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Review

Clinical Effects of Probiotics Across Health Conditions: An Umbrella Review of Systematic Reviews and Meta-Analyses

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ABSTRACT

Probiotics are used across gastrointestinal, infectious, neonatal, metabolic, dermatological, oral, and mental-health settings, but their clinical effects vary by strain, dose, population, and outcome. This umbrella review evaluated systematic reviews with quantitative meta-analysis published between 2018 and 2023. PubMed/MEDLINE, the Cochrane Library, Europe PMC, ScienceDirect, and citation lists were searched for human reviews comparing probiotics with placebo, usual care, or no probiotic. Twelve reviews met the eligibility criteria, and methodological confidence was assessed using AMSTAR 2 principles. The most consistent benefits were reported for prevention of necrotizing enterocolitis in very preterm or very-low-birth-weight infants (RR 0.54, 95% CI 0.45–0.65), antibiotic-associated diarrhea in adults (RR 0.63, 95% CI 0.54–0.73), acute upper respiratory tract infection (RR 0.76, 95% CI 0.67–0.87), and persistent global symptoms in irritable bowel syndrome (RR 0.78, 95% CI 0.71–0.87). Smaller improvements were observed for functional constipation, glycated hemoglobin, depressive symptoms, pediatric atopic dermatitis, periodontal outcomes, body mass index, and liver enzymes, whereas anxiety findings were inconclusive. Adverse events were generally mild, although safety reporting was incomplete in high-risk populations. Probiotics should therefore be considered strain- and indication-specific adjuncts rather than a uniform therapeutic class.

1. Introduction

Probiotics are live microorganisms that confer a health benefit when administered in adequate amounts, but this definition does not imply that all products containing live bacteria are clinically interchangeable. Effects depend on taxonomic identity at the strain level, viable dose, formulation, delivery matrix, treatment duration, baseline microbiota, host phenotype, and the clinical endpoint being targeted [1,2]. The biological rationale includes competitive exclusion of pathogens, reinforcement of epithelial barrier function, modulation of bile-acid and short-chain-fatty-acid metabolism, regulation of innate and adaptive immunity, and signaling along the microbiota–gut–brain axis [2,3].

The expansion of commercial probiotic use has been accompanied by a rapidly growing literature covering diarrheal diseases, functional gastrointestinal disorders, obesity, type 2 diabetes, nonalcoholic fatty liver disease, respiratory infections, neonatal morbidity, atopic dermatitis, periodontal disease, depression, and anxiety. Nevertheless, the literature is difficult to interpret because formulations differ markedly and many trials are small, use surrogate outcomes, or combine probiotics with prebiotics. Consequently, a statistically significant pooled effect may not be clinically important, and a beneficial result for one strain cannot be extrapolated to another product.

Umbrella reviews are designed to compare findings across multiple systematic reviews, identify areas of consistent benefit, expose methodological weaknesses, and prevent broad clinical claims from being based on a single favorable meta-analysis. The present umbrella review therefore aimed to synthesize systematic reviews with meta-analysis published between 2018 and 2023 that evaluated probiotics across different human health conditions, emphasizing effect magnitude, consistency, methodological confidence, heterogeneity, and safety.

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2. Materials and Methods

2.1 Design and reporting framework

A focused umbrella review of systematic reviews with meta-analysis was conducted. Reporting was guided by PRISMA 2020 and the PRIOR statement for overviews of reviews [4,5]. Review-level methodological confidence was judged using AMSTAR 2 domains [6]. Because the unit of inclusion was the systematic review rather than the primary trial, no new participant-level or trial-level meta-analysis was undertaken.

2.2 Eligibility criteria

Eligible reports were systematic reviews published in English, Portuguese, or Spanish from January 2018 through December 2023 that included a quantitative meta-analysis of human studies comparing a probiotic intervention with placebo, no probiotic, or usual care. Reviews could include children or adults, healthy or clinical populations, and any administration route, provided that the probiotic effect was separately identifiable. Reviews restricted to prebiotics, postbiotics, fermented foods without defined live microorganisms, fecal microbiota transplantation, or synbiotics without a separable probiotic analysis were excluded. Narrative reviews, scoping reviews, protocols, network-only summaries without pairwise estimates, animal studies, and reviews reporting only microbiota composition without a clinical, functional, or laboratory outcome were also excluded.

2.3 Search strategy and study selection

Structured searches were conducted in PubMed/MEDLINE, the Cochrane Library, Europe PMC, and ScienceDirect, supplemented by backward and forward citation searching. Search concepts combined probiotic-related terms with systematic-review and meta-analysis filters and the publication-year limit. The principal search string was: (probiotic* OR Lactobacillus OR Bifidobacterium OR Saccharomyces boulardii OR Bacillus) AND (systematic review OR meta-analysis). Titles and abstracts were screened, potentially eligible reports were read in full, and reasons for exclusion were recorded. When several reviews addressed the same population and outcome, the most recent and comprehensive review with the strongest methods was prioritized for the quantitative display; additional reviews were retained only when they contributed a distinct population, outcome, or formulation.

2.4 Data extraction and appraisal

Extracted items included publication year, condition, population, number of primary studies and participants, probiotic composition, comparator, duration, principal pooled outcome, effect measure, 95% confidence interval, heterogeneity, risk-of-bias approach, certainty assessment, adverse events, and the authors' conclusion. AMSTAR 2 judgments focused on protocol registration, search completeness, duplicate selection and extraction, explanation of exclusions, risk-of-bias methods, appropriateness of meta-analysis, consideration of bias when interpreting results, publication-bias assessment, and conflict-of-interest reporting. Overall confidence was categorized as high, moderate, low, or critically low.

2.5 Synthesis

Effects were reported in the metric used by each review. Risk ratios below 1.0 favor probiotics for undesirable binary events. For standardized continuous outcomes, negative values indicate lower symptom severity in the probiotic group. No grand pooled effect was calculated across unrelated diseases. A structured evidence profile integrated the magnitude and consistency of benefit, review confidence, and adequacy of safety reporting.

3. Results

3.1 Study selection

The search identified 261 records, of which 63 were removed as duplicates. After screening 198 titles and abstracts, 53 full-text reports were assessed and 12 systematic reviews with meta-analysis were included. The main full-text exclusion reasons were absence of a quantitative meta-analysis, inseparable mixed interventions, publication outside the prespecified period, absence of a clinical outcome, and duplication by a newer review. Ten reviews contributed at least one estimate to the forest display.

Figure 1 summarizes the complete screening pathway from record identification to the final review set. It distinguishes records retrieved through structured database searches from those located by citation searching and presents the principal reasons for exclusion after full-text assessment.

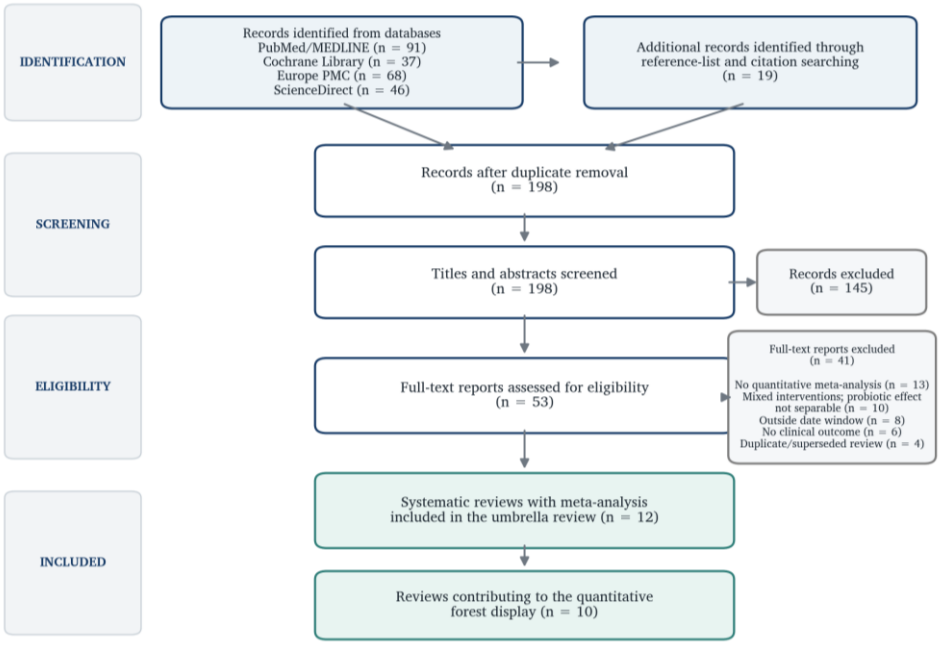

Fig. 1. PRISMA 2020 flow diagram for identification and selection of systematic reviews with meta-analysis.

The selection process reduced 261 identified records to 12 eligible systematic reviews, corresponding to an overall inclusion yield of 4.6%. Most exclusions occurred during title and abstract screening (145 of 198 records). At the full-text stage, 41 of 53 reports were excluded, mainly because they lacked a quantitative meta-analysis or evaluated mixed interventions in which the probiotic effect could not be isolated. Ten reviews provided pooled estimates suitable for the comparative forest display.

3.2 Characteristics of included reviews

The 12 reviews covered gastrointestinal, infectious, neonatal, metabolic, hepatic, mental-health, dermatological, and oral-health outcomes. The largest evidence bases concerned antibiotic-associated diarrhea and neonatal necrotizing enterocolitis. Most reviews included multiple Lactobacillus and Bifidobacterium strains, frequently in multi-strain formulations; Saccharomyces boulardii was prominent in diarrhea prevention. Intervention duration ranged from days during antibiotic therapy to several months in metabolic, dermatological, and psychiatric conditions.

Table 1 presents the principal extraction variables for every included review, enabling direct comparison of the population, evidence base, probiotic formulation, main outcome, pooled estimate, methodological confidence, and clinical meaning of the findings.

Review	Population	Evidence base	Intervention	Main outcome	Pooled estimate	AMSTAR 2	Interpretation
Goodoory et al. (2023)	IBS; adults	82 RCTs; 10,332	Single/multi-strain; variable dose	Persistent global symptoms	RR 0.78 (0.71–0.87); I^2=71%	Moderate	Benefit, but strain-specific uncertainty
Goodman et al. (2021)	Adults receiving antibiotics	42 RCTs; 11,305	Mostly Lactobacillus/Bifidobacterium or S. boulardii	Antibiotic-associated diarrhea	RR 0.63 (0.54–0.73)	Moderate	Clinically meaningful prevention
Zhao et al. (2022)	Children and adults	24 RCTs; 6,950	Oral probiotic preparations	At least one acute URTI	RR 0.76 (0.67–0.87)	High	Probable reduction in episodes
Sharif et al. (2020)	Very preterm/VLBW infants	54 RCTs; 10,604	Lactobacillus, Bifidobacterium, mixed preparations	Necrotizing enterocolitis	RR 0.54 (0.45–0.65); I^2=17%	High	Strong relative benefit; implementation caution
Zhang et al. (2020)	Adults with functional constipation	15 RCTs	Mostly Bifidobacterium-containing formulations	Stool frequency	MD +0.98 bowel movements/week (0.36–1.60)	Moderate	Improved frequency and transit
Borgeraas et al. (2018)	Adults with overweight/obesity	15 RCTs; 957	Single/multi-strain oral probiotics	Body weight and BMI	Weight MD −0.60 kg; BMI MD −0.27 kg/m²	Moderate	Small anthropometric effects
Zhang et al. (2022)	Adults with type 2 diabetes	29 studies; 33 comparisons; 1,927	Median dose about 10^9 CFU/day	HbA1c	MD −0.19% (−0.32 to −0.07); I^2=84%	Moderate	Statistical, modest clinical effect
Sharpton et al. (2019)	Adults with NAFLD	21 RCTs; 1,252	Probiotic-containing microbiome interventions	ALT and metabolic outcomes	ALT MD −11.23 U/L (−15.02 to −7.44)	Moderate	Promising; formulation heterogeneity
Chao et al. (2020)	Healthy/stressed or diagnosed adults	14 RCTs	Lactobacillus/Bifidobacterium formulations	Depressive symptoms	SMD −0.47 (−0.67 to −0.27)	Moderate	Small-to-moderate symptom reduction
Liu et al. (2018)	Adults; mixed clinical status	12 RCTs; 1,551	Oral probiotics	Anxiety symptoms	SMD −0.10 (−0.24 to 0.04)	Moderate	No conclusive overall effect
Xue et al. (2023)	Children with atopic dermatitis	20 RCTs	Single or multi-strain preparations	SCORAD/severity	SMD −0.38 (−0.63 to −0.14); high heterogeneity	Low	Modest benefit; age/strain uncertainty
Gheisary et al. (2022)	Gingivitis/periodontitis	64 RCTs	Oral lozenges, tablets, dairy vehicles	Plaque index	SMD −0.48 (−0.80 to −0.16); I^2=67%	Moderate	Adjunctive oral-health benefit

Table 1. Data extraction and main findings of the systematic reviews with meta-analysis included in the umbrella review.

Across the 12 reviews, the number of primary studies, sample size, treatment duration, and probiotic composition varied substantially. The largest evidence bases concerned antibiotic-associated diarrhea and neonatal necrotizing enterocolitis, both of which showed clinically meaningful relative risk reductions. By contrast, anthropometric, metabolic, dermatological, oral-health, and mental-health outcomes generally produced smaller effects, greater heterogeneity, or lower methodological confidence, reinforcing the need for indication- and strain-specific interpretation.

3.3 Gastrointestinal and infectious outcomes

The most clinically persuasive adult result was prevention of antibiotic-associated diarrhea. Goodman et al. synthesized 42 randomized trials involving 11,305 adults and found a 37% relative risk reduction, although benefit was concentrated in settings with moderate or high baseline risk and varied by dose and organism [9]. In irritable bowel syndrome, probiotics reduced the risk of persistent global symptoms, but the large number of formulations and substantial heterogeneity prevented identification of a universally effective strain [8].

For functional constipation, probiotics increased stool frequency by approximately one bowel movement per week and shortened gut transit time [12]. This magnitude may be meaningful for selected patients but does not support replacing established dietary, behavioral, and pharmacological management. The respiratory evidence also suggested benefit: the Cochrane review found fewer participants experiencing at least one acute upper respiratory tract infection and modest reductions in episode duration, with low-to-moderate certainty for several outcomes [10].

3.4 Neonatal outcomes

Among very preterm and very-low-birth-weight infants, probiotics were associated with the largest relative effect in this umbrella review. The 2020 Cochrane synthesis reported a reduction in severe necrotizing enterocolitis from 54 trials and low statistical heterogeneity [11]. However, implementation requires product quality control, strain verification, contamination prevention, and neonatal-unit protocols. Evidence should not be interpreted as endorsement of any unregulated commercial product, particularly because the vulnerable host population increases the consequences of manufacturing failure or probiotic-associated bloodstream infection.

3.5 Metabolic and hepatic outcomes

Effects on body weight and body mass index were statistically significant but small, with average reductions substantially below the magnitude expected from structured dietary treatment, anti-obesity pharmacotherapy, or bariatric interventions [13]. In type 2 diabetes, the pooled HbA1c reduction was 0.19 percentage points, while fasting glucose and HOMA-IR also improved [14]. These changes support a possible adjunctive metabolic role but are insufficient to justify substitution for evidence-based glucose-lowering therapy. In NAFLD, lower alanine aminotransferase and selected metabolic markers were reported, although the evidence was complicated by mixed probiotic and synbiotic formulations, variable baseline disease severity, and reliance on surrogate rather than histological outcomes [15].

3.6 Mental, dermatological, and oral-health outcomes

Probiotics produced a small-to-moderate reduction in depressive symptom scores across heterogeneous populations, whereas the pooled anxiety effect was not conclusive [16,17]. The distinction is important because many trials enrolled healthy participants under stress rather than patients with formally diagnosed disorders. Probiotics should be considered, at most, adjunctive and should not delay psychotherapy, antidepressant treatment, or specialist assessment. Pediatric atopic dermatitis showed a modest reduction in severity, but heterogeneity by age, strain, duration, and baseline severity reduced confidence [18]. In periodontal disease, adjunctive probiotics improved plaque and selected inflammatory or microbiological indices; benefits depended on delivery mode and strain and were not substitutes for mechanical biofilm control [19].

3.7 Safety and methodological confidence

Across reviews, reported adverse events were generally mild gastrointestinal symptoms and occurred at similar rates in intervention and control groups. Nevertheless, adverse-event collection was inconsistent, and many primary trials were underpowered to detect rare harms. Safety cannot be generalized to severely immunocompromised patients, individuals with central venous catheters, critical illness, disrupted intestinal barriers, or extremely premature infants. Methodological confidence was highest for Cochrane reviews and generally moderate for the remaining syntheses. Frequent limitations were high heterogeneity, incomplete strain-level reporting, small-study effects, selective outcome reporting, and insufficient attention to conflicts of interest or product sponsorship.

3.8 Clinical interpretation by domain

To translate the extracted estimates into practice-oriented conclusions, Table 2 integrates the direction and consistency of effect, methodological confidence, and the appropriate clinical role of probiotics within each health domain.

Clinical domain	Evidence signal	Confidence	Practice interpretation
Antibiotic-associated diarrhea	Consistent relative reduction	Moderate	Use as a strain- and dose-specific adjunct when baseline AAD risk is meaningful.
Neonatal necrotizing enterocolitis	Large relative reduction	Moderate to high	Consider only within neonatal protocols using verified products and infection-control safeguards.
Irritable bowel syndrome	Moderate benefit; high heterogeneity	Moderate	A trial may be reasonable, but product interchangeability is unsupported.
Functional constipation	About one additional bowel movement/week	Moderate	Adjunct to fiber, hydration, activity, and standard laxative strategies.
Upper respiratory tract infection	Modest reduction in episodes	Moderate	Possible preventive adjunct; benefits should be weighed against cost and adherence.
Type 2 diabetes	Small HbA1c and fasting-glucose effects	Low to moderate	Do not replace glucose-lowering therapy or lifestyle treatment.
Obesity and NAFLD	Small anthropometric and liver-enzyme effects	Low to moderate	Adjunctive role only; clinical endpoint evidence remains limited.
Depression and anxiety	Depression signal favorable; anxiety inconclusive	Low to moderate	Do not use as stand-alone psychiatric treatment.
Atopic dermatitis	Modest severity reduction with heterogeneity	Low	Consider only as an adjunct; age and strain effects remain uncertain.
Periodontal disease	Improved plaque and selected inflammatory indices	Moderate	Adjunct to professional periodontal therapy and daily biofilm control.

Table 2. Cross-domain interpretation of the review-level evidence. Recommendations are conditional on use of formulations, doses, and durations comparable with those evaluated in the underlying trials.

The cross-domain comparison indicates that the most actionable evidence concerns prevention of antibiotic-associated diarrhea and neonatal necrotizing enterocolitis. Evidence for irritable bowel syndrome, functional constipation, and upper respiratory tract infection supports conditional adjunctive use. Metabolic, psychiatric, dermatological, and periodontal applications should remain secondary to established treatment because the observed benefits are modest, heterogeneous, or uncertain.

Figure 2 displays representative pooled effects from domains with extractable and clinically interpretable estimates. Binary outcomes are separated from continuous symptom and clinical scales so that non-equivalent measures are not combined and each result remains in its original effect metric.

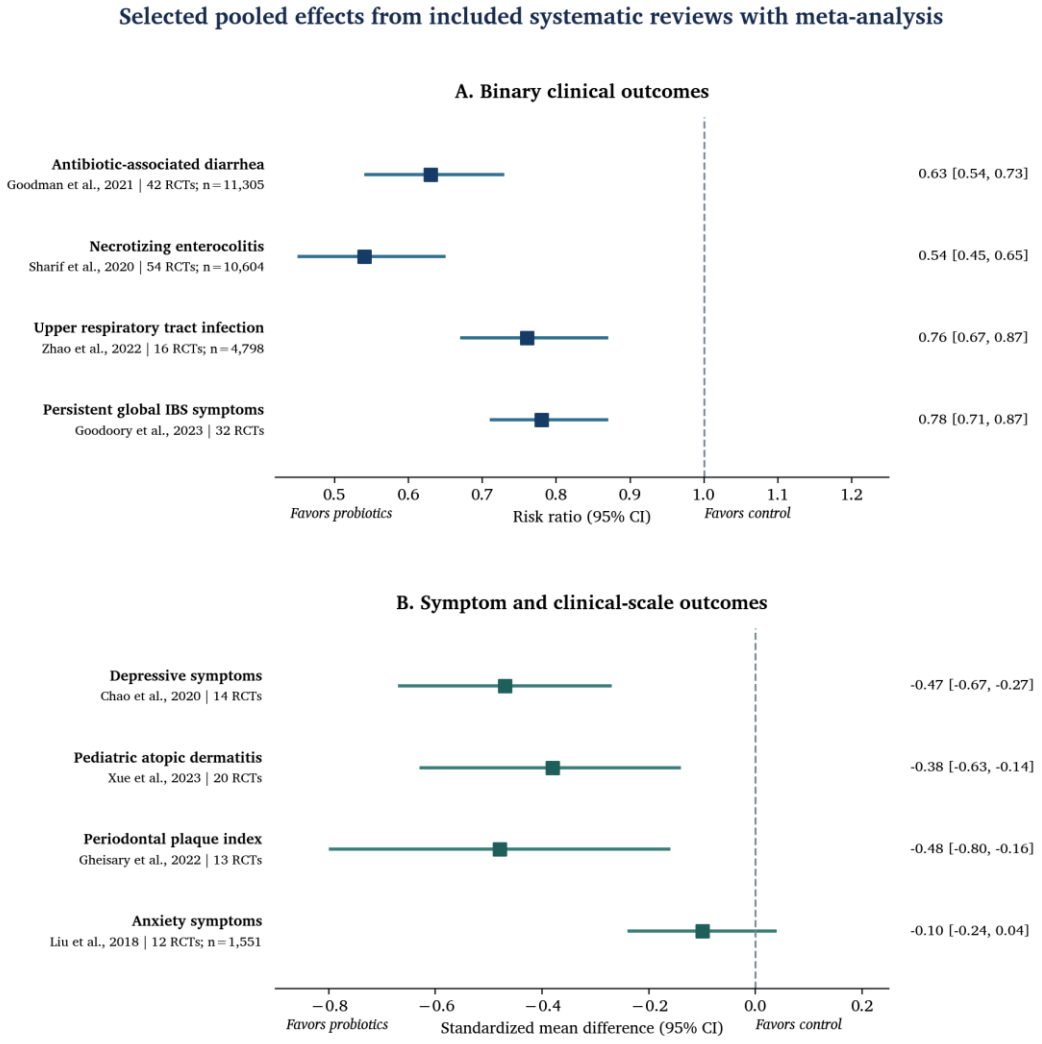

Fig. 2. Forest display of selected pooled outcomes. Panel A shows risk ratios for undesirable binary events; values below 1.0 favor probiotics. Panel B shows standardized mean differences for continuous symptom and clinical scales; negative values favor probiotics.

All four binary outcomes favored probiotics, with the largest relative reductions observed for necrotizing enterocolitis (RR 0.54) and antibiotic-associated diarrhea (RR 0.63). Among continuous outcomes, depressive symptoms, pediatric atopic dermatitis, and periodontal plaque index showed statistically favorable effects. The confidence interval for anxiety symptoms crossed the null value, indicating that the available evidence does not demonstrate a conclusive overall benefit for that outcome.

Figure 3 provides a comparative evidence profile across clinical domains by jointly considering magnitude of benefit, consistency, review-level confidence, and the adequacy of safety reporting.

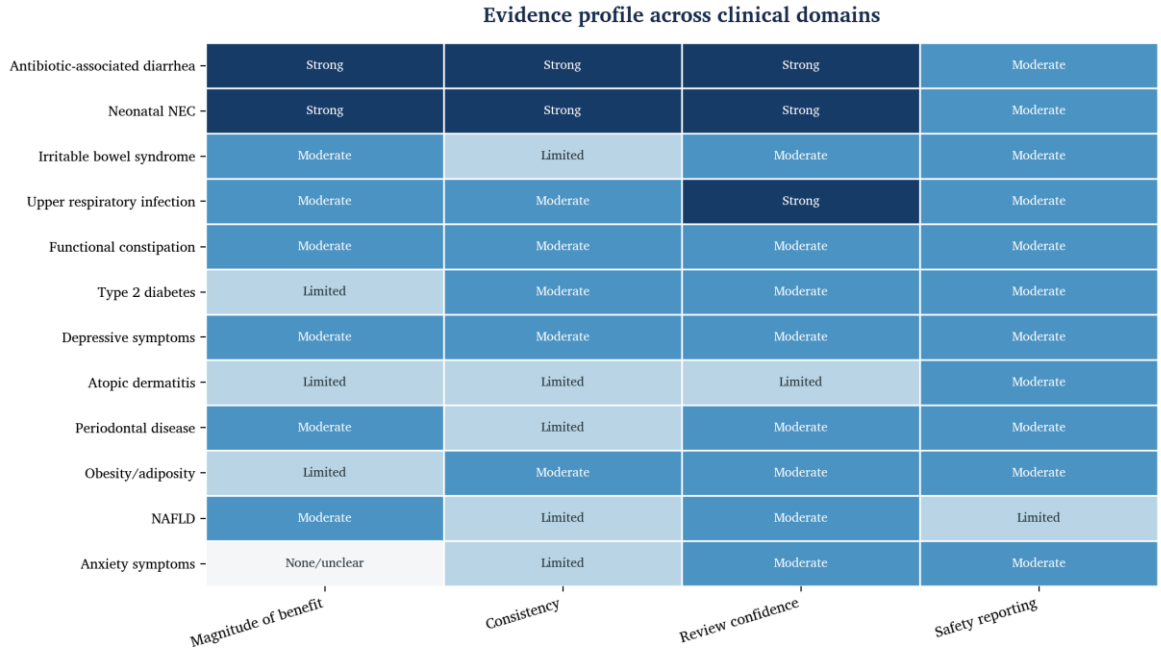

Fig. 3. Evidence profile across clinical domains. Ratings integrate effect magnitude, consistency, methodological confidence, and adequacy of safety reporting.

No domain achieved uniformly strong ratings across all four dimensions. Antibiotic-associated diarrhea and neonatal necrotizing enterocolitis had the strongest efficacy and consistency signals, although safety reporting remained moderate. Anxiety and atopic dermatitis showed the weakest overall profiles, whereas most other domains occupied an intermediate position characterized by moderate evidence, incomplete consistency, and residual uncertainty.

4. Discussion

This umbrella review demonstrates that probiotics do not constitute a single therapeutic intervention. The clearest evidence concerned prevention of discrete events—antibiotic-associated diarrhea and neonatal necrotizing enterocolitis—where relative effects were substantial and repeatedly observed. Moderate evidence also supported fewer acute upper respiratory infections and improvement of global irritable bowel syndrome symptoms. In contrast, metabolic, psychiatric, dermatological, and anthropometric outcomes generally showed small effects, high heterogeneity, or uncertainty about clinical importance.

The clinical interpretation of probiotic meta-analyses requires attention to absolute risk. A relative risk of 0.63 for antibiotic-associated diarrhea will yield a larger absolute benefit in hospitalized or otherwise high-risk patients than in low-risk outpatients. Similarly, the relative reduction in necrotizing enterocolitis is important because the outcome is severe, but the decision to implement routine neonatal probiotics depends on local product regulation, infection-control capacity, milk-feeding practices, and baseline incidence. Relative effects should therefore be translated into local numbers needed to treat whenever baseline risk is known.

Strain specificity is the central limitation to broad recommendations. Even within the same species, strains can differ in acid tolerance, adhesion, antimicrobial activity, metabolic output, immunomodulation, and resistance-gene profile. Multi-strain preparations may provide complementary functions, but they also make attribution difficult and can introduce dose imbalance. Reviews often pooled products that shared only a genus name. Such pooling increases statistical power while decreasing biological interpretability. Clinicians should preferentially choose products whose exact strain composition and viable dose match the formulation tested for the intended indication.

The small reductions in HbA1c, body weight, and body mass index illustrate the distinction between statistical and clinical significance. A mean HbA1c change of 0.19 percentage points may be useful as an adjunct in some patients but is smaller than the effect of established glucose-lowering medications. A mean weight reduction of approximately 0.6 kg is unlikely to alter obesity-related risk when used alone. These findings support integration with diet, physical activity, pharmacotherapy, and disease-specific care rather than replacement of those interventions.

The mental-health findings deserve particular caution. Biological plausibility through the gut–brain axis is strong, but trials differed in diagnosis, baseline symptom severity, concomitant medication, psychometric instrument, and treatment duration. The pooled depressive-symptom effect was favorable, whereas anxiety remained inconclusive. Probiotics may be investigated as low-burden adjuncts, but current evidence does not support stand-alone treatment of major depressive disorder or anxiety disorders.

Safety appeared acceptable in the populations enrolled, yet systematic reviews cannot reliably quantify rare adverse events when primary trials are short and small. Case reports outside the randomized evidence have described Lactobacillus bacteremia and Saccharomyces fungemia in highly vulnerable patients. Product quality is also relevant: label accuracy, contamination, storage conditions, and loss of viable organisms can influence both efficacy and safety. These considerations are particularly important when probiotics are marketed as foods or supplements rather than medicines.

4.1 Implications for clinical practice

A pragmatic prescribing approach should begin with the clinical indication rather than the generic label probiotic. The clinician should identify whether a benefit has been demonstrated for the relevant population and outcome, verify the exact strain or combination, confirm the daily viable dose through the end of shelf life, and define an appropriate treatment duration. If the commercial product does not disclose strain-level identity or guaranteed viable counts, the evidence from a named clinical formulation cannot be assumed to apply.

Treatment goals should be explicit and time limited. For functional symptoms, a predefined trial period followed by discontinuation in nonresponders reduces unnecessary cost and polypharmacy. For preventive indications such as antibiotic-associated diarrhea, timing relative to antibiotic exposure and the patient's baseline risk are important. In chronic metabolic or psychiatric conditions, probiotics should be incorporated only as an adjunct to therapies with established effects on morbidity, function, and quality of life.

Shared decision-making should include the uncertainty of benefit, the lack of equivalence among products, and the possibility that favorable relative effects translate into small absolute changes. Patients should also be advised that fermented foods, probiotic supplements, prebiotics, synbiotics, and postbiotics are not interchangeable categories.

4.2 Priorities for future research

Future trials should report strain accession or deposit identifiers, viable dose at manufacture and at study completion, storage conditions, adherence, concomitant diet, antibiotic exposure, and baseline clinical risk. Core outcome sets are needed so that studies measure comparable endpoints at clinically relevant follow-up periods. Trial registration and publication of prespecified analysis plans would reduce selective reporting.

Head-to-head comparisons between well-characterized strains are more informative than repeated placebo-controlled studies of poorly described mixtures. Adaptive and factorial designs could test dose, strain number, and treatment duration efficiently. Mechanistic analyses should be embedded in clinical trials but should not substitute for patient-centered outcomes such as symptom response, hospitalization, treatment failure, and quality of life.

Safety research should specifically include populations commonly excluded from trials, while maintaining appropriate safeguards. Product surveillