-text access was not available
Primary evidence, prioritized in the following order: Randomized clinical trial, cohort studies, case control studies, case series and reports	Secondary evidence including systematic reviews
Articles published in peer-reviewed journals	Preprints or non-peer reviewed publications
Studies published within the last 15 years (2010-2025)	Studies published more than 15 years ago
Using keywords and related to the PICO question	Not using the selected keywords or not relevant to the PICO question
In vivo studies (or studies including extractable in vivo human data)	In vitro or animal studies
Clearly identified probiotic strains	Studies not using identified probiotics strains
Conducted on adult participants, or in mixed-aged samples with adult data available	Conducted exclusively on pediatric populations
Conducted on healthy participants or population without systemic disease	Participants with systemic diseases affecting immune function
Participants not going under head and neck radiotherapy	Participants undergoing head and neck radiotherapy
Assessment of dental caries or caries-associated outcomes (clinical and/or microbiological)	Studies not assessing dental caries or caries-associated outcomes (e.g., studies limited to plaque index alone or periodontal disease only)
Oral hygiene habits not modified during the study period	Studies in which oral hygiene habits were modified during the intervention

Table 1. Inclusion and exclusion criteria of the selected studies.

3.3 Search strategy

3.3.1 Databases

The scientific literature search was conducted using the PubMed and MEDLINE databases to identify relevant clinical studies on the effects of probiotics on dental caries and associated outcomes.

3.3.2 Keywords and MeSH terms

To carry the research on the previously cited databases, keywords were selected, and MeSH terms were identified through the National Library of Medicine MeSH database and included to encounter relevant studies related to the documentary research.
The keywords, also known as Free Terms and MeSH terms were grouped according to the PICO question, and given in the following table:

PICO	*MeSH Terms*	*Free Terms*
Population (adult)	"Adult" [Mesh]	adult, adults, adult population, over 18 years old
Intervention (Probiotics)	"Probiotics" [Mesh], "*Streptococcus salivarius*" [Mesh], "*Lactobacill*us" [Mesh]	Probiotics, Oral Probiotics, Probiotic Therapy, Probiotic Supplement, *Streptococcus Salivarius, Streptococcus Salivarius M18, S. salivarius K12, Lactobacillus Rhamnosus, Lactobacillus Reuteri, Bifidobacterium*
Comparison (Placebo/ no intervention)	"Placebo" [Mesh]	Placebo, Control Group, No Probiotic use.
Outcomes (tooth decay)	"Dental Caries" [Mesh], "Tooth Demineralization" [Mesh], "Dental Plaque" [Mesh], "*Streptococcus mutans*" [Mesh]	Prevention, Tooth decay, Dental caries, Caries incidence, Caries risk, Oral biofilm, Plaque pH, Oral Microbiome, Demineralization, *Streptococcus mutans* count

Table 2. Keywords and MeSH terms used for literature search based on the PICO framework.

3.3.3 Boolean operators

Different combinations were made of the selected keywords and MeSH term. These equations were applied on MEDLINE and PubMed and tested to find the most relevant articles:
The main equation was: (probiotic OR probiotics OR "oral probiotics" OR "*Streptococcus salivarius M18*" OR "*Lactobacillus rhamnosus*") AND ("dental caries" OR "tooth decay" OR (caries, dental [MeSH Terms]))

3.3.4 Study selection

After applying the defined keywords, Boolean combination and exclusion criteria, the articles were studied and selected on three different levels.
In a first phase, articles' titles were reviewed to remove the ones that were clearly unrelated to the topic. Studies were excluded at this stage if they did not involve probiotic, were not related to dentistry or dental caries, were not written in English or were laboratory or animal studies.
The following step consisted in reading the abstracts, keeping in mind the inclusion and exclusion criteria previously established, of the articles that passed the title selection. Articles were excluded if the intervention did not involve clearly identified probiotic strains, if the outcomes were unrelated to dental caries incidence or cariogenic bacteria, addressed periodontal diseases only. Articles that were not primary research were also excluded. Additionally, studies containing a population with systemic diseases or undergoing head and neck radiotherapy were excluded at this stage.
The remaining articles were then read in their entirety. They were excluded when the full text was not accessible, when adult data could not be extracted from mixed-age samples, did not provide caries-related outcomes. Studies were also excluded if oral hygiene habits were significantly modified during the intervention period or if the article was not published in a peer-reviewed journal.
Only studies that met all the criteria were included in the final review.

