



Effectiveness and Safety of Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Children: A Systematic Review

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CONFLICT OF INTEREST
None declared.



GRANT SUPPORT
None declared.



FINANCIAL SUPPORT
None Declared.



ABSTRACT

Background: Antibiotic-associated diarrhea (AAD) is a clinically important gastrointestinal complication of antibiotic therapy in children. Probiotic effects are biologically and clinically strain-specific, and differences in formulation, dose, outcome definition, and study setting can influence observed effectiveness. This systematic review evaluated the effectiveness and safety of probiotics for prevention of AAD in children receiving antibiotic therapy.

Methods: A systematic review was conducted in accordance with PRISMA 2020. PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library were searched using controlled vocabulary and free-text terms for children, probiotics, antibiotics, and AAD. Randomized controlled trials and prospective observational studies reporting comparative pediatric outcomes were eligible. The primary outcome was AAD incidence; secondary outcomes included diarrhea severity and duration, stool frequency and consistency, gastrointestinal symptoms, and adverse events. Randomized trials were assessed with Cochrane Risk of Bias 2 and the observational study with the Newcastle-Ottawa Scale. Because of substantial clinical and methodological heterogeneity, results were synthesized narratively rather than pooled.

Results: Five studies enrolled 1,224 children, of whom 1,104 were included in the final analyses reported by the individual studies; four studies were randomized controlled trials and one was prospective observational. *Lactobacillus rhamnosus* GG was associated with lower AAD incidence than placebo in Arvola et al. (5% vs 16%; treatment effect -11%, 95% CI -21% to 0%; $p = 0.05$) and Vanderhoof et al. (8% vs 26%; $p < 0.001$). A multi-strain probiotic yogurt reduced severe diarrhea (0% vs 16.7%; $p = 0.025$) and minor diarrhea (2.9% vs 58.3%; $p < 0.001$). *Lactobacillus plantarum* DSM 9843 did not significantly reduce AAD (2.8% vs 4.1%; $p = 0.40$). In the observational study, probiotic prophylaxis was associated with lower AAD incidence (12.4% vs 41.8%; RR 0.30, 95% CI 0.19-0.46). No consistent increase in reported adverse events was identified.

Conclusion: The included studies suggest that selected probiotic preparations, particularly *Lactobacillus rhamnosus* GG-containing interventions, may reduce pediatric AAD, whereas benefit was not demonstrated for all strains. The findings support strain-specific interpretation and cautious application because of heterogeneity in interventions, outcome definitions, study design, and sample size.

Keywords

Probiotics; antibiotic-associated diarrhea; children; pediatric patients; *Lactobacillus rhamnosus* GG; antibiotics; gastrointestinal symptoms; prevention

Acknowledgement

The author acknowledges the investigators whose published studies contributed to the evidence synthesized in this systematic review.

Ashraf M et al. Short Title

Probiotics for Pediatric Antibiotic-Associated Diarrhea





INTRODUCTION

Antibiotic-associated diarrhea (AAD) is commonly defined as otherwise unexplained diarrhea occurring during antibiotic exposure or within a period after treatment, although exact stool-frequency, consistency, and timing criteria vary across studies. Antibiotics can disrupt the composition and metabolic function of the intestinal microbiota, reduce colonization resistance, and alter carbohydrate and bile-acid metabolism, thereby contributing to loose stools and other gastrointestinal symptoms. In children, these effects are clinically relevant because antibiotic exposure is common and diarrhea may impair treatment tolerance, hydration, and adherence [1,2]. Probiotics are live microorganisms administered with the intention of conferring a health benefit through mechanisms that may include restoration of microbial balance, competitive inhibition of pathogens, modulation of epithelial barrier function, and interaction with mucosal immune responses. Evidence in pediatric AAD has repeatedly shown that efficacy cannot be assumed to be a uniform class effect. Outcome definitions, strain identity, daily dose, formulation, timing relative to antibiotics, baseline AAD risk, and clinical setting all influence interpretation [1-4]. A 2020 scoping review also demonstrated substantial heterogeneity in how pediatric antibiotic-associated gastrointestinal outcomes were defined and measured, emphasizing the need to interpret trial findings in relation to their specific outcome definitions [3].

Recent evidence syntheses and clinical guidance published before 2022 generally support a preventive role for selected probiotics, particularly *Lactobacillus rhamnosus* GG (LGG), while also emphasizing that evidence for other strains and combinations is less consistent [1,2,4,5]. Prevention of *Clostridioides difficile*-associated diarrhea is a related but distinct clinical question and should not be considered equivalent to prevention of all-cause AAD [6]. These distinctions are important when translating pooled or class-level conclusions into strain-specific pediatric practice. The present systematic review therefore aimed to evaluate the effectiveness and safety of probiotic preparations used to prevent AAD in children receiving antibiotic therapy, with particular attention to AAD incidence, diarrhea severity and duration, stool-related outcomes, gastrointestinal symptoms, adverse events, and differences between probiotic strains and formulations.

