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The Use of Probiotics and Synbiotics in the Prevention and Treatment of Post-Antibiotic Diarrhea in Children, with Particular Emphasis on the Future of Such Therapy

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ABSTRACT

Post-antibiotic diarrhea (AAD) is a significant problem in children undergoing antibiotic therapy and is a visible symptom of gut microbiota depletion. To prevent this occurrence, probiotics such as *Lactobacillus rhamnosus* GG, *Saccharomyces boulardii* CNCM I-745, and *Limosilactobacillus reuteri* DSM 17938 may prove to be effective; they work by strengthening the intestinal barrier, modulating the immune system, influencing the metabolome, and through direct antagonism. Future therapy involves not only the use of such preparation but also nanocoating technology, which involves applying protective coatings at the single-cell level; analysis of the patient's baseline microbiome structure to determine which strain is dominant and enable personalized therapy, as well as multiomic analytics and shotgun metagenomics, so that it is possible not only to monitor the composition of the patient's bacteria but also their functional stability and the evolution of the resistome. Combining precision probiotic therapy with modern delivery systems and microbiome analytics represents the future of safe antibiotic therapy in the pediatric population.

Keywords: Post-antibiotic diarrhea, children, probiotics

1. INTRODUCTION

Antibiotics are among the most commonly used medications in the pediatric population. The frequency of their prescription in Western countries ranges from 0.5 to 1.6 courses per child per year, and although they are essential in combating serious diseases, they can themselves cause many negative effects: a reduction in the diversity of commensal microorganisms in the gut, or even disruptions to the

functioning of the developing immune system. Dysbiosis occurring at such an early stage of life therefore has many complications, and one long-term effect is antibiotic-associated diarrhea (Dierikx et al., 2024). AAD is defined as diarrhea occurring during antibiotic treatment or persisting for up to 8 weeks after discontinuation. The frequency of this condition depends, among other factors, on the child's age and is most common in children under 2 years of age; the type of antibiotic used is also significant; the broader the spectrum, the more frequent diarrhea is as a complication (Dinleyici et al., 2025).

AAD is not only a bothersome symptom but also a serious challenge for clinicians, which can result in patient dehydration, the need to discontinue the antibiotic, and possible hospitalization (Merenstein et al., 2026). To prevent this, the use of probiotics - "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" as well as synbiotics, i.e., a combination of probiotics and prebiotics - a nutrient source for beneficial bacteria, which, however, would not be sufficient on its own to counteract AAD (Dinleyici et al., 2025).

2. REVIEW METHODS

The review was done using the PubMed database. The search strategy involved using the following keywords: probiotics, antibiotic-associated diarrhea, children, linked by the AND operator. Studies published in English between January 2021 and February 2026 were taken into consideration. Exclusion criteria included articles for which full text was not available, publications in languages other than English, and studies on species other than humans (studies on mice were excluded). The final selection involved analyzing the titles and abstracts of the chosen articles; finally, after reading and studying the full text, the publications used in this paper were selected. The results of the review are presented in Figure 1.