4. RESULTS

4.1 Selection of the studies

The process of articles selection is represented in the PRISMA diagram.

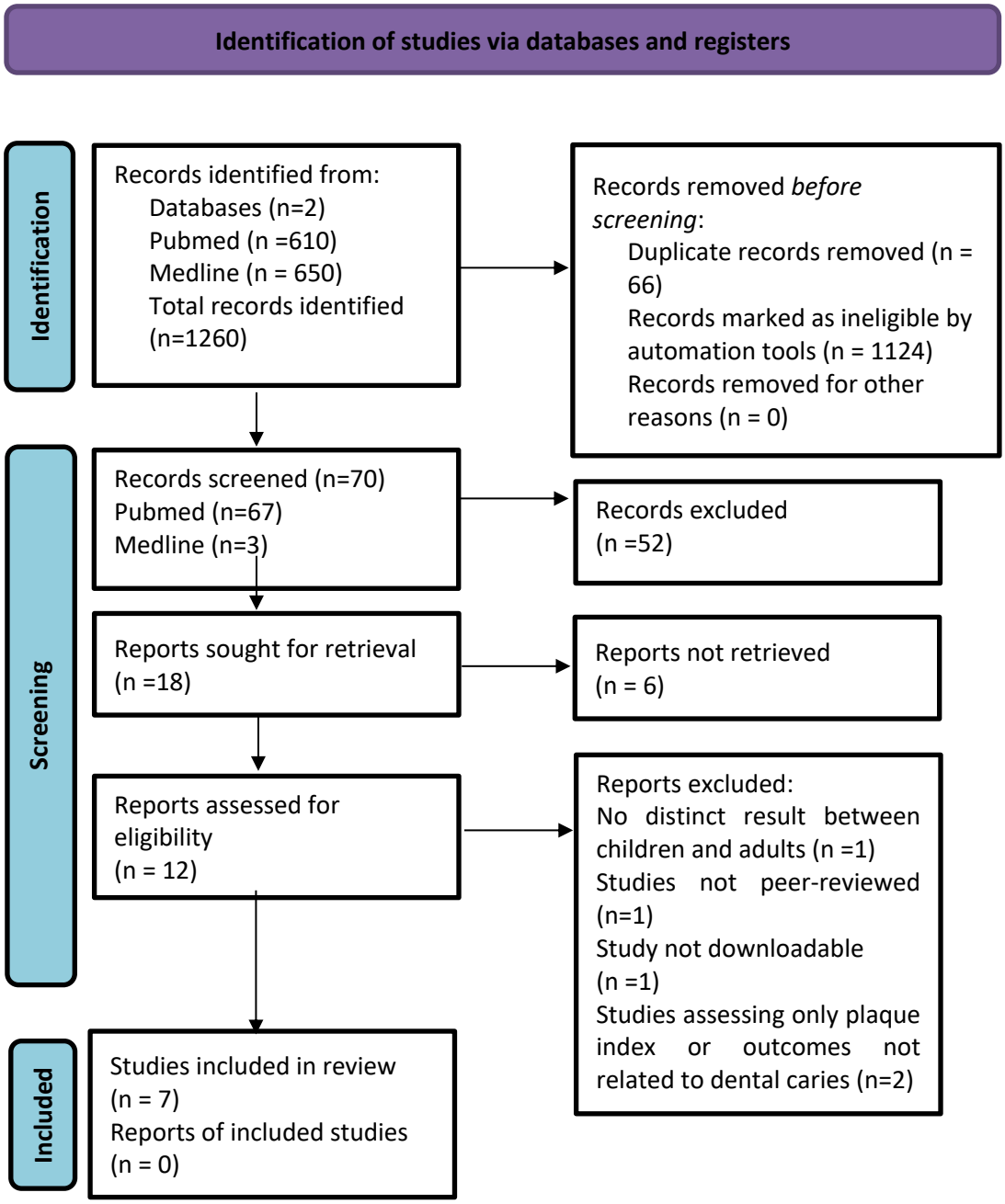


Figure 1. PRISMA 2020 flowchart (35).

4.2 Synthesis of the results

The seven selected studies were randomized controlled trials (RCTs) evaluating the effects of probiotics on parameters related to caries risk. The studies were conducted in adult populations and included between 26 and 150 participants. Several probiotic strains were studied, mainly from *Lactobacillus*, *Bifidobacterium* and *Streptococcus* family. Probiotics were administered in various forms, such as tablets, yogurt, milk and cheese. The duration of the interventions varied between studies, ranging from a few weeks to several months.

The evaluated outcomes focused mainly on microbiological and clinical parameters associated with caries risk, including salivary levels of *Streptococcus mutans*, dental biofilm characteristics, certain salivary parameters and, in some cases, the progression of caries lesions.

The main characteristics of the selected studies are summarized in the following table.

Authors and year	*Study design*	*Population*	*Probiotic strain + Modeof administration*	*Duration*	*Microbiological outcomes*	*Clinical outcomes and other caries-related parameters*
Campus et al. (36) 2025	Double-blind RCT, crossover, in vivo ± ex vivo/in vitro (Only the in vivo part of the study is included)	26 adults Probiotic group n= 13 Control group n=13	*Lactobacillus brevis CD2* Lozenge	4 weeks	**<u>Plaque microorganisms</u>** (relative abundance; % of total viable bacteria): ***S. mutans:*** <u>Probiotic group</u> Baseline: 0.02 ± 0.0005 Day 28: 0.12 ± 0.006 <u>Control group:</u> Baseline: 0.11 ± 0.006 Day 28: 0.86 ± 0.05 ***Lactobacilli:*** <u>Probiotic group:</u> Baseline: 0.05 ± 0.002 Day 28: 0.10 ± 0.004 <u>Control group</u> Baseline: 0.01 ± 0.0004 Day 28: 0.01 ± 0.0003 **Total streptococci**: <u>Probiotic group:</u> Baseline: 35.00 ± 0.44 Day 28: 19.99 ± 0.19 <u>Control group:</u> Baseline: 23.05 ± 10.84 Day 28: 23.22 ± 0.34	**<u>Plaque acidogenicity</u>** (after 10% sucrose rinse): **Minimal pH value** <u>Probiotic group</u>: Baseline:5.32 ± 0.42 Day 28: 5.49 ± 0.53 <u>Control group</u>: Baseline :5.39± 0.48 Day 28: 5.2± 0.53 **Maximal pH fall** <u>Probiotic group:</u> Baseline: 1.55 ± 0.48 Day 28: 1.32 ± 0.49 <u>Control group:</u> Baseline :1.41 ± 0.36 Day 28: 1.52 ± 0.50 **<u>Plaque index</u>** (Silness-Löe score): <u>Probiotic group:</u> Baseline: 1.60 ± 0.50 Day 28: 1.46 ± 0.42 <u>Placebo group</u>: Baseline: 1.29 ± 0.60 Day 28: 1.58 ± 0.49

Ghasemi E. et al. (37) 2017	RCT	50 adults (age: 19-37) Probiotic group n= Control group n=	*Lactobacillus acidophilus ATCC 4356* and *Bifidobacterium bifidum ATCC29521* Probiotic Yogurt	2 weeks (Follow up: 4 weeks)	**Salivary *Streptococcus mutans*** (×10^5 CFU/mL) Probiotic group: Baseline: 23.62 ± 4.38 Week 2: 4.03 ± 1.37 4 weeks post intervention: 7.86 ± 4.30 Control group: Baseline: 22.28 ± 5.97 Week 2: 5.26 ± 2.01 4 weeks post intervention: 9.04 ± 3.00	No clinical outcomes reported
Ferrer M.D et al. (38) 2020	Double- blind RCT	59 adults (age: 18-65) Probiotic group n= 30 Control group n= 29	*Streptococcus dentisani* 7746 Buccal gel in dental splint	30 days (Follow up: 45 days)	**Salivary and plaque *Streptococcus dentisani*** (qPCR; relative abundance)**:** Probiotic group: Baseline: not numerically reported D15, D30, D45: increased Control group: Baseline: not numerically reported D15–D45: no relevant change	**Salivary flow** (mL/5 min): *(*days 0, 30 and 45: values estimated from graphical data) Probiotic group: Baseline~3.4 Day 15 =4.24 Day 30 ~4.5 Day 45 ~4.8 Control group: Base line ~3.3 Day 15 = 3.24 Day 30 ~3.5 Day 45 ~3.8

Plaque index: (Silness & Löe index)
(values estimated from graphical data)

Probiotic group:
Baseline ~0.9
Day 15 ~0.8
Day 30 ~0.65
Day 45 ~0.6
Control group:
Baseline~ 0.9
Day 15 ~0.95
Day 30 ~1.05
Day 45 ~1

Salivary Calcium (mg/L, saliva)
Probiotic group
Baseline ~75mg/L
Day 30 ~100mg/L
Control group: values not clearly reported

Salivary Ammonium (mg/L, saliva)
Probiotic group:
Baseline ~100mg/L
Day 30 ~150mg/L
Control group: values not clearly reported

Salivary pH:
Values not numerically reported

Teanpaisan R. & Piwat S.(39) 2013	RCT	40 adults (age: 18-25) Randomized into: Probiotic and control group	*Lactobacillus paracasei SD1* Milk powder	4 weeks	**Salivary *Streptococcus mutans*** (log10 CFU/mL): Probiotic group: Baseline: 3.77 ± 0.53 Week 4: 1.45 ± 0.63 Control group: Baseline: 2.44 ± 0.66 Week 4: 2.04 ± 0.63 **Salivary *lactobacilli*** (log10 CFU/mL): Probiotic group: Baseline: 5.66 ± 0.65 Week 46.73 ± 0.67 Control group: Baseline: 5.94 ± 0.43 Week 4: 6.40 ± 0.44	No clinical outcomes reported
Nishihara T. et al.(40) 2014	Open-label RCT	64 adults (Mean age: 24,8 ±2,3) 4 groups: *Lactobacillus salivarius WB21* group (n=17)	*Lactobacillus salivarius WB21* and *TI 2711* Tablets	2 weeks	**Salivary *mutans streptococci*** (score units; change from baseline,Δ): *L. salivarius WB21*: 0.0 (−1.0 to 0.0) *L. salivarius TI2711*: 0.0 (0.0 to 1.3) Control group: 0.0 (0.0 to 2.0) no difference between groups	**Salivary flow** (mL/3 min): *L. salivarius WB21*: Baseline 4.8 (3.3–5.8). Δ 0.0 (−0.5 to 0.0) *L. salivarius TI2711*: Baseline 7.3 (5.8–8.8); Δ 0.0 (−0.4 to 0.5) Control group: Baseline: 5.5 (3.6–7.0); Δ −0.5 (−1.1 to 0.0)

		Lactobacillus salivarius) TI 2711 group (n=16) Ovalgen group (n= 13) Control group (n=18)			***Salivary lactobacilli*** (score units,Δ): *L. salivarius WB21:* 3.0 (2.0–3.0) *L. salivarius TI2711*: 2.5 (2.0–3.0) Control group**:** 0.0(-0,3-0,0) higher values in probiotic groups	**Buffering capacity** (Δ): *WB21:* Δ 0.0 (−0.4 to 0.3) *TI2711:* Δ 0.0 (−0.2 to 0.4) Control group: Δ −0.3 (−0.6 to −0.1) **Salivary pH** (Δ): *WB21*: Δ 0.0 (0.0 to 0.2) *TI2711:* Δ 0.2 (0.0 to 0.3) Control group: Δ 0.0 (−0.1 to 0.3)
Nishihara T. et al.(40) 2014	Short-term administration trial	8 adults	*Lactobacillus salivarius WB21* Tablets	2 weeks	**Salivary *mutans streptococci*** (log_{10} CFU/mL) Probiotic group: Day 0: 6.0 (4.9–6.3) Day 14: 5.5 (4.8–6.1	No clinical outcomes reported

Petersson L.G. et al.(41) *2011*	Double- blind RCT	160 adults (age: 58-64) with at least 2 Primary root caries Lesions Randomized into: Control group, Probiotic+ Fluor group, Probiotic group, Fluor group	*Lactobacillus rhamnosus* LB21 Probiotic milk	15 months	**Salivary and plaque *Streptococcus mutans* and *lactobacilli*** (score 0–3, based on CFU levels): Baseline → 6 months → 15 months No statistically significant differences reported between groups. (Probiotic group, Probiotic + Fluor group, Control group)	**Root Caries Index** (garde 1 (inactive (remineralized) lesions, % of lesions) Probiotic group: Baseline: 0 15 months: 37 Probiotic group + fluor group: Baseline: 0 Month 15: 59 Placebo group: Baseline: 0 Month 15:16 **Electric Caries Monitor** (kΩ – higher values indicate remineralization): Baseline → 15 months Probiotic group: 306 → 581 Probiotic + fluor group: 256 → 1127 Placebo group: 277 → 364 (Not significant)

Chuang L.C. et al. (42) 2010	Double- blind RCT	80 adults (age: 20-26) Probiotic group (n= 42) Control group (n= 38)	*Lactobacillus paracasei GMNL-33* Tablets	2 weeks (Follow up:2 weeks)	**Salivary *Streptococcus mutans*** (score 0–3, based on CFU/mL levels): Probiotic group: Baseline: 2 (0–3) Week 2: 2 (0–3) Weeks 4 (2 weeks post intervention): 1 (0–3) Control group: Baseline: 1.5 (0–3) Weeks 2: 2 (0–3) Week 4: 2 (0–3)	**Salivary buffer capacity** (score 0–2, based on pH buffering capacity): Probiotic group: Baseline: 2 (1–2) Week 2: 2 (1–2) Week 4: 2 (1–2) Control group Baseline: 2 (1–2) Week 2: 2 (1–2) Week 4: 2 (1–2)

Table 3. Characteristics and caries-related outcomes of included clinical studies assessing probiotics in adults.

5. DISCUSION

5.1 Summary of the main findings

Based on the results of the included studies, probiotics tend to show heterogeneous effects on caries-related outcomes in adults. Overall, the results suggest that probiotic interventions may influence several factors associated with caries risk, although these effects were not uniform across studies.

Changes in cariogenic bacteria were frequently examined. Several studies reported a decrease in *Streptococcus mutans* levels following probiotic use, often reflected by a decrease in bacterial levels over the course of the intervention (37,39,42). However, these findings were not consistent, as some studies did not observe significant differences between probiotic and control groups (40,41), and in certain cases, reductions were also reported in control groups.

In addition to microbiological outcomes, some studies reported modifications in plaque and salivary parameters. These changes included reduced plaque acidogenicity and changes in salivary composition, such as increased levels of calcium and ammonium (38). However, other studies found no significant changes in salivary flow, pH, or buffering capacity (40,42).

Only a limited number of studies evaluated clinical outcomes directly related to dental caries. (41) Among these, improvements in early lesions, particularly root caries, were observed in longer-term studies lasting up to 15 months (41). In contrast, shorter interventions, typically lasting only a few weeks (37,40,42), mainly reported changes in microbiological or biochemical parameters rather than direct clinical outcomes.

Overall, these findings suggest that probiotics may influence factors involved in caries development, while evidence for a direct impact on clinical caries outcomes in adults remains limited.

5.2 Interpretation of the results

The results suggest that the effects of probiotics cannot be explained by a simple and direct antibacterial action. Although reductions in *Streptococcus mutan*s were observed in some studies, these findings were not consistent and were sometimes also present in control groups, indicating that other mechanisms are likely involved.

Some studies also reported an increase in *lactobacill*i levels, suggesting that probiotic use may influence the overall microbial balance rather than only specific cariogenic bacteria (36,39,40).
The variability observed across studies may be explained by differences in probiotic strains, duration of exposure, and individual oral conditions. In some cases, the observed effects appeared to be transient and diminished after the end of the intervention (37).
Rather than acting on a single parameter, probiotics appear to influence several components of the oral environment. The reduction in plaque acidogenicity observed in some studies suggests a decrease in acid production by the biofilm, which may limit enamel demineralization. In addition, changes in salivary composition, such as increased calcium and ammonium levels (38), may contribute to a less cariogenic environment. Calcium is involved in remineralization processes, while ammonium may contribute to acid neutralization and support buffering capacity.
Overall, these findings support the idea that probiotics act by modifying the conditions that favor caries development, rather than by directly targeting a specific pathogenic species. This is in line with the ecological plaque hypothesis, which considers dental caries as the result of an imbalance in the oral microbiota.
In summary, probiotics seem to influence the oral environment in a way that may help limit disease progression, although their direct impact on established lesions remains uncertain.

5.3 Clinical relevance

Probiotics should be considered as an adjunct to conventional preventive measures in dentistry rather than a replacement for established oral hygiene practices such as toothbrushing and fluoride use. Their main advantage lies in their ease of integration into daily life, as they can be consumed through commonly available food products or administered as supplements, which may enhance their acceptability in preventive strategies for adults.
From a clinical perspective, probiotics may be particularly relevant for individuals at higher risk of caries, where preventive approaches are essential. Their potential benefit appears to lie mainly in early intervention and risk reduction, rather than in the management of established carious lesions, which is consistent with the limited clinical outcomes observed in the included studies.
However, their effectiveness in real-life conditions may vary between individuals. This variability is likely related to differences in oral microbiota composition, as well as to individual responses to probiotic intake. In addition, adherence may not always be optimal in daily practice, and

irregular consumption may limit their potential benefits.

These considerations suggest a possible role for more personalized preventive approaches in the future, where probiotic use could be adapted to individual caries risk profiles and oral conditions.

Overall, probiotics may represent a simple and accessible way to support preventive strategies, but their use should remain integrated within a comprehensive approach to oral health.

5.4 Safety and limitations of probiotic use

Probiotics are generally considered safe when used in oral or dietary contexts, with very few adverse effects reported in the included studies. However, their main limitation in clinical practice is not related to safety, but rather to the variability and instability of their effects under real-life conditions.

Their clinical effectiveness appears to depend on continuous and regular intake and may be transient if consumption is interrupted. This is consistent with the short-term nature of many interventions and the limited evidence on long-term outcomes.

In addition, it remains unclear whether probiotics can maintain their effects over time in the oral environment, which may contribute to the variability of their effects.

This lack of stability, together with significant individual variability in the oral microbiota, limits the predictability and reproducibility of their clinical outcomes. As a result, their integration into preventive dental care remains a challenge.

5.5 Limitations of the included studies

Although most of the included studies were randomized controlled trials, several methodological limitations should be considered when interpreting the findings.

First, many studies involved relatively small sample sizes, which may limit their statistical power and the generalizability of the results to broader adult populations. In addition, the duration of the interventions was often short, preventing the assessment of long-term effects of probiotics, particularly on the development and progression of dental caries. The relatively small number of included studies also makes it difficult to reach strong conclusions.

Another important issue is the high variability between studies. Differences in probiotic strains, dosages, modes of administration, and study protocols make direct comparisons difficult and limit the identification of optimal conditions for probiotic use. In addition, the use of different measurement methods and units, makes the comparison between the results harder.

Furthermore, the outcomes varied a lot between studies. Most studies focused on microbiological or salivary parameters, while only a limited number evaluated clinically relevant outcomes such as caries lesion progression.

Moreover, most studies were conducted on healthy adult populations and excluded individuals with systemic diseases, which may limit the applicability of the findings to more medically complex or higher-risk patients. In addition, participants using antibiotics were often excluded, although antibiotic use is common in clinical practice and may significantly influence the oral microbiota and the effects of probiotics.

Finally, certain methodological aspects, including participant adherence and long-term follow-up, were not consistently reported, and study conditions were often controlled, which may not fully reflect real-life clinical settings. These factors may introduce bias and affect the reliability and external validity of the results.

Overall, these limitations suggest that, despite promising findings, current evidence remains insufficient to draw strong conclusions regarding the effectiveness of probiotics in reducing caries risk or incidence in adults.

5.6 Future perspectives and recommendations

Based on the results and their limitations, several recommendations can be made for future research. Larger-scale studies with longer follow-up periods are still needed to better assess the long-term effects of probiotics. Likewise, better standardization of study protocols, particularly regarding the probiotic strains used and modes of administration, would improve the comparability of results. The use of standardized outcome measures would also improve comparisons across studies.

Beyond these general recommendations, more specific research directions should be explored. It is important to better define the conditions of probiotic use, especially the frequency of consumption and the duration of interventions, in order to identify potocols that are both effective and applicable in practice.

Furthermore, taking into account the baseline oral microbiota of patients could be an interesting approach to better understand the observed variability in responses. Identifying specific microbiological profiles would help determine which patients are most likely to benefit from this type of intervention. Future research should also include more diverse populations, particularly individuals at higher risk of caries or with systemic conditions. In addition, studies conducted under real-life conditions would be valuable to better reflect clinical practice.

Finally, greater attention should be given to clinically relevant outcomes, such as the onset or progression of carious lesions, to better evaluate the impact of probiotics on oral health.

6. CONCLUSIONS

This documentary research project aimed to explore whether probiotics can reduce the risk or incidence of dental caries in adults, and to review the current evidence and its limitations.

Overall, the results suggest that probiotics may influence factors involved in caries development, such as cariogenic bacteria, plaque properties, and salivary parameters. However, these effects were variable across studies, and current evidence does not allow a clear conclusion regarding their impact on the incidence or progression of dental caries in adults.

These findings should be interpreted with caution, given several methodological limitations, including small sample sizes, short study durations, and significant heterogeneity between studies.

In clinical practice, probiotics may be considered as a supportive approach in caries prevention, particularly in early intervention and risk reduction. However, they should remain complementary to established preventive measures such as oral hygiene and fluoride use.

Future research is needed to better understand the conditions of use and identify the populations that may benefit the most from probiotics.

7. SUSTAINABILITY

The use of probiotics in caries prevention in adults can be considered from a sustainability point of view, particularly in relation to social and economic aspects. This approach could fit with Sustainable Development Goal 3 (SDG 3), one of the 17 goals of Sustainable Development defined by the United Nations (43), which focuses on improving health and well-being, as well as with SDG 10 (Reduced Inequalities) and SDG 12 (Responsible Consumption and Production).

From a social point of view, probiotics may offer a simple and accessible way to support oral health. Because they can be easily integrated into daily habits, they could help the reinforcement of preventive approaches, particularly for populations with limited access to dental care or at higher risk of caries. Including probiotics in public health programs and improving the education of both patients and healthcare professionals, could help increase their use in prevention. However, their effectiveness depends on regular use and remains uncertain, which may limit their real impact.

From an economic perspective, probiotics could contribute to a more preventive approach to oral health that may help reduce costs. However, they do not replace necessary dental treatments. In addition, their accessibility may vary depending on cost and availability, which could limit their use in certain populations.

Overall, while probiotics alone cannot solve the issue of dental caries, they may represent a complementary approach towards more preventive and accessible oral healthcare.

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