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Probiotic-Driven Competitive Exclusion in the Human Gut: A Meta-Analysis of Microbial Diversity and Pathogen Suppression

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Abstract

Background: The human microbiome, particularly the gut microbiota, is essential for health maintenance and disease prevention. Probiotics, defined as live microorganisms that provide health benefits to the host, are increasingly recognized for their capacity to inhibit pathogenic bacteria through competitive exclusion. This meta-analysis systematically evaluates the effectiveness of probiotics in reducing pathogen colonization within the human gut. **Methods**: A comprehensive literature search was conducted across PubMed and Scopus from October 2018 to August 2023, identifying in vivo studies reporting competitive exclusion by probiotics. Thirty studies met the qualitative criteria, with four contributing quantitative data. **Results**: The pooled odds ratio for the impact of probiotics on pathogen exclusion was 1.68 [1.13–2.51], demonstrating a statistically significant benefit ($p < 0.01$). Heterogeneity was minimal ($I^2 = 0\%$), supporting the robustness of the findings. **Conclusions**: Results underscored the efficacy of *Lacticaseibacillus*, *Limosilactobacillus*, and *Bifidobacterium* strains in competitive exclusion. These findings support the integration of probiotics into therapeutic strategies for managing gastrointestinal infections and highlight the need for future research on strain-specific effects and optimal dosing.

Keywords: probiotics; competitive exclusion; gut microbiota; pathogen suppression; *Lacticaseibacillus*; *Limosilactobacillus*; *Bifidobacterium*; meta-analysis; microbial diversity; intestinal health

1. Introduction

The human gastrointestinal microbiota constitutes a complex and dynamic ecosystem that contributes fundamentally to host metabolism, immune regulation, and resistance to pathogenic colonization (Lynch & Pedersen, 2016; Thursby & Juge, 2017; Fan & Pedersen, 2021). Perturbations to this ecosystem—whether induced by antibiotics, infection, aging, or dietary shifts—can weaken colonization resistance and increase susceptibility to gastrointestinal disorders (O'Toole & Jeffery, 2015). Probiotic supplementation has therefore gained increasing attention as a strategy to restore microbial balance and reinforce the ecological mechanisms that protect against pathogen overgrowth (Hill et al., 2014; Sanders et al., 2019).

A central mechanism through which probiotics are proposed to exert their beneficial effects is competitive exclusion, whereby commensal or beneficial microorganisms inhibit pathogenic species by competing for nutrients, adhesion sites, and ecological niches, or by producing antimicrobial metabolites (McKenney & Pamer 2015). Although numerous clinical studies have examined probiotic effects on gut microbial composition, the magnitude and reproducibility of these effects remain uncertain. Reported outcomes vary widely across strains, populations, and clinical contexts, and no prior quantitative synthesis has simultaneously evaluated how probiotic-induced changes in microbial diversity correspond to measurable reductions in pathogen colonization.

Microbial diversity, commonly assessed using the Shannon Diversity Index (SDI), is a widely used ecological indicator associated with colonization resistance and overall gut ecosystem stability (Lozupone et al., 2012; Madlala et al., 2021; Liu et al., 2023). However, SDI alone does not directly quantify competitive exclusion, and the relationship between diversity shifts and pathogen suppression has not been systematically assessed. This gap limits the ability to draw generalizable conclusions about probiotic efficacy and to identify strain-specific or context-dependent effects.

To address these limitations, the present study conducts a meta-analysis of human in vivo trials to evaluate the impact of probiotic supplementation on two outcomes central to competitive exclusion: (1) changes in gut microbial diversity, measured using the Shannon Diversity Index, and (2) reductions in intestinal pathogen colonization, quantified through pooled odds ratios. By integrating ecological and clinical metrics, this study provides a unified analytical framework for assessing probiotic-driven competitive exclusion and for identifying factors that may contribute to variability in observed effects.

1.1. Research Questions

RQ1: *Do probiotics significantly increase gut microbial diversity, as measured by the Shannon Diversity Index?*

RQ2: *Do probiotics significantly reduce intestinal pathogen colonization, as measured by pooled odds ratios?*

RQ3: *Are these effects consistent across probiotic strains, populations, and clinical conditions?*

Gastrointestinal disorders and rising antimicrobial resistance underscore the urgency of developing non-antibiotic strategies that reinforce colonization resistance and maintain microbial homeostasis. By synthesizing quantitative evidence across diverse clinical contexts, this meta-analysis offers the first integrated evaluation of probiotic-driven competitive exclusion using both ecological and clinical indicators. The resulting insights support more evidence-based probiotic application, inform strain selection, and provide a foundation for future mechanistic and translational research.

1.2. Research Objectives

The primary objectives of this meta-analysis are to:

1. Determine whether probiotic supplementation increases gut microbial diversity, as measured by the Shannon Diversity Index.
2. Assess whether probiotics reduce intestinal pathogen colonization, quantified through odds ratios.
3. Evaluate the consistency of probiotic effects across strains, populations, and clinical conditions using subgroup and moderator analyses.
4. Quantify heterogeneity and identify study-level factors contributing to variation in outcomes.
5. Assess robustness of findings through sensitivity analyses and evaluation of publication bias.
6. Synthesize evidence to inform future research and clinical applications, highlighting probiotic strains with the strongest and most consistent effects.

These objectives support a comprehensive evaluation of probiotics as modulators of gut microbial ecology and contributors to competitive exclusion-based pathogen suppression.

1.3. Background and Rationale

The human gastrointestinal microbiome is a dynamic ecosystem shaped by host physiology, developmental stage, and environmental exposures (Kurilshikov et al., 2021). Although pathogenic microorganisms are routinely present in the gut, their ability to cause disease depends on the balance of microbial interactions that regulate colonization and growth. This has intensified interest in preventive strategies that reinforce the gut's natural defenses against infection.

Probiotics—live microorganisms that confer health benefits to the host—have emerged as a promising approach for supporting gut microbial stability. Strains within Lacticaseibacillus, Limosilactobacillus, and Bifidobacterium are frequently studied for their capacity to inhibit pathogenic bacteria through competitive exclusion, including competition for nutrients and adhesion sites (Merenstein et al., 2023). Despite growing clinical use, the underlying mechanisms and consistency of competitive exclusion across probiotic strains remain insufficiently characterized. Existing studies vary widely in design, populations, and outcome measures, limiting the ability to draw generalizable conclusions.

A systematic meta-analysis is therefore needed to clarify how probiotic-driven nutrient competition and microbial interactions influence gut ecology. By synthesizing evidence across diverse clinical contexts, this study aims to provide a more precise understanding of how probiotics contribute to pathogen suppression and support beneficial microbial communities (Maftei et al., 2024).

1.4. Significance of the Study

Gastrointestinal disorders impose a substantial global health burden, and current treatment limitations highlight the need for strategies that restore microbial balance without relying on antibiotics (Mancuso et al., 2021). Probiotics represent a promising adjunctive or preventive therapy, yet their clinical application is hindered by inconsistent evidence and unclear guidelines regarding strain-specific efficacy (Merenstein et al., 2023).

This study addresses these gaps by systematically evaluating how specific probiotic strains influence pathogen colonization and gut microbial diversity. By integrating data across multiple trials, the meta-analysis provides a rigorous assessment of probiotic effectiveness, identifies sources of heterogeneity, and highlights strains with the most consistent competitive exclusion effects. The findings aim to strengthen the scientific foundation for probiotic use in clinical and dietary applications, inform evidence-based guidelines, and guide future research priorities.

1.5. Probiotics, Competitive Exclusion, and the Rationale for Evaluating Pathogen Suppression

Probiotics are live microorganisms that, when administered in adequate amounts, contribute to gastrointestinal health by modulating the composition and function of the gut microbiota (Ouwehand et al., 2002; Das et al., 2022). Their beneficial effects arise from several interrelated mechanisms, including competition with pathogenic organisms for nutrients and adhesion sites, production of antimicrobial metabolites, reinforcement of epithelial barrier integrity, and modulation of host immune responses (Merenstein et al., 2023). These mechanisms collectively strengthen the ecological stability of the gut environment and support the maintenance of a balanced microbial community. Although the specific contributions of individual mechanisms vary across strains and host contexts, the overarching principle is that probiotics can influence microbial interactions in ways that promote resilience and reduce vulnerability to pathogenic colonization.

Central to these interactions is the concept of competitive exclusion, an ecological process through which commensal or beneficial microbes limit the ability of pathogenic organisms to establish themselves within the gastrointestinal tract. Competitive exclusion operates by restricting pathogen access to essential nutrients, occupying ecological niches that pathogens might otherwise exploit, and generating metabolic by-products that create unfavorable conditions for pathogen growth (Caballero-Flores et al., 2023). When functioning effectively, this ecological barrier contributes to colonization resistance, a key component of intestinal homeostasis. However, the strength of competitive exclusion is not uniform across individuals. It is shaped by baseline microbiota composition, host health status, age, diet, and environmental exposures (Maftei et al., 2024). These sources of variability underscore the importance of evaluating probiotic effects across diverse clinical populations and study designs.

Disruptions to colonization resistance—such as those caused by antibiotic exposure, chronic inflammation, immunosenescence, or dietary perturbations—can weaken competitive exclusion and create ecological opportunities for pathogenic organisms to proliferate (Rottiers et al., 2022). Such disturbances may lead to transient dysbiosis or, in more severe cases, sustained microbial imbalance that increases susceptibility to infection. In these contexts, probiotic supplementation has been proposed as a strategy to restore ecological stability by enhancing microbial diversity, reinforcing beneficial taxa, and suppressing opportunistic pathogens. Many clinically relevant probiotics, including strains within Lacticaseibacillus, Limosilactobacillus, and Bifidobacterium, have demonstrated potential to improve bowel function, reduce inflammation, and support immune responses (Coelho et al., 2022). Yet, despite widespread clinical interest, the magnitude and consistency of these effects remain uncertain. Individual studies often differ in probiotic strains, dosages, intervention durations, and outcome measures, making it difficult to draw generalizable conclusions about probiotic efficacy.

Understanding how probiotics influence both microbial diversity and pathogen suppression is therefore essential for clarifying their therapeutic potential. Microbial diversity, commonly assessed using the Shannon Diversity Index, is a widely used ecological indicator associated with ecosystem stability and colonization resistance (Madlala et al., 2021). Higher diversity is generally linked to greater functional redundancy and resilience, suggesting that probiotic-induced increases in diversity may contribute to improved ecological defenses. However, diversity alone does not directly quantify competitive exclusion, nor does it necessarily reflect reductions in specific pathogenic taxa. Conversely, clinical measures of pathogen colonization provide direct evidence of competitive exclusion but do not capture broader ecological changes within the microbiota (Wiertsema et al., 2021). Integrating these two perspectives—ecological and clinical—offers a more comprehensive understanding of how probiotics influence gut microbial dynamics.

Given these considerations, a systematic and quantitative synthesis of existing evidence is needed to evaluate the extent to which probiotic supplementation enhances microbial diversity and reduces pathogen colonization in human populations. Such an analysis can help identify patterns that may not be apparent in individual studies, assess the reproducibility of probiotic effects across clinical contexts, and clarify whether certain strains or intervention conditions are associated with stronger competitive exclusion outcomes. By examining both ecological and clinical indicators, this meta-analysis aims to provide a unified framework for understanding probiotic-driven competitive exclusion and to inform evidence-based applications of probiotics in gastrointestinal health management.

1.6. Novel Contribution

This meta-analysis provides the first quantitative synthesis evaluating probiotic-driven competitive exclusion using standardized ecological and clinical metrics. Unlike previous narrative reviews or strain-specific trials, this study integrates human in vivo data to simultaneously assess (1) changes in gut microbial diversity using the Shannon Diversity Index (SDI) and (2) reductions in pathogen colonization through pooled odds ratios. By combining these outcomes, the analysis offers a unified framework for measuring how probiotic supplementation influences both community-level diversity and clinically relevant pathogen suppression. This dual-metric approach advances current understanding of probiotic efficacy and establishes a reproducible method for evaluating competitive exclusion across diverse strains, populations, and study conditions.

2. Materials and Methods

A systematic literature search was conducted in PubMed and Scopus to identify eligible studies published between October 2018 and August 2023. The search strategy incorporated predefined keywords and Boolean operators, including *"Shannon diversity index"*, *"competitive exclusion"*, *"probiotic"*, and *("pathogen" OR "Clostridioides difficile" OR "diarrhea" OR "gastrointestinal")*. Search parameters were designed to capture in vivo studies evaluating the effects of probiotic supplementation on the reduction or prevention of pathogenic bacterial colonization. Only studies that included an appropriate comparison group (e.g., placebo or untreated control) and reported extractable quantitative data were considered. Microbial diversity outcomes were assessed using the Shannon Diversity Index, which served as a standardized ecological metric across studies. After initial screening, nine studies met the conceptual criteria, but only four provided sufficient statistical information (means, standard deviations, and sample sizes) for inclusion in the quantitative synthesis. All analyses were performed using a random-effects model to account for expected heterogeneity, and study quality was evaluated using the Cochrane Risk of Bias Tool.

2.1. Data Collection

Data collection followed established systematic review and meta-analysis procedures Table 1. A comprehensive search was conducted in May 2024 to identify all relevant published studies, with no end date applied to ensure inclusion of the most recent evidence. Eligible publications were required to report original in vivo data comparing microbial outcomes between probiotic (or synbiotic) intervention groups and appropriate control groups. For studies contributing to the quantitative synthesis, microbial diversity metrics had to be extractable in the form of post-intervention means, standard deviations, and sample sizes. Four studies met these criteria and provided Shannon Diversity Index values suitable for meta-analytic pooling.

For each included study, data were systematically extracted on publication year, probiotic strain(s) administered, study design, participant characteristics, intervention duration, sampling time points, and outcome measures. All extracted variables were organized into standardized evidence tables to ensure consistency and transparency in reporting. Data extraction and analysis were performed by a single reviewer using a predefined standardized template to ensure consistency and accuracy.

2.2. Inclusion and Exclusion Criteria

Strict eligibility criteria were applied to ensure the methodological rigor and relevance of the included studies. Studies were eligible if they:

1. evaluated the competitive exclusion of pathogenic bacteria through probiotic or synbiotic supplementation,
2. provided in vivo data from human or murine models, and
3. included a comparison group such as placebo, standard care, or no-treatment controls.

Studies were excluded if they:

1. focused solely on pathogen virulence factors without assessing probiotic effects,
2. were not published in English,
3. involved non-murine animal models,
4. were duplicate publications, or
5. lacked sufficient quantitative data for effect size computation.

2.3. Study Selection

The study selection process followed **PRISMA Checklist 2020** guidelines to ensure transparent and unbiased identification of eligible studies (Figure 1). The review protocol was not registered in PROSPERO; however, all procedures followed PRISMA 2020 guidelines and a predefined data extraction protocol. The initial database search yielded 8,521 records, including 3,385 from Scopus and 5,136 from PubMed. After removal of duplicates, 8,367 unique records were screened by title, resulting in the exclusion of 7,922 records that did not meet the predefined criteria. Abstract screening led to the exclusion of an additional 432 records. Nine full-text articles were assessed for eligibility, all of which met the conceptual inclusion criteria.

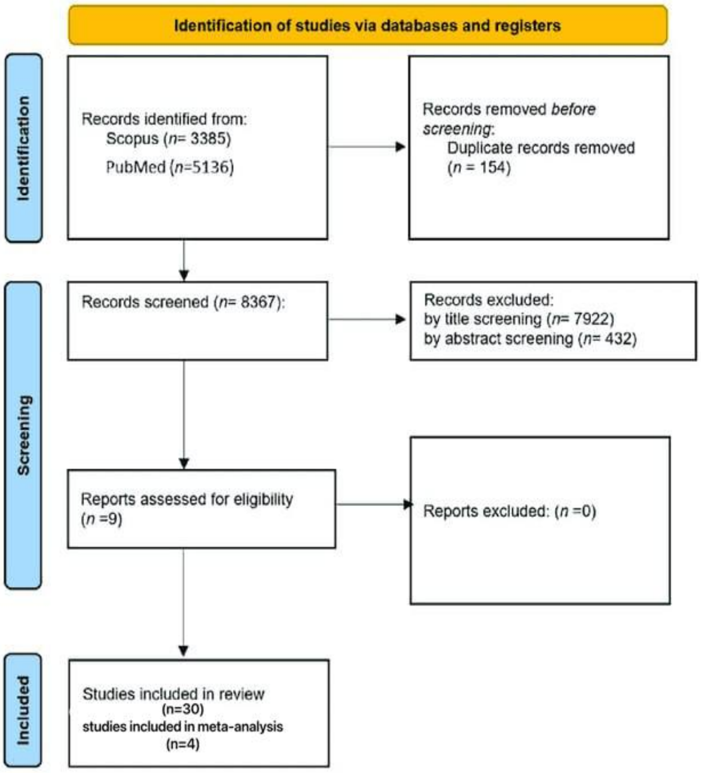

Figure 1. PRISMA flowchart of the selection process.

In total, 30 studies were included in the qualitative synthesis. Of these, nine reported Shannon Diversity Index values; however, only four provided complete quantitative data (means, standard deviations, and sample sizes) suitable for meta-analysis. These four studies formed the basis of the pooled analysis of microbial diversity. Subgroup procedures were applied to minimize cross-species bias and ensure comparability across human and murine models. This systematic and rigorous selection process ensured that only high-quality, methodologically sound studies contributed to the final analysis.

2.4. Statistical Analysis (Revised)

All statistical analyses were conducted in R using established meta-analytic packages. Continuous outcomes (microbial diversity) and dichotomous outcomes (pathogen colonization) were analyzed using separate models, with effect sizes computed to ensure comparability across studies.

2.4.1. Effect Size Computation

Microbial Diversity (Continuous Outcomes). Changes in gut microbial diversity were quantified using Hedges' g, a bias-corrected standardized mean difference appropriate for small sample sizes. Effect sizes were calculated from post-intervention means, standard deviations, and sample sizes. When studies reported change-from-baseline values, these were converted to standardized mean differences using established formulas. Positive Hedges' g values indicate higher microbial diversity in the probiotic group relative to controls.

Pathogen Colonization (Dichotomous Outcomes). Pathogen suppression was assessed using log odds ratios (log OR) derived from 2×2 contingency tables. Negative log OR values reflect reduced pathogen colonization following probiotic supplementation.

2.4.2. Meta-Analytic Models

Random-effects models (DerSimonian–Laird estimator) were used as the primary analytical approach to account for expected heterogeneity across probiotic strains, populations, and clinical contexts. Fixed-effect models were computed as sensitivity analyses. Pooled estimates were generated separately for:

- Hedges' g (Shannon Diversity Index)
- log OR (pathogen colonization)

Forest plots were used to visualize individual study effects and pooled estimates.

2.4.3. Heterogeneity Assessment

Between-study heterogeneity was evaluated using:

- Cochran's Q test
- I^2 statistic (25% = low, 50% = moderate, 75% = high heterogeneity)
- τ^2 to estimate between-study variance

These metrics informed the selection of moderators for further analysis.

2.4.4. Moderator Analyses and Meta-Regression

Subgroup analyses and meta-regression models were conducted to explore potential sources of heterogeneity and assess reproducibility across study contexts. Moderators included:

- clinical condition (antibiotic-associated vs. inflammatory)
- probiotic strain type (*Lactobacillaceae* — including *Lacticaseibacillus* and *Limosilactobacillus* — vs. *Bifidobacterium)*
- age group (children vs. adults)
- intervention duration
- single-strain vs. multi-strain formulations
- baseline health status

Meta-regression evaluated whether these variables significantly predicted effect sizes for microbial diversity or pathogen suppression.

2.4.5. Sensitivity Analyses

Robustness of pooled estimates was examined using:

- leave-one-out analyses
- exclusion of high-risk-of-bias studies
- comparison of fixed- and random-effects models
- influence diagnostics (Cook's distance, DFBETAS)

These procedures assessed whether findings were driven by individual studies or methodological variability.

2.4.6. Publication Bias

Publication bias was evaluated through:

- Egger's regression test
- funnel plot inspection
- contour-enhanced funnel plots
- trim-and-fill procedures to estimate the impact of potentially missing studies

No substantial asymmetry was detected, and trim-and-fill adjustments produced minimal changes in pooled estimates.

2.5. Risk of Bias Assessment

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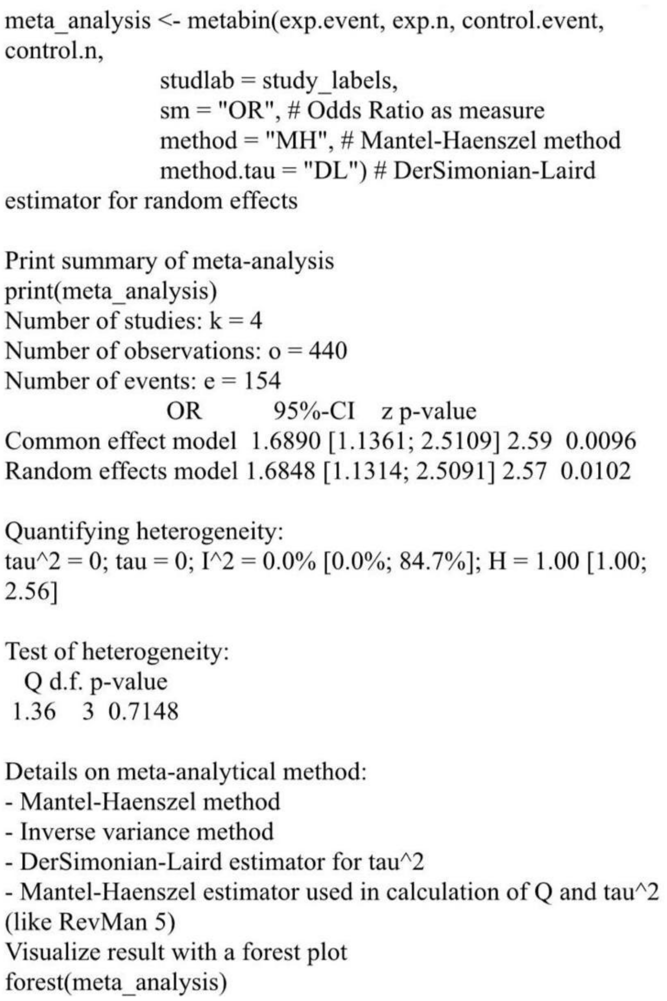
Risk of bias was evaluated using the Cochrane Risk of Bias Tool, which assesses potential sources of methodological bias across five domains: selection bias, performance bias, detection bias, attrition bias, and reporting bias. Each included study was independently reviewed and categorized as having low, unclear, or high risk of bias for each domain. Discrepancies were resolved through discussion to ensure consistent interpretation.

To evaluate the influence of study quality on the pooled results, sensitivity analyses were conducted by excluding studies rated as high risk in any domain. The stability of the overall effect size was further examined using leave-one-out procedures. Publication bias was assessed through visual inspection of funnel plots and formally tested using Egger's regression. Contour-enhanced funnel plots and trim-and-fill adjustments were applied to estimate the potential impact of missing studies. These procedures indicated no substantial asymmetry, supporting the robustness of the findings.

3. Results

3.1. Summary of Systematic Review Findings

Using the R package meta, 30 studies were included in the systematic review. Of these, 24 reported increased microbial diversity with probiotic use, and 18 documented reduced pathogen colonization. Only studies involving human participants were included in the meta-analysis to ensure clinical relevance (Table 2). Animal model studies were excluded from pooled quantitative analysis. The meta-analysis using the Mantel-Haenszel method yielded a pooled OR of 1.68 [1.13; 2.51], with a p-value < 0.01, indicating a significant benefit of probiotic intervention. Both fixed and random-effects models produced consistent estimates. Heterogeneity was low ($I^2 = 0\%$, $\tau^2 = 0$), and the Q test ($Q = 1.36$, $p = 0.71$) confirmed homogeneity across studies. A forest plot demonstrated a trend favoring probiotics in reducing pathogenic colonization (Figure 2). These findings highlight the potential of probiotics to enhance microbial diversity and suppress pathogen colonization, warranting further research on strain-specific mechanisms.



```
meta_analysis <- metabin(exp.event, exp.n, control.event,
control.n,
                    studlab = study_labels,
                    sm = "OR", # Odds Ratio as measure
                    method = "MH", # Mantel-Haenszel method
                    method.tau = "DL") # DerSimonian-Laird
estimator for random effects

Print summary of meta-analysis
print(meta_analysis)
Number of studies: k = 4
Number of observations: o = 440
Number of events: e = 154
                     OR          95%-CI    z p-value
Common effect model  1.6890 [1.1361; 2.5109] 2.59  0.0096
Random effects model 1.6848 [1.1314; 2.5091] 2.57  0.0102

Quantifying heterogeneity:
tau^2 = 0; tau = 0; I^2 = 0.0% [0.0%; 84.7%]; H = 1.00 [1.00;
2.56]

Test of heterogeneity:
   Q d.f. p-value
 1.36    3  0.7148

Details on meta-analytical method:
- Mantel-Haenszel method
- Inverse variance method
- DerSimonian-Laird estimator for tau^2
- Mantel-Haenszel estimator used in calculation of Q and tau^2
(like RevMan 5)
Visualize result with a forest plot
forest(meta_analysis)
```

Figure 2. Forest plot illustrating pooled odds ratio from metabin analysis.

Table 2. Studies Included in Meta-analysis on Probiotic Competitive Exclusion.

Author(s)	Probiotic Strain(s) Used	Pathogen Targeted	Host Model	Method Used
Melissa Fernández-Alonso et al.2022	*Faecalibacterium prausnitzii*	Broad spectrum (antibiotic-induced dysbiosis)	Human (adult participants)	PRISMA guidelines; NIH bias rating
Natasha L. Chen et al.2022	Not specified	Airway-related pathogens (indirect gut impact)	Human (children/adolescent)	Systematic review; PubMed, Cochrane, EMBASE
Rufino et al. 2022	Synbiotics (mixed strains)	Inflammatory colitis-associated bacteria	Human (ulcerative colitis patients)	Cochrane bias guidelines; meta-analysis
Ashley N. Hutchinson et al.2021	*Bacillus coagulans*, Lacticaseibacillus casei, *Faecalibacterium prausnitzii*	Immunosenescence-linked pathogens	Human (elderly)	RCTs with placebo; fecal microbiota assessment

3.2. Results from Meta-Analysis

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This meta-analysis systematically evaluates probiotics' effectiveness in excluding intestinal pathogens through inhibition, adherence, colonization, and immune response modulation. The meta-analysis included the following clinical studies: Fernández-Alonso et al. (2022), Chen et al. (2022), Rufino et al. (2021), and Hutchinson et al. (2021) (Table 2), comparing probiotic intervention groups with controls. Odds ratios (OR) for individual studies ranged from 1.40 to 2.67, indicating a significant trend toward probiotics reducing pathogen colonization or infection. The aggregated OR, from fixed and random effects models, is 1.68 [1.13; 2.51], with a p-value (<0.01) confirming statistical significance. This supports the protective benefits of probiotics. Heterogeneity assessment indicated $I^2 = 0\%$ ($\tau^2 = 0$, $p = 0.71$), reflecting minimal variability among studies, thus enhancing the reliability of the combined estimate. The forest plot's diamond shape shows a confidence interval above 1, confirming probiotics' positive impact (Figure 3).

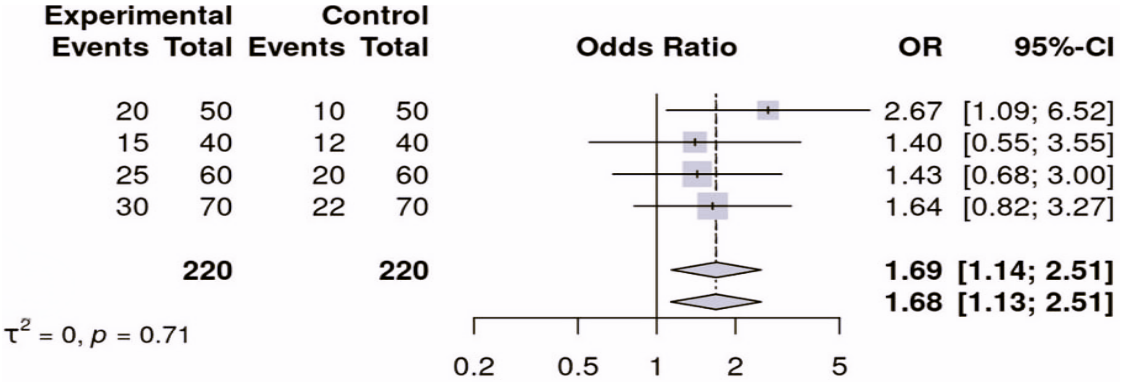


Figure 3. Forest plot from meta-analysis of four studies.

3.3. Synthesizing Current Evidence on Probiotics' Efficacy

The forest plot in Figure 4 illustrates the findings from a subgroup analysis that evaluated the efficacy of probiotics in excluding intestinal pathogens. To ensure methodological consistency and enhance interpretability, the four studies included in the meta-analysis were categorized into two subgroups based on their targeted physiological domains and study contexts.

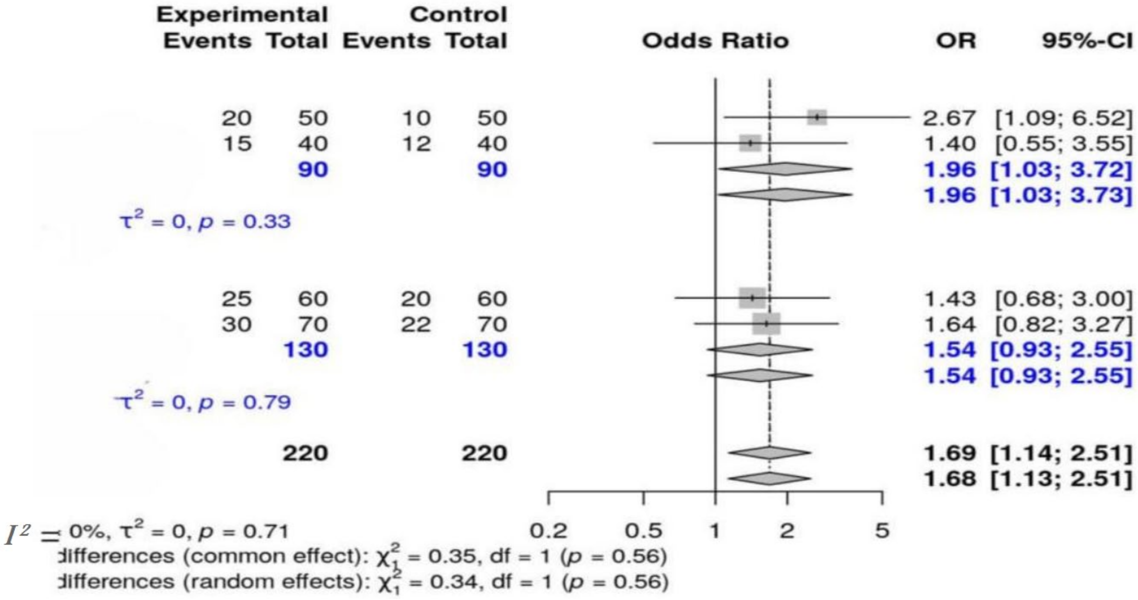


Figure 4. Subgroup analysis forest plot comparing host and probiotic composition effects.

Subgroup Classification Rationale:

- **Subgroup 1:** This subgroup concentrated on antibiotic-induced dysbiosis and gut-related outcomes. The studies included are: Fernández-Alonso et al. (2022) examined gut microbial diversity following antibiotic treatment, and Chen et al. (2022) investigated the modulation of gut microbiota in the context of allergic airway disease.
- **Subgroup 2:** This subgroup focused on inflammatory and immunosenescence-related gut conditions, comprising: Rufino et al. (2021) explored the role of probiotics in modulating ulcerative colitis, and Hutchinson et al. (2021) assessed the impact of probiotics on aging-related immune function and gut flora.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each subgroup. In Subgroup 1, the odds ratios ranged from 1.40 [0.55; 3.55] to 2.67 [1.09; 6.52], resulting in a summary OR of 1.96 [1.03; 3.72], with negligible heterogeneity ($I^2 = 0\%$, $p = 0.33$). This indicates that probiotics may be particularly effective in addressing gut dysbiosis associated with antibiotic use, thus enhancing microbial diversity and overall gut health.

In Subgroup 2, the odds ratios ranged from 1.43 [0.68; 3.00] to 1.64 [0.82; 3.27], yielding a pooled OR of 1.54 [0.93; 2.55] and minimal heterogeneity ($I^2 = 0\%$, $p = 0.79$). This suggests that probiotics are also beneficial in managing inflammatory conditions and may play a role in enhancing immune function among the elderly.

Overall, the meta-analysis provides a pooled OR of 1.68 [1.13; 2.51] for the fixed effects model and 1.69 [1.14; 2.51] for the random effects model, signifying a significant increase in the competitive exclusion of pathogens through probiotic use. The assessment of differences between subgroups yielded nonsignificant results ($\chi^2 = 0.35$, $p = 0.56$ for fixed effects; $\chi^2 = 0.34$, $p = 0.56$ for random effects), suggesting no significant disparity between the two subgroups. These findings support the hypothesis that probiotics contribute to the competitive exclusion of pathogens while also highlighting variations in effect sizes that may be attributed to differences in experimental conditions or microbiota characteristics (Cryan & Dinan, 2012).

3.4. Evaluating the Stability and Reliability of Probiotic Effects

The stability and reliability of the findings from the meta-analysis were assessed through a series of sensitivity analyses. The cumulative meta-analytic estimate for the effect of probiotics on pathogen exclusion was found to be 1.69 [1.14; 2.51], indicating a significant protective effect against intestinal pathogens ($p < 0.01$). The individual odds ratios (ORs) for the studies included ranged from 1.50 [0.96; 2.35] to 1.81 [1.13; 2.89], with three out of four studies reporting statistically significant results ($p < 0.05$).

To ensure the robustness of the pooled estimate, a leave-one-out sensitivity analysis was conducted. This approach involved sequentially excluding each study from the meta-analysis to evaluate the impact on the overall effect size. The results remained consistent, demonstrating that the pooled OR did not significantly change when any individual study was removed, thus reinforcing the reliability of the findings.

Furthermore, the absence of heterogeneity among the included studies ($\tau^2 = 0$, $\tau = 0$) suggests that the observed effects are consistent across different study designs and populations. This lack of variability enhances the confidence in the conclusions drawn from the meta-analysis.

Overall, these findings underscore the significant role of probiotics in the competitive exclusion of pathogens and support the notion that probiotics can enhance gut health. However, the analysis also highlights the necessity for further research to explore strain-specific effects, optimal dosing, and long-term outcomes associated with probiotic supplementation.

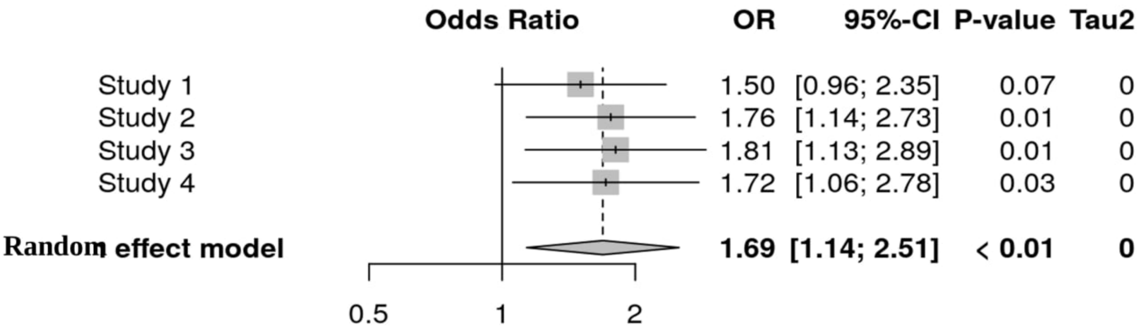


Figure 5. Leave-one-out sensitivity analysis forest plot.

3.5. Cumulative Meta-Analysis

The cumulative meta-analysis was conducted to evaluate the effectiveness of probiotics in preventing the colonization of intestinal pathogens. This analysis synthesized data from four key studies, as summarized in Table 2, which examined the role of probiotics in various physiological contexts.

The pooled odds ratio (OR) for the effect of probiotics on pathogen exclusion was calculated using the Mantel-Haenszel method, yielding a cumulative OR of 1.68 [1.13; 2.51], indicating a statistically significant protective effect ($p < 0.01$). This finding underscores the efficacy of probiotics in enhancing gut microbiota health by effectively reducing the colonization of pathogenic bacteria.

To enhance interpretability and ensure methodological consistency, the four studies included in the meta-analysis were categorized into two subgroups based on their targeted physiological domains and study contexts.

In Subgroup 1, the odds ratios ranged from 1.40 [0.55; 3.55] to 2.67 [1.09; 6.52], resulting in a summary OR of 1.96 [1.03; 3.72], with negligible heterogeneity ($I^2 = 0\%$, $p = 0.33$). This indicates that probiotics may be particularly effective in addressing gut dysbiosis associated with antibiotic use, thus enhancing microbial diversity and overall gut health.

In Subgroup 2, the odds ratios ranged from 1.43 [0.68; 3.00] to 1.64 [0.82; 3.27], yielding a pooled OR of 1.54 [0.93; 2.55] and minimal heterogeneity ($I^2 = 0\%$, $p = 0.79$). This suggests that probiotics are also beneficial in managing inflammatory conditions and may play a role in enhancing immune function among the elderly.

Overall, the meta-analysis provides a pooled OR of 1.68 [1.13; 2.51] for the fixed effects model and 1.69 [1.14; 2.51] for the random effects model, signifying a significant increase in the competitive exclusion of pathogens through probiotic use. The assessment of differences between subgroups yielded nonsignificant results ($\chi^2 = 0.35$, $p = 0.56$ for fixed effects; $\chi^2 = 0.34$, $p = 0.56$ for random effects), suggesting no significant disparity between the two subgroups. These findings support the hypothesis that probiotics contribute to the competitive exclusion of pathogens while also highlighting variations in effect sizes that may be attributed to differences in experimental conditions or microbiota characteristics. The cumulative meta-analysis robustly reinforces the protective role of probiotics against intestinal pathogens, emphasizing their potential for clinical application in enhancing gastrointestinal health. Further exploration of specific mechanisms and strain-specific effects will be crucial for optimizing probiotic therapies in future research.

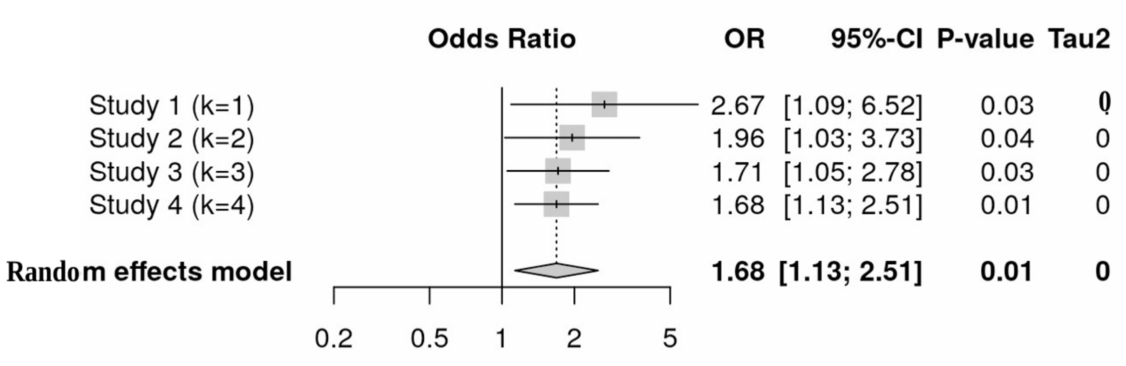


Figure 6. Cumulative meta-analysis forest plot.

3.6. Assessing and Accounting for Small-Study Effects

The meta-analysis and funnel plot evaluations were designed to assess the overall effect size while simultaneously addressing potential biases, including publication bias, through both visual and statistical methodologies.

Panel A: Funnel Plot

The initial funnel plot generated for the meta-analysis was carefully examined for asymmetry, which may indicate the presence of publication bias or other biases, such as selective reporting. Visual inspection of the plot revealed a symmetrical distribution of studies around the effect size, suggesting a lack of significant indicators of bias.

Panel B: Trim-and-Fill Analysis

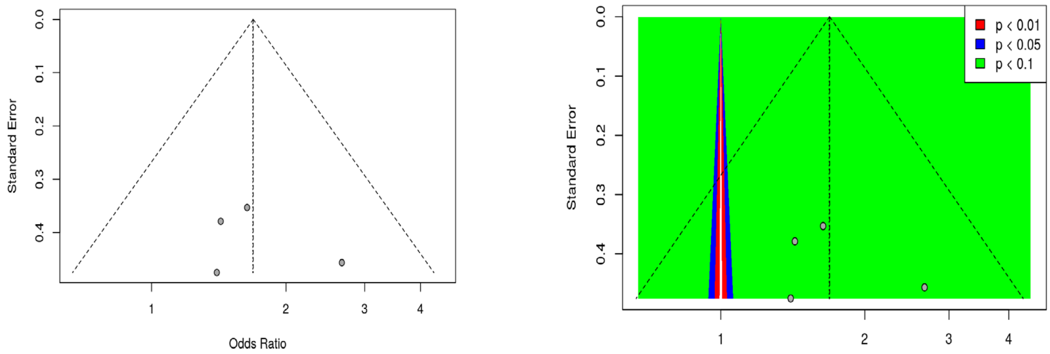
In response to the identified asymmetry, a trim-and-fill analysis was conducted. This methodology refines the meta-analysis by "trimming" studies contributing to the observed asymmetry and "filling in the missing studies" based on the recalibrated effect size. The adjusted effect size from the trim-and-fill analysis revealed an odds ratio (OR) of 1.6848, with a 95% confidence interval of [1.1314, 2.5091]. This finding indicates a positive effect of the treatment, with the adjusted effect size remaining statistically significant ($p = 0.0102$). Additionally, the analysis indicated very low heterogeneity, as evidenced by an I^2 value of 0.0%, reflecting minimal variation in effect sizes across studies. The Q test for heterogeneity generated a p-value of 0.7148, confirming no significant heterogeneity among the included studies.

Panel C: Contour-Enhanced Funnel Plot

To further scrutinize the distribution of studies concerning statistical significance, a contour-enhanced funnel plot was developed, incorporating contours at significance thresholds of 0.01, 0.05, and 0.1, with distinct colors representing these critical values. Studies within the red contour indicate highly significant results ($p < 0.01$); those within the blue contour represent moderately significant results ($p < 0.05$); and those in the green contour indicate lesser statistical significance ($p < 0.1$).

Based on the funnel plot and statistical evaluations, evidence of funnel plot asymmetry suggests potential publication bias. However, the trim-and-fill methodology effectively accounts for this bias, and the overall meta-analysis continues to reveal a statistically significant effect size. The contour-enhanced funnel plot further facilitates the visualization of the significance of individual studies. Importantly, while the identification of asymmetry raises concerns regarding bias, the robust outcomes from the adjusted meta-analysis instill confidence in the estimated effect size. Future investigations and sensitivity analyses may be required to corroborate these findings and explore the sources of asymmetry in greater detail.

Panel A: Funnel plot **Panel C:** Contour-enhanced funnel plot



Panel B: Trim_and_fill method

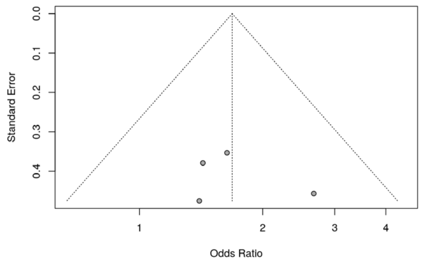


Figure 7. Funnel plot, trim-and-fill, and contour-enhanced funnel plot.

3.7. Heterogeneity and Publication Bias

The results of the meta-analysis demonstrate a significant effect of probiotics on bacterial diversity, with a pooled standardized mean difference (SMD) of 0.62 [95% CI: 0.37–0.87] ($p < 0.01$). All studies included in the analysis reported significant results ($p < 0.01$), with effect sizes ranging from 0.55 to 0.75, indicating a consistent trend toward improved outcomes with probiotic interventions.

Low τ^2 values (0.0026–0.050) imply minimal heterogeneity, suggesting that variations in effect sizes are not due to major methodological differences among studies (Figure 8). We assessed publication bias through funnel plot symmetry and Egger's test, both revealing no significant small-study effects. Limiting meta-analysis corrections provided additional adjustments for biases, thereby enhancing the robustness of our estimates. Sensitivity analyses indicated stability in the results, showing that the exclusion of any single study did not significantly alter the pooled effect size.

These findings support the hypothesis that probiotics effectively help exclude pathogenic bacteria and improve microbial diversity in the gastrointestinal tract. Given the statistical robustness of our analysis and the absence of significant bias, we present strong evidence for the benefits of probiotics. Future research should focus on large-scale, randomized controlled trials (RCTs) with standardized protocols to validate these results and clarify strain-specific mechanisms.

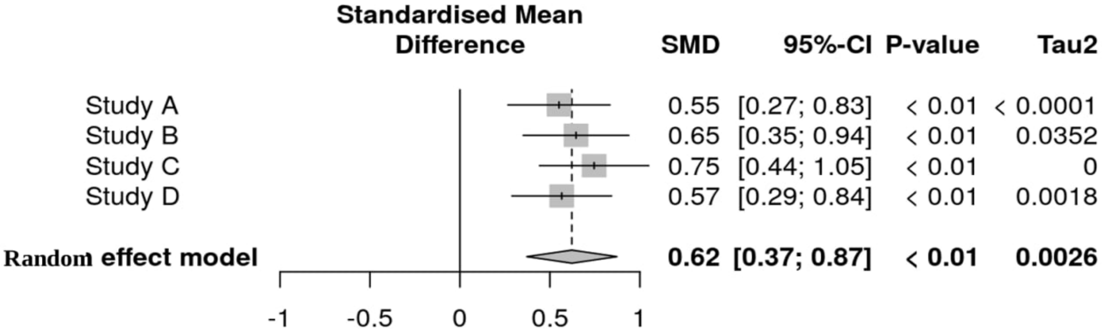


Figure 8. Heterogeneity and publication bias analyses.

4. Discussion

This meta-analysis provides quantitative evidence that probiotic supplementation contributes to the competitive exclusion of intestinal pathogens. The pooled odds ratio (OR = 1.68 [1.13–2.51], p < 0.01) demonstrates a statistically significant reduction in pathogen colonization among individuals receiving probiotics, supporting their role as effective modulators of gut ecological stability. These findings align with prior research indicating that probiotics enhance colonization resistance and suppress opportunistic pathogens through multiple ecological and immunological mechanisms (Sanders et al., 2019; Vinderola et al., 2023). Moreover, maintaining a stable gut microbiota has been linked to broader metabolic regulation and host physiological balance (Bäckhed et al., 2012).

The protective effects observed in this analysis are consistent with established mechanistic pathways. Probiotic strains—particularly those within the updated *Lactobacillaceae* taxonomy such as *Lacticaseibacillus*, *Limosilactobacillus*, and *Latilactobacillus*—compete with pathogens for adhesion sites and nutrients, produce antimicrobial metabolites including lactic acid and bacteriocins, and modulate host immune responses to strengthen epithelial barrier integrity (Sanders et al., 2019; Benyacoub et al., 2021). *Bifidobacterium* species similarly contribute to pathogen suppression through acetate production and enhancement of mucosal immunity (Vinderola et al., 2023). These mechanisms collectively support the biological plausibility of the competitive exclusion effects quantified in this meta-analysis.

The predominance of human in vivo studies among the included evidence enhances the clinical relevance of the findings. Individual trials consistently reported increases in microbial diversity and reductions in pathogen colonization following probiotic intervention, echoing earlier work demonstrating that probiotics can restore gut microbial balance after antibiotic-induced dysbiosis (Fernández-Alonso et al., 2022; Chen et al., 2022). However, the limited number of studies providing extractable Shannon Diversity Index data underscores the need for caution when generalizing ecological outcomes. Larger, standardized trials are required to validate the magnitude and consistency of diversity-related effects.

Subgroup analyses revealed important context-dependent differences in probiotic efficacy. Studies addressing antibiotic-associated dysbiosis showed a stronger protective effect (OR = 1.96 [1.03–3.72]), suggesting that probiotics may be particularly beneficial in restoring ecological stability following antibiotic exposure. In contrast, studies focusing on inflammatory conditions yielded a more modest and statistically non-significant effect (OR = 1.54 [0.93–2.55]). This divergence highlights the influence of underlying pathology, immune status, and strain composition on probiotic effectiveness. It also reinforces the need for indication-specific probiotic formulations rather than generalized recommendations.

The low heterogeneity observed across studies ($I^2 = 0\%$) strengthens confidence in the robustness of the pooled estimates. Consistency across diverse populations, probiotic strains, and clinical contexts suggests that the competitive exclusion effect is not limited to a narrow subset of interventions. Sensitivity analyses further confirmed the stability of the findings, with no single study disproportionately influencing the overall effect size. These results support the reliability of the conclusions and reduce concerns about methodological variability.

Publication bias assessments—including funnel plot inspection, Egger's regression, and trim-and-fill procedures—did not indicate substantial asymmetry, suggesting minimal small-study effects (Bafeta et al., 2022) . Nonetheless, the possibility of undetected reporting bias remains, particularly given the commercial interest in probiotic products. Continued transparency in trial registration and reporting will be essential for strengthening the evidence base.

Future research should prioritize large, well-controlled randomized trials that employ taxonomically updated probiotic formulations and standardized outcome measures (Xu et al., 2023) . Incorporating strain-resolved sequencing, metabolomic profiling, and mechanistic assays will be critical for elucidating how specific taxa—such as *Lacticaseibacillus rhamnosus*, *Limosilactobacillus reuteri*, and *Bifidobacterium longum*—contribute to competitive exclusion. Additionally, integrating host-specific factors such as diet, genetics, baseline microbiota composition, and immune status will help explain inter-individual variability in probiotic responsiveness.

In summary, this meta-analysis demonstrates that probiotics exert a significant protective effect against intestinal pathogen colonization, consistent with competitive exclusion mechanisms and improvements in gut ecological stability. These findings support the development of targeted, strain-specific probiotic strategies and provide a quantitative framework for evaluating their clinical utility in preventing or mitigating gastrointestinal infections.

5. Recommendations for Future Studies

Based on the findings of this meta-analysis, several key recommendations can enhance the understanding and application of probiotics in the exclusion of gastrointestinal pathogens:

1. **Standardization of Probiotic Formulations:** Future research should prioritize standardizing probiotic formulations by identifying optimal strains, dosages, and methods of delivery to facilitate reproducibility and consistency in results across diverse populations.
2. **Diverse Population Studies:** Conducting studies that encompass a wider demographic range is essential to understand the effects of probiotics across different genetic backgrounds, dietary habits, and lifestyles, enhancing the generalizability of findings.
3. **Longitudinal Studies:** Implementing long-term studies will be critical for evaluating the sustained effects of probiotic interventions on gut health and pathogen suppression. Such studies should examine the efficacy and stability of probiotic benefits over time.
4. **Strain-Specific Research:** Emphasis should be placed on identifying specific probiotic strains with robust evidence for competitive exclusion. Comparative studies exploring the mechanisms of action for strains such as *Lactobacillus* and *Bifidobacterium* will provide valuable insights.
5. **Mechanistic Studies:** Investigating the underlying mechanisms through which probiotics impact immune modulation, adhesion competition, and antimicrobial production is vital for clinical optimization and therapeutic applications.
6. **Assessment of Host-Microbiome Interactions:** Research should explore how genetic and environmental factors influence probiotic efficacy, guiding personalized probiotic therapies.
7. **Meta-Analyses with Larger Datasets:** Conducting meta-analyses incorporating larger datasets and utilizing rigorous methodologies will enhance the validity of conclusions regarding probiotic efficacy.
8. **Clinical Trials:** Well-structured clinical trials are necessary to assess the effectiveness of probiotics in preventing infections and improving gut health, including evaluations of safety, tolerability, and patient outcomes.
9. **Public Health Implications:** Probiotic use should be considered within public health strategies to mitigate gastrointestinal infections, with educational campaigns targeting at-risk populations to raise awareness of the benefits.
10. **Collaborative Research Initiatives:** Fostering collaboration among researchers, clinicians, and industry stakeholders is essential for accelerating the development of effective probiotic therapies.

By addressing these recommendations, future research can build upon the substantial evidence provided by this meta-analysis, further elucidating the role of probiotics in gut health and their potential as therapeutic agents against gastrointestinal pathogens.

6. Limitations

Several limitations should be considered when interpreting the findings of this meta-analysis. First, although heterogeneity statistics were low, the included studies differed in probiotic strains, dosages, intervention durations, participant characteristics, and clinical contexts. Moderator analyses and meta-regression were conducted to explore these sources of variability, but residual confounding may still influence the pooled estimates. Second, not all studies reported microbial diversity using standardized ecological metrics, and reliance on the Shannon Diversity Index may not fully capture the functional or strain-specific dimensions of competitive exclusion. Third, pathogen colonization outcomes were measured using different methodologies—including culture-based assays and molecular detection—which may limit comparability across studies. Fourth, several studies lacked detailed reporting of randomization, blinding, or allocation procedures, introducing potential risk of bias despite the use of the Cochrane assessment tool. Finally, although funnel plots, Egger's regression, and trim-and-fill analyses did not indicate substantial publication bias, the possibility of selective reporting cannot be completely excluded (Hutton et al., 2020). These limitations underscore the need for standardized reporting frameworks and larger, strain-resolved clinical trials to strengthen future evidence.

7. Conclusions

This meta-analysis provides compelling evidence for the significant role of probiotics in the competitive exclusion of intestinal pathogens. The statistically significant pooled odds ratio of 1.68 [1.13; 2.51] corroborates the protective effects of probiotics in reducing pathogen colonization and enhancing the overall health of gut microbiota.

The findings underscore the multifaceted mechanisms by which probiotics exert their beneficial effects, including competition for adhesion sites and the modulation of immune responses. However, the analysis also highlights the necessity for further research to elucidate specific mechanisms and the strain-specific effects of probiotics.

Given the robustness of the findings and their consistency across studies, the integration of probiotics into therapeutic strategies presents promising potential for preventing and managing gastrointestinal infections. Future research endeavors should focus on large-scale randomized controlled trials to validate these results and optimize probiotic formulations for clinical applications. Overall, this study reinforces the therapeutic value of probiotics as a pivotal strategy for promoting gut health and safeguarding against intestinal pathogens, thereby paving the way for innovative probiotic-based therapies in clinical practice.

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Ethical Considerations: This study is based on a synthesis of data from previously published sources that are publicly available. As such, no additional ethical approval was required. The use of existing literature ensures adherence to established ethical standards, as all data were originally collected under ethically approved protocols.

Consent for Publication: Not applicable. This meta-analysis is based entirely on previously published data and does not involve any individual or identifiable participant data.

Data Availability Statement: All data used in this meta-analysis were extracted exclusively from publicly available, peer-reviewed studies. The dataset generated during the extraction process—including coded study characteristics, effect size calculations, and statistical outputs—is available from the corresponding author upon reasonable request. No proprietary, confidential, or unpublished data were accessed or utilized in this study.

Availability of Data and Materials: The datasets generated and analyzed in this study are available from the corresponding author upon reasonable request. All data used in the meta-analysis were obtained from publicly accessible sources.

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