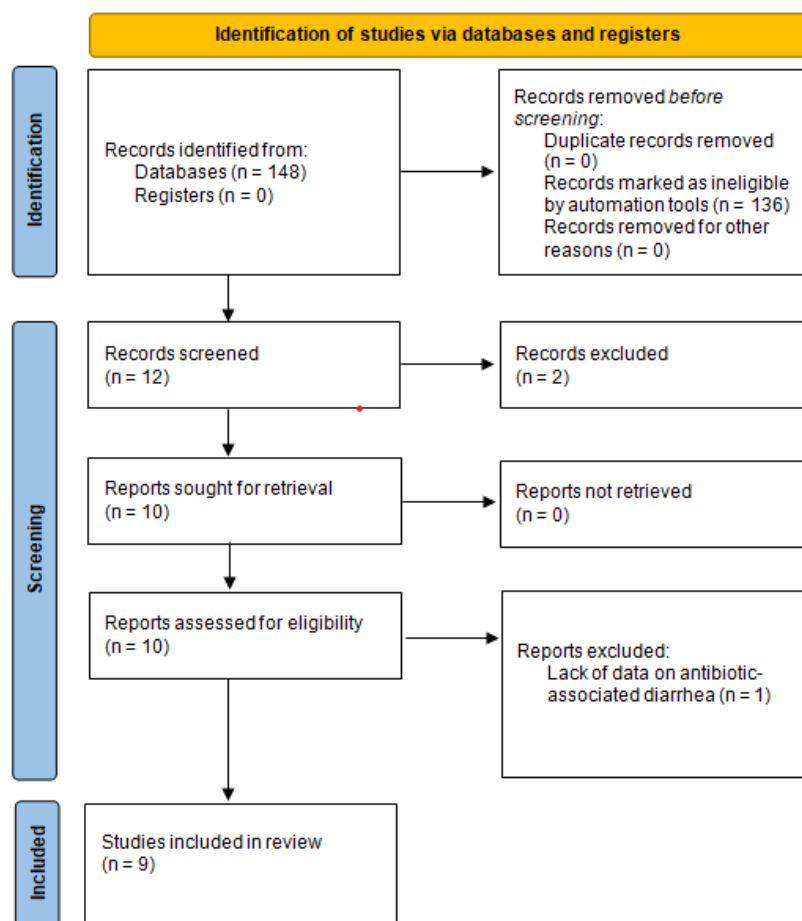


Figure 1. PRISMA Chart

3. RESULTS AND DISCUSSION

Pathophysiology of Diarrhea

Broad-spectrum antibiotics, such as amoxicillin with clavulanic acid or cephalosporins, deplete the diversity of bacteria inhabiting the intestines, including those of the order Bifidobacterium, Lactobacillus, and the families Lachnospiraceae and Ruminococcaceae, while leading to an increase in the population of dangerous bacteria such as resistant *Escherichia coli* or *Clostridioides difficile* (Waitzberg et al., 2024) .

Gut bacteria are needed for the fermentation of undigested carbohydrates into short-chain fatty acids (SCFA). SCFAs are necessary for absorbing water and sodium in the large intestine and for maintaining the integrity of the intestinal barrier; a decrease in the number of gut bacteria causes osmotic diarrhea due to the accumulation of carbohydrates and lack of SCFAs (Dierikx et al., 2024).

Reducing the number of gut bacteria causes colonization resistance. This allows dangerous strains of bacteria like *C. difficile* to multiply and do harm (Waitzberg et al., 2024), resulting in almost 1-2% of AAD cases in children being caused by this pathogen (Merenstein et al., 2026). Symptoms can range from mild diarrhea to a life-threatening condition, which is *pseudomembranous colitis* (Dinleyici et al., 2025). The characteristics of high-risk AAD patients are presented in Table 1.

Table 1. High risk AAD patient

RISK FACTOR	DESCRIPTION
Patient Age	Children under 2 years
Type of Antibiotic	Broad-spectrum antibiotics, e.g., aminopenicillins with a β-lactamase inhibitor
Medical History	Previous episodes of AAD during treatment
Clinical Condition	Need for hospitalization and intravenous antibiotics

Preventive Strategies - The Role of Selected Strains

The effects of using probiotics in preventing AAD depend on the strain used. Promising results for one strain do not mean the same therapeutic success with another (Dinleyici et al., 2025).

Lactobacillus rhamnosus LGG

The LGG strain is one of the most thoroughly studied prebiotics in pediatrics. Its effectiveness stems from the fact that this strain is highly stable in the acidic environment of the stomach and in the presence of bile salts, which allows it to reach the intestines in an active state. Its mechanism of action involves having polysaccharides and protein projections on its surface. These make attachment to the mucosal membrane and temporary colonization possible. The strain then forms a biofilm that protects the epithelium, along with specific soluble factors that maintain intestinal barrier integrity and inhibit host cell apoptosis (Boggio Marzet et al., 2022).

LGG is strongly recommended for the prevention of AAD in children, provided that a sufficiently high dose is used, i.e., at least 5 billion CFU per day (Szajewska et al., 2023). If supplementation starts on the same day as antibiotic therapy, the risk of diarrhea may be reduced by up to 51%. In addition to its direct effect on the microbiota, LGG also regulates the immune system. The strain stimulates immunoglobulin production and promotes a Th1-type immune response (Boggio Marzet et al., 2022).

Saccharomyces boulardii CNCM I-745

Saccharomyces boulardii CNCM I-745 is a yeast; because it is a eukaryotic organism, it is resistant to antibiotics, making it an ideal candidate for use during antimicrobial therapy. This probiotic acts in multiple ways. At the molecular level, this probiotic suppresses key inflammatory pathways such as NF-κB, ERK1/2, and JNK. In addition, it works with epithelial and immune cells to fortify the mucosal barrier while boosting immunoglobulin secretion to regulate immunity (Liu et al., 2025). Administering this probiotic after starting antibiotic therapy, or within 48 hours of its initiation, can significantly reduce the risk of AAD (Waitzberg et al., 2024), to achieve this, the recommended dose is ≥5 billion CFU/day (250–750 mg/day) (Szajewska et al., 2023). *Saccharomyces boulardii* reduces the risk of AAD and *C. difficile*-associated diarrhea (Waitzberg et al., 2024). It also lowers diarrhea severity more effectively than preparations containing *Bifidobacterium* (Liu et al., 2025).

***Limnosilactobacillus reuteri* DSM 17938**

Limnosilactobacillus reuteri DSM 17938 is a natural component of the human microbiota and is distinguished by its ability to survive in the acidic environment of the stomach and its strong adhesion to the intestinal epithelium. The mechanisms of action of this probiotic are: strengthening the intestinal barrier, limiting microbial translocation, and producing antimicrobial substances. Another significant advantage of this strain is its lack of sensitivity to amoxicillin with clavulanic acid, which allows for safe co-administration with this medication. A study conducted on 654 children treated with this antibiotic for otitis media or sinusitis in a prospective, multicenter, randomized, double-blind trial demonstrated the efficacy of this strain in preventing AAD compared to placebo (7.9% vs. 16.7%) at a dose of 2 × 108 CFU/day. The most noticeable effect was observed in the youngest children (6–24 months) and in patients treated with antibiotics for otitis media (Dinleyici et al., 2025).

Multistrain formulations

The use of a multistrain preparation is intended to restore the gut ecosystem more comprehensively. A probiotic containing *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51, *Lactobacillus acidophilus* W37, *Lactobacillus acidophilus* W55, *Lacticaseibacillus paracasei* W20, *Lactiplantibacillus plantarum* W62, *Lacticaseibacillus rhamnosus* W71, and *Ligilactobacillus salivarius* W24 has been studied and found that, when administered at a dose of 10 billion CFU/day throughout the entire course of antibiotic therapy and for 7 days after its completion, do not reduce the risk of AAD, but do lower the risk of any type of diarrhea during antibiotic therapy (Lukasik et al., 2022).

Factors Affecting Treatment Efficacy

Antibiotic spectrum

Narrow-spectrum antibiotics, such as amoxicillin, rarely cause diarrhea (2% of cases) because the disruption to the microbiome is not as severe. It is advisable to prescribe short-term, narrow-spectrum antibiotics; in situations like this, probiotics do not provide any additional benefits. Broad-spectrum antibiotics, such as amoxicillin with clavulanic acid, can cause severe dysbiosis, which justifies probiotic supplementation (Merenstein et al., 2026).

Dosage and Timing

Patients should receive a daily dose consisting of at least 5 billion CFU. For the best results, timing is very important: probiotics should be given as fast as possible - within 24 to 48 hours of the first antibiotic dose and continued for 7-14 days after finishing treatment to speed up gut flora recovery (Szajewska et al., 2023).

Mechanisms of Action

Probiotics are not only intended to replace bacteria lost due to broad-spectrum antibiotic therapy; they also perform several other functions, which are presented in Table 2.

Table 2. Mechanisms of probiotic action

Strengthening the Intestinal Barrier	Strains such as LGG stimulate the production of tight junction proteins, which results in increased intestinal wall integrity (Dierikx et al., 2024).
Immunological Modulation	Through interactions with epithelial cells, macrophages, and lymphocytes, immunoglobulin secretion is increased and local inflammatory processes are inhibited (Waitzberg et al., 2024).
Effect on the Metabolome	Probiotics can support carbohydrate digestion and SCFA production, which directly counteracts the mechanisms of osmotic diarrhea (Dierikx et al., 2024).
Direct Antagonism	The production of bacteriocins and competition for nutrients make it difficult for dangerous pathogens, such as <i>Clostridioides difficile</i> , to colonize these sites (Boggio Marzet et al., 2022).

Safety

Probiotics are considered safe (GRAS status) and well tolerated by children, with uncommon side effects; when they do occur, they are usually mild and include gas, bloating, and nausea. However, special caution should be taken when giving them to high-risk patients, such as:

1. Children with severe immunodeficiencies.
2. Critically ill patients or those hospitalized in an intensive care unit.
3. Children with central lines - in the case of *S. boulardii*, there is a risk of fungemia; in other cases, there is a risk of bacteremia (Waitzberg et al., 2024).

Innovations and Future Research Directions

The concept of “nano-weapons” is one of the most promising areas of innovation. Nanotechnology is used to protect probiotic cells from the harmful effects of antibiotics and stomach acid. The defense mechanism involves creating nanocapsules for individual beneficial bacterial cells using a supramolecular network composed of tannic acid and iron ions-this creates a coating approximately 20 nm thick, which protects the bacteria through intermolecular interactions such as hydrogen bonds, hydrophobic interactions, and electrostatic interactions. As a result, antibiotic molecules are absorbed before they reach the probiotic’s cell membrane.

In vitro studies have shown that nanoparticle-coated probiotics can survive exposure to doses of antibiotics such as levofloxacin, gentamicin, and ciprofloxacin that are many times higher than their minimum bactericidal concentration (MBC). In experiments performed on rats, a protective nano-coating cover was used on probiotics during levofloxacin therapy, resulting in stable gut colonization, reducing the risk of AAD and relieving the state of drug-induced inflammation. This technology is temporary: when cells divide, the protective layer is destroyed, so as antibiotic levels start to decrease, gut bacteria can return to their natural form (Pan et al., 2022).

The future of probiotic therapy lies in its personalization, as evidence suggests that its success depends on the individual characteristics of a patient’s gut microbiota. Three main microbiome enterotypes have been identified in children: one dominated by *Bacteroides*, one dominated by *Enterococcus*, and a mixture of *Prevotella* and *Bacteroides*. Each of these enterotypes is characterized by a different level of stability. The *Bacteroides* cluster is highly stable: following the administration of antibiotics and probiotics, changes in species composition were minimal. The other two clusters mentioned are more susceptible to the negative effects of antibiotic therapy, making patients with these clusters more challenging to treat with probiotics. With awareness of these differences, it will be possible in the near future to administer probiotic therapy to selected patients who will benefit most from the intervention, while avoiding routine use of probiotics in individuals with a naturally stable microbiome. This approach will minimize the risk of unjustified probiotic use and, consequently, the costs associated with the therapy (Szajewska et al., 2023).

Research on AAD is constantly evolving: it now encompasses not only a simple description of species composition based primarily on 16S rRNA gene sequencing, but also comprehensive functional analysis using multi-omic technologies; this allows for the determination not only of the gut microbiota’s composition but also of its functions and how they change under the influence of antibiotic administration. It is extremely important to analyze the metabolic products of gut bacteria with a particular focus on SCFAs. As a side effect of antibiotic therapy, SCFA production becomes reduced, which results in less water absorption and causes diarrhea. Modern research allows for the measurement of these metabolites as a kind of “marker” of gut health; this may turn out to be even more reliable than analyzing taxonomic diversity (Dierikx et al., 2024).

Advanced shotgun metagenomic sequencing provides insight into the full genetic potential of the gut ecosystem. An innovative approach is resistome profiling, which involves monitoring the presence and changes in the abundance of antibiotic resistance genes (ARGs). Tools such as ShortBRED allow us to assess how probiotic administration affects the spread of resistance genes among bacteria during antibiotic treatment.

The ability of the microbiota to return to a state of balance after disruptions caused by antibiotic therapy is called resilience. Because the microbiome retains its metabolic functions much more easily than its original species composition, future therapies should focus on protecting the function of the entire gut ecosystem, rather than merely restoring specific bacterial strains (Waitzberg et al., 2024).

Modern AAD prevention involves not only using probiotics but, more importantly, rational thinking about antibiotic therapy. Using narrow-spectrum antibiotics minimizes disruptions to the microbiome and the risk of AAD, which may turn out to be enough to reduce the risk of diarrhea. It is crucial to raise physicians’ awareness of the impact of medications on the microbiota in order to make treatment more targeted and safer (Waitzberg et al., 2024).

4. CONCLUSION

Post-antibiotic diarrhea is one of the most troublesome complications in children and represents a symptom of intestinal dysbiosis. The effectiveness of probiotics depends on the specific strain; the strongest efficacy has been demonstrated for *Lactobacillus rhamnosus* and *Saccharomyces boulardii* CNCM I-745. Multistrain preparations show efficacy in reducing the overall risk of diarrhea. High doses - at least 5 billion CFU per day - are recommended. Probiotics should be given right after the first dose of antibiotics or within 48 hours, continuing throughout treatment and for 7–14 days after to restore gut microbiota. With broad-spectrum antibiotics, the risk of AAD is higher, and probiotics should be recommended. Patients at elevated risk - such as children under two, hospitalized patients, or those with past episodes - should consider probiotics. Probiotics should not be administered to patients in intensive care, children with severe immune system compromise, or anyone carrying a central venous catheter. Future advances include microbiome analysis and protective nanocoatings.

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Ethical approval

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on the reasonable request to the corresponding author.

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