METHODOLOGY

Study Design and Reporting Framework

This systematic review was structured in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [7]. The review question was framed around pediatric patients receiving antibiotics, prophylactic probiotic exposure, an appropriate comparison group, and subsequent antibiotic-associated gastrointestinal outcomes.

Search Strategy

A comprehensive literature search was conducted in PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library. Controlled vocabulary, including Medical Subject Headings where applicable, was combined with free-text terms using Boolean operators. The core search concepts were: (Child OR Pediatric OR Paediatric* OR Infant* OR Adolescent*) AND (Probiotic* OR *Lactobacillus* OR *Bifidobacterium* OR *Saccharomyces* OR Synbiotic*) AND (Antibiotic* OR Antimicrobial*) AND ("Antibiotic-associated diarrhea" OR "Antibiotic-associated diarrhoea" OR "Antibiotic associated diarrhea" OR "Antibiotic associated diarrhoea" OR AAD). Syntax was adapted to the indexing and search functions of each database. Reference lists of eligible studies and relevant reviews were also examined to identify additional potentially eligible publications.

Eligibility Criteria

Eligibility was defined using the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) framework. Studies were eligible when they involved children or adolescents receiving antibiotic therapy, evaluated a probiotic preparation intended to prevent antibiotic-associated gastrointestinal symptoms, included placebo, no-probiotic, or standard-care comparison data, and reported AAD incidence or a closely related gastrointestinal, stool, duration, or safety outcome. Randomized controlled trials and prospective observational studies published as full-text articles in English were eligible. Prospective observational evidence was included to complement controlled trial findings on effectiveness and safety in routine pediatric care; randomized and observational findings were interpreted separately according to design. Reviews, meta-analyses, editorials, commentaries, letters, conference abstracts, case reports, case series, animal studies, studies involving non-pediatric populations, studies evaluating interventions unrelated to probiotics, duplicate publications, secondary analyses of the same population, and studies that did not report relevant comparative outcomes were excluded.

Study Selection

Retrieved records were screened against the predefined eligibility criteria after removal of duplicate records. Screening was conducted in two stages: title/abstract assessment followed by full-text assessment of potentially eligible reports. Reasons for exclusion were categorized at the full-text stage. Five studies satisfied the final eligibility criteria and were included in the review.

Data Extraction

A standardized extraction structure was used to capture author, year, country, study design, sample size, age, clinical setting, antibiotic exposure, probiotic strain or formulation, dose, duration, comparator, AAD definition, follow-up, efficacy outcomes, safety outcomes, event counts, percentages, effect estimates, confidence intervals, and p-values as reported in the original studies. Enrolled or randomized sample sizes were distinguished from the numbers completing follow-up or included in the final analysis.





Outcome Measures

The primary outcome was the incidence of antibiotic-associated diarrhea. Secondary outcomes included diarrhea severity and duration, stool frequency and consistency, gastrointestinal symptoms, and adverse events. Because included studies used different operational definitions of diarrhea, outcome definitions were retained at the individual-study level rather than forced into a single post hoc definition.

Risk-of-Bias and Methodological Quality Assessment

The four randomized controlled trials were assessed using Cochrane Risk of Bias 2 (RoB 2), which evaluates bias arising from the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result [8]. Judgments were categorized as low risk, some concerns, or high risk. The prospective observational study was assessed using the Newcastle-Ottawa Scale (NOS), considering cohort selection, comparability of exposed and non-exposed groups, and outcome assessment/follow-up.

Data Synthesis and Statistical Interpretation

A narrative synthesis was undertaken because the included studies differed substantially in probiotic strain and formulation, dose, treatment duration, antibiotic exposure, AAD definition, follow-up, participant setting, and study design. Randomized and observational evidence was not combined into a single pooled estimate. Study-specific event counts, percentages, relative risks, confidence intervals, treatment effects, and p-values were reported when available. A two-sided p value <0.05 was interpreted as statistically significant, while results at p = 0.05 were described cautiously in relation to their confidence intervals.

Ethical Considerations

This review synthesized aggregate information from previously published studies and involved no direct recruitment, intervention, or collection of new participant-level data.

RESULTS

Study Selection Process

A total of 573 records were identified across the four electronic databases. After removal of 211 duplicates, 362 records underwent title and abstract screening and 106 were excluded. Of 256 reports sought for retrieval, 3 could not be retrieved, leaving 253 reports for full-text eligibility assessment. A further 248 reports were excluded because of wrong population (n = 134), wrong intervention (n = 56), wrong outcomes (n = 49), or conference-abstract publication (n = 9). Five studies met the predefined eligibility criteria and were included in the systematic review (Figure 1).

Characteristics of Included Studies

The five included studies enrolled 1,224 children in total. Based on the final or analyzed populations reported by the individual studies, 1,104 participants contributed to the reported final analyses. Four studies were randomized, double-blind, placebo-controlled trials and one was a prospective observational study. Studies were conducted in Finland, the United States, Australia, Poland, and Italy, and participant ages ranged from 1 month to 17 years. Interventions included LGG, *L. plantarum* DSM 9843 (LP299V), a multi-strain probiotic yogurt, and clinician-selected probiotic preparations. Study designs, dosing schedules, AAD definitions, and follow-up differed substantially (Tables 1A and 1B).

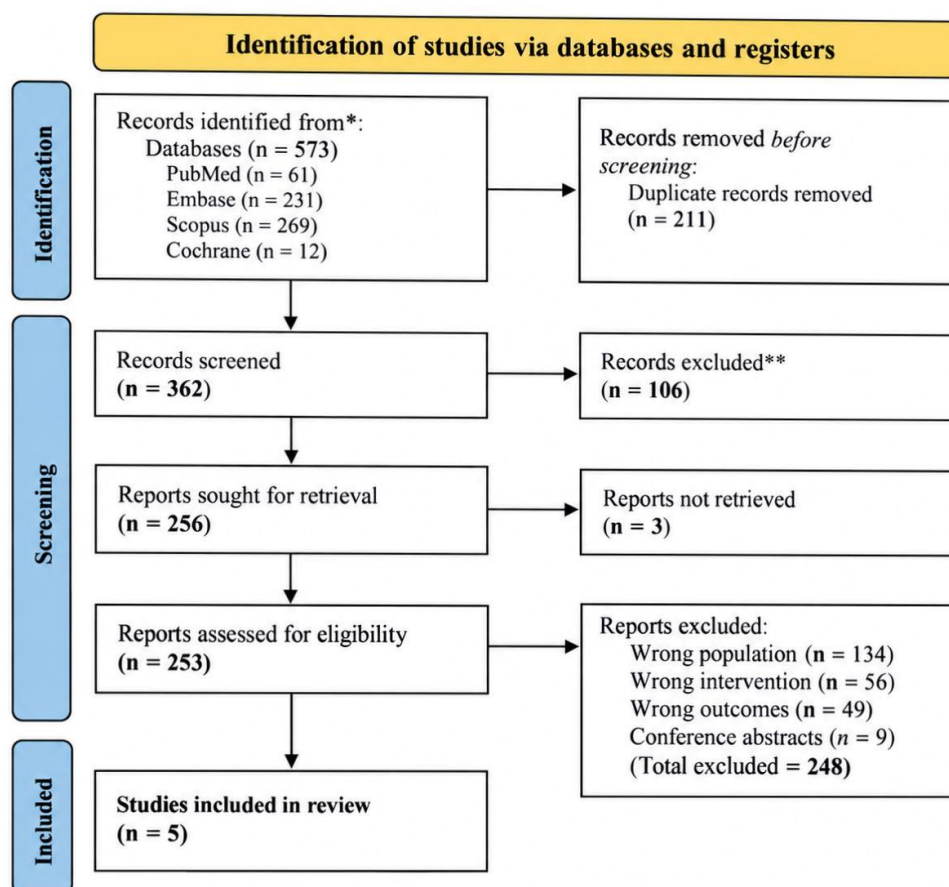


Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility, and inclusion.



Table 1A. Design and participant characteristics of included studies

Study	Country / design	Sample size	Age	Antibiotic / clinical setting	Follow-up
Arvola et al. [9]	Finland; randomized, double-blind, placebo-controlled	167 enrolled; 119 final	2 weeks-12.8 years; mean 4.5 y	Acute respiratory infections; oral penicillin, amoxicillin, cephalosporins, erythromycin, trimethoprim-sulfa	Primary outcome during first 2 weeks; symptom diary for 3 months
Vanderhoof et al. [10]	USA; double-blind randomized placebo-controlled	202 enrolled; 188 completed	6 months-10 years; median 4 years	Acute respiratory, urinary, and skin/soft-tissue infections; 10-day oral antibiotics	During 10-day antibiotic course; contacted every 3 days
Fox et al. [11]	Australia; multisite randomized, double-blind, placebo-controlled	72 commenced; 70 completed	1-12 years; mean 6.6 +/- 3.0 y	Broad-spectrum oral antibiotics in outpatient children	Antibiotic treatment plus 1 week
Olek et al. [12]	Poland; prospective multicenter randomized, double-blind, placebo-controlled	447 randomized; 438 analyzed	1-11 years; mean 5.2 +/- 2.7 y	Outpatient antibiotic therapy for respiratory, throat, ear, or urinary infections	15-28 days total
Baù et al. [13]	Italy; prospective observational study	336 enrolled; 289 completed	1 month-17 years; mean 57.1 +/- 47.4 months	Emergency/inpatient children receiving antibiotics; mainly protected penicillins, cephalosporins, macrolides	Assessment at 2 and 4 weeks; additional recall if symptoms persisted

Table 1B. Intervention and outcome characteristics of included studies

Study	Intervention	Dose and duration	Comparator	AAD definition / outcome	AAD cases / incidence
Arvola et al. [9]	L. rhamnosus GG	2 x 10 ¹⁰ CFU twice daily during antibiotic treatment	Placebo capsule	>=3 watery/loose stools/day for >=2 consecutive days	3/61 (5%) vs 9/58 (16%)
Vanderhoof et al. [10]	Lactobacillus GG	10 billion CFU/day (<12 kg) or 20 billion CFU/day (>=12 kg)	Placebo capsule	>=2 liquid stools/day on >=2 observation periods	7/93 (8%) vs 25/95 (26%)
Fox et al. [11]	Probiotic yogurt: LGG + B. lactis Bb-12 + L. acidophilus La-5	200 g/day; LGG 5.2 x 10 ⁹ , Bb-12 5.9 x 10 ⁹ , La-5 8.3 x 10 ⁹ CFU/day	Pasteurized yogurt	Severe: >=3 stools/day + consistency >=6 for >=2 days; minor: >=2 stools/day + consistency >=5 for >=2 days	Severe 0/34 vs 6/36; minor 1/34 vs 21/36
Olek et al. [12]	L. plantarum DSM 9843 (LP299V)	1 x 10 ¹⁰ CFU once daily, 2-3 h after antibiotic; antibiotic period + 1 week	Placebo capsule	>=3 loose/watery stools/24 h beginning >=2 h after antibiotic initiation	6/218 (2.8%) vs 9/220 (4.1%)
Baù et al. [13]	Clinician-selected probiotics; mainly LGG, L. reuteri, multispecies products	Not standardized; clinician-selected products/strains	No probiotic prophylaxis	>=3 loose/liquid stools/day during antibiotics or within 14 days after treatment, excluding other etiologies	26/210 (12.4%) vs 33/79 (41.8%); RR 0.30



Risk-of-Bias Assessment

Among the randomized trials, Fox et al. [11] and Olek et al. [12] were judged to have low overall risk of bias. Arvola et al. [9] and Vanderhoof et al. [10] were judged as having some concerns overall, principally because of limitations in the reporting of randomization and/or missing outcome data. Across individual domains, all four trials were at low risk for outcome measurement and selection of the reported result. The corrected domain-level judgments are shown in Figure 2, and the corresponding percentages are shown in Figure 3.

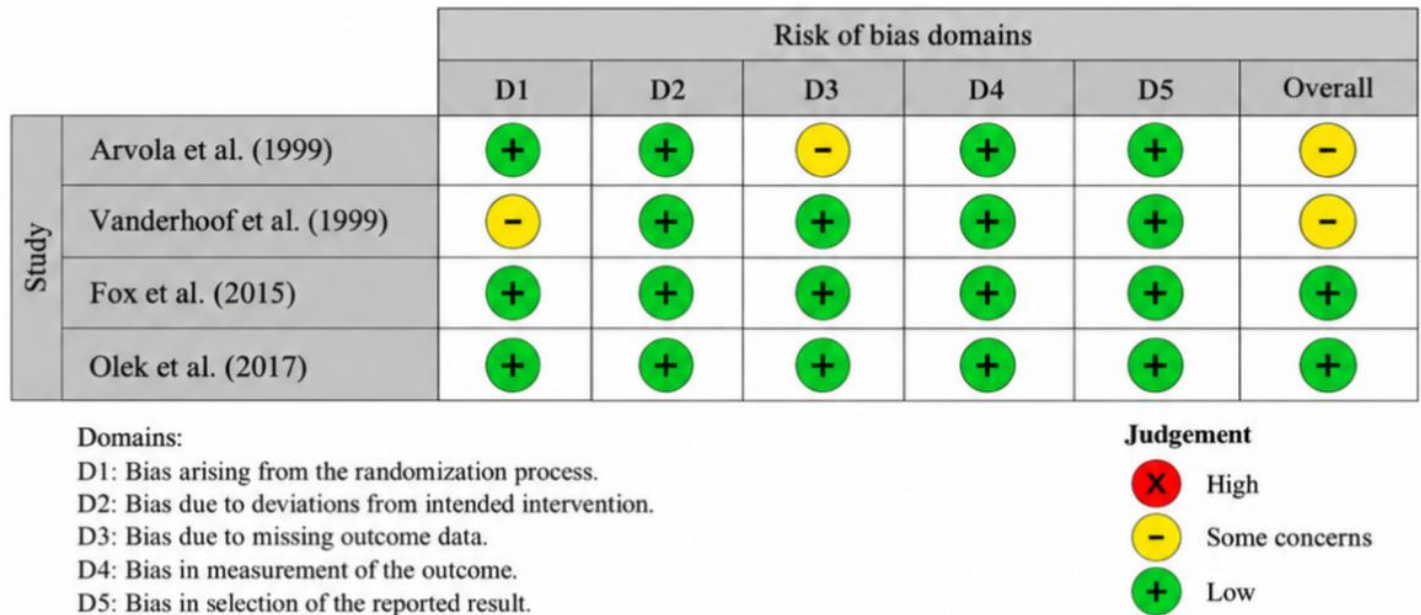


Figure 2: Traffic Light Plot of Domains Showing Risk of Bias for Included Studies Using RoB 2.0

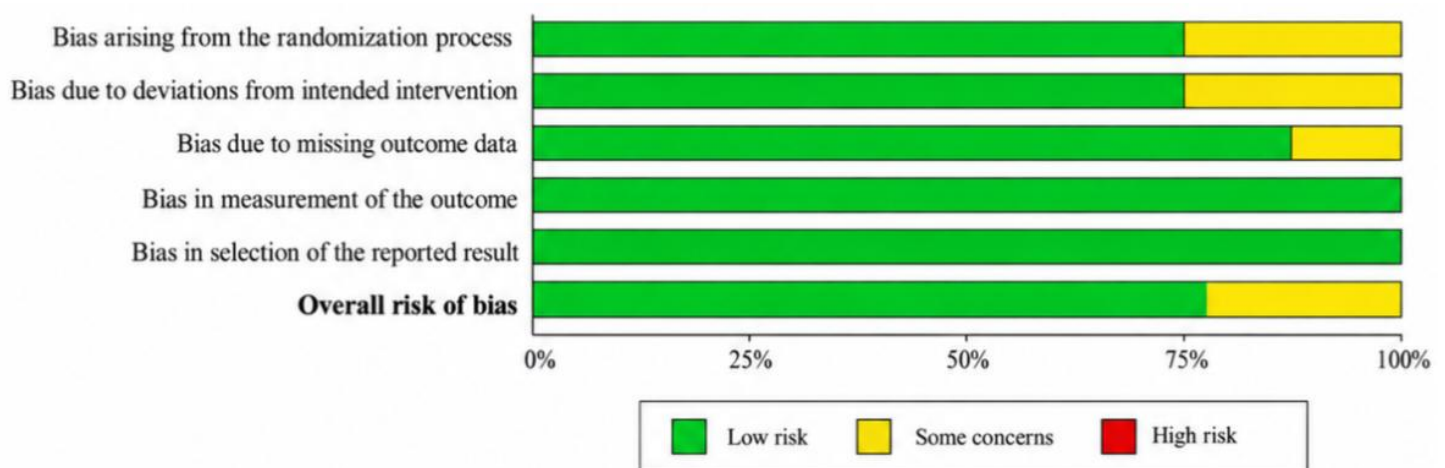


Figure 3: Traffic Light Plot Summary for Included Studies Using RoB 2.0

Newcastle-Ottawa Scale Assessment

Baù et al. [13] received 7 of 9 possible NOS stars, reflecting strengths in cohort selection, exposure ascertainment, outcome assessment, and follow-up. No comparability stars were assigned because the primary probiotic comparisons were based on non-randomized exposure and crude between-group estimates rather than design-based matching or multivariable adjustment for key confounding variables. This limitation is important when interpreting the magnitude of the observed association.

Table 2. Newcastle-Ottawa Scale assessment of the prospective observational study

Study	Exposed	Non-exposed	Exposure	Outcome absent	Comparability	Outcome / follow-up	Total
Baù et al. (2020) [13]	★	★	★	★	☆☆	★★★	7/9





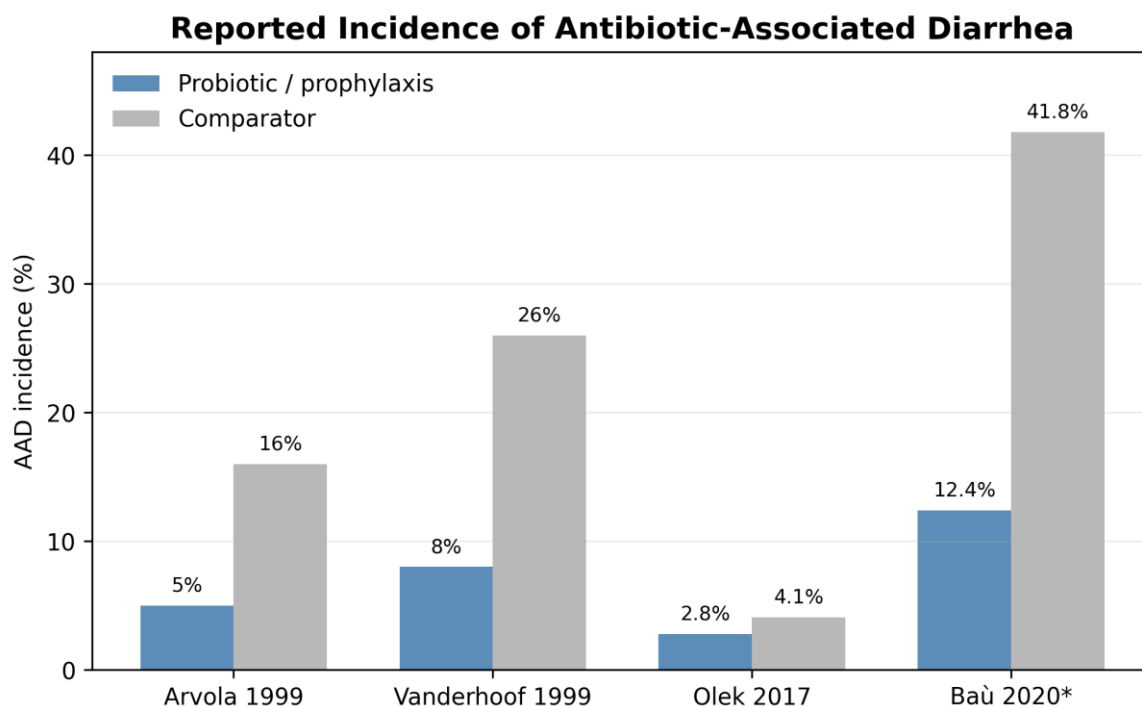
Efficacy Outcomes

Incidence of Antibiotic-Associated Diarrhea

Arvola et al. [9] reported AAD in 3/61 children (5%) receiving LGG and 9/58 (16%) receiving placebo, corresponding to an absolute treatment effect of -11% (95% CI -21% to 0%) with $p = 0.05$. This result indicates a lower observed incidence with LGG, although the confidence interval reached the null boundary. Vanderhoof et al. [10] reported AAD in 7/93 (8%) LGG recipients and 25/95 (26%) placebo recipients ($p < 0.001$), supporting a protective effect for LGG in that trial.

Fox et al. [11] used severity-specific diarrhea definitions rather than a single AAD endpoint. Severe diarrhea occurred in 0/34 children receiving probiotic yogurt compared with 6/36 (16.7%) receiving pasteurized yogurt (Fisher exact $p = 0.025$), while minor diarrhea occurred in 1/34 (2.9%) versus 21/36 (58.3%), respectively ($p < 0.001$). In contrast, Olek et al. [12] found no statistically significant reduction in AAD with LP299V: 6/218 (2.8%) versus 9/220 (4.1%) ($p = 0.40$).

In the prospective observational study by Baù et al. [13], AAD occurred in 26/210 children (12.4%) who received probiotic prophylaxis and 33/79 (41.8%) who did not, yielding RR 0.30 (95% CI 0.19-0.46). Because probiotic exposure was not randomized, this association should be interpreted as supportive real-world evidence rather than as a causal effect equivalent to a randomized comparison. The reported incidences for studies with a directly comparable AAD endpoint are illustrated in Figure 4.



*Baù et al. was a prospective observational study; the other displayed studies were randomized trials.

Figure 4. Reported AAD incidence in probiotic/prophylaxis and comparator groups for studies with a directly reported AAD endpoint. No pooled estimate is shown because of clinical and methodological heterogeneity. Diarrhea Severity, Duration, and Stool Outcomes

Arvola et al. [9] reported a mean diarrhea duration of 4 days (range 2-8) and approximately 5 stools/day during diarrheal episodes, with comparable severity between treatment groups. Vanderhoof et al. [10] reported improved stool frequency and consistency with LGG by day 10 and a shorter mean diarrhea duration (4.7 vs 5.9 days; $p = 0.05$). Fox et al. [11] demonstrated substantially fewer severe and minor diarrheal episodes with the multi-strain probiotic yogurt. Olek et al. [12] found no significant difference in the incidence of loose/watery stools (39.0% vs 44.5%; $p = 0.26$) or mean number of loose/watery stools (3.9 ± 3.5 vs 4.7 ± 6.3 ; $p = 0.90$). These findings reinforce that benefits observed with LGG-containing interventions cannot be assumed for every probiotic strain.

Safety and Adverse Events

Across the included studies, probiotic use was not associated with a consistent increase in reported adverse events. Fox et al. [11] reported fewer gastrointestinal and general adverse events in the probiotic group than in the comparator group. Olek et al. [12] reported adverse events in 17.9% of children receiving LP299V and 27.3% receiving placebo ($p = 0.02$), with no serious adverse events attributed to the intervention. Arvola et al. [9] did not identify a probiotic-related safety signal. Because the evidence base was limited in size and adverse-event reporting differed between studies, these findings support short-term tolerability in the studied populations but do not establish the absence of rare harms.





Table 3A. Comparative efficacy outcomes of included studies

Study	Intervention / comparator	Relevant outcome	Statistical finding
Arvola et al. [9]	LGG 2 x 10 ¹⁰ CFU twice daily vs placebo	AAD: ≥3 loose/watery stools/day for ≥2 days	Treatment effect -11% (95% CI -21% to 0%); p = 0.05
Vanderhoof et al. [10]	LGG 1 x 10 ¹⁰ -2 x 10 ¹⁰ CFU/day vs placebo	AAD during 10-day antibiotic course	p < 0.001; stool frequency/consistency improved by day 10
Fox et al. [11]	LGG + B. lactis Bb-12 + L. acidophilus La-5 yogurt vs pasteurized yogurt	Severe and minor diarrhea	Severe p = 0.025; minor p < 0.001
Olek et al. [12]	LP299V 1 x 10 ¹⁰ CFU daily vs placebo	AAD and loose/watery stools	AAD p = 0.40; loose/watery stools p = 0.26; mean stool count p = 0.90
Baù et al. [13]	Clinician-selected probiotics vs no prophylaxis	AAD during antibiotics or within 14 days	RR 0.30 (95% CI 0.19-0.46); LGG RR 0.37; L. reuteri RR 0.35

Table 3B. Study-specific results and interpretation

Study	Probiotic / intervention result	Comparator result	Interpretation
Arvola et al. [9]	3/61 (5%)	9/58 (16%)	Lower observed AAD incidence with LGG; estimate reached the null boundary.
Vanderhoof et al. [10]	7/93 (8%)	25/95 (26%)	LGG reduced AAD incidence in this trial.
Fox et al. [11]	Severe 0/34; minor 1/34	Severe 6/36; minor 21/36	Multi-strain yogurt reduced both severity-defined outcomes.
Olek et al. [12]	AAD 6/218 (2.8%); loose/watery stools 85/218 (39.0%)	AAD 9/220 (4.1%); loose/watery stools 98/220 (44.5%)	No statistically significant efficacy signal for LP299V.
Baù et al. [13]	26/210 (12.4%)	33/79 (41.8%)	Lower AAD incidence was associated with prophylaxis; observational design limits causal inference.

DISCUSSION

Summary and Interpretation of Principal Findings

This systematic review identified heterogeneous but clinically informative evidence regarding probiotics for prevention of pediatric AAD. The most consistent preventive signals were observed in the two early LGG trials [9,10] and in the LGG-containing multi-strain yogurt trial [11]. By contrast, LP299V did not significantly reduce AAD or related stool outcomes [12]. The prospective observational study [13] also showed a lower incidence of AAD among children receiving probiotic prophylaxis, but its non-randomized design and lack of adjustment for important confounders require more cautious interpretation. Taken together, the evidence supports a strain- and formulation-specific interpretation rather than a universal probiotic class effect.

The pattern observed in the included studies is broadly consistent with larger evidence syntheses available before 2022. The 2019 Cochrane review of pediatric AAD reported a moderate overall protective effect of probiotics, while emphasizing heterogeneity across strains and suggesting greater benefit with higher probiotic doses [1]. Mantegazza et al. similarly highlighted LGG and *Saccharomyces boulardii* as among the preparations with the most consistent pediatric evidence, while noting that strain identity and antibiotic susceptibility can influence effectiveness [2]. A network meta-analysis across AAD trials also demonstrated clinically meaningful differences among probiotic interventions rather than equivalence across all preparations [4].

Outcome heterogeneity is an important explanation for differences in observed effect size. The included studies used thresholds ranging from at least two liquid stools on repeated observations to at least three loose or watery stools per day over consecutive days,





while Fox et al. [11] used separate severe and minor diarrhea definitions incorporating stool consistency. A pediatric scoping review published in 2020 identified similar variability in outcome definitions and measurement across probiotic-antibiotic studies [3]. This variability limits direct comparison of absolute event rates and is one reason a pooled meta-analysis was not considered appropriate for the present evidence set.

Dose and formulation may also contribute to between-study variability. The effective LGG trials used daily doses in the range of approximately 10^{10} CFU or higher, while the multi-strain yogurt provided several probiotic organisms concurrently. Larger pediatric reviews have suggested a stronger effect at higher probiotic doses, although dose-response relationships should not be generalized across strains because biological activity is strain-specific [1,2]. The null result with LP299V [12] further illustrates that a dose expressed only as CFU does not make different organisms clinically interchangeable.

The observational findings of Baù et al. [13] are clinically relevant because they reflect routine practice and included commonly used strains such as LGG and *L. reuteri*. However, probiotic choice was clinician-directed and the primary comparisons were unadjusted for several factors associated with AAD risk. The magnitude of the association therefore may reflect both probiotic exposure and differences in age, infection type, route of antibiotic administration, previous AAD, clinical severity, or other patient-level factors. This distinction between randomized efficacy and observational effectiveness should be maintained when considering practice implications.

CLINICAL AND RESEARCH IMPLICATIONS

The findings support a selective rather than indiscriminate approach to probiotic prophylaxis in children receiving antibiotics. Evidence should be interpreted at the level of the specific strain or defined combination, dose, target population, and clinical outcome. Contemporary pediatric evidence and guidance available before 2022 also favored selected strains rather than generic probiotic products [1,2,5]. Clinicians should additionally consider baseline AAD risk, age, antibiotic class and duration, clinical setting, and host vulnerability when deciding whether prophylaxis is appropriate.

Future trials should use adequately powered multicenter randomized designs, prespecify a standardized AAD definition, clearly identify probiotic strain and dose, report timing relative to antibiotic administration, and use consistent follow-up periods. Reporting should distinguish all-cause AAD from *C. difficile*-associated diarrhea and should include clinically important harms as well as efficacy outcomes. Harmonized outcome definitions would improve the comparability of future studies and facilitate more reliable strain-specific meta-analysis [3,6].

STRENGTHS

The review considered both randomized controlled evidence and prospective real-world evidence, evaluated multiple clinically relevant outcomes beyond a single diarrhea endpoint, and preserved study-specific AAD definitions to avoid artificial harmonization. Risk of bias was assessed according to study design, and the synthesis explicitly separated randomized from observational evidence. The revised presentation also distinguishes enrolled from analyzed participant totals and corrects the risk-of-bias summary percentages.

LIMITATIONS

Several limitations should be considered. First, the included evidence was clinically and methodologically heterogeneous with respect to probiotic strain, formulation, dose, antibiotic exposure, patient setting, AAD definition, and follow-up, precluding a meaningful single pooled effect estimate. Second, the review included only five studies and several randomized trials were relatively small, limiting precision and the ability to evaluate uncommon adverse events. Third, the inclusion of one non-randomized study adds real-world context but also introduces confounding that cannot be equated with randomized treatment effects. Fourth, restriction to English-language full-text publications may contribute to language or publication bias. Finally, with only five included studies, formal assessment of small-study effects using funnel-plot methods would not be informative. These limitations support cautious, strain-specific interpretation of the findings.

CONCLUSION

Selected probiotic preparations may reduce antibiotic-associated diarrhea in children, with the clearest preventive signals in the included studies observed for *Lactobacillus rhamnosus* GG-containing interventions. Benefit was not demonstrated for all probiotic strains, and differences in formulation, dose, outcome definition, and study design limit broad generalization. Probiotic prophylaxis should therefore be interpreted on a strain-specific basis, and further well-designed pediatric randomized trials with standardized outcomes are needed to clarify optimal preparations and dosing.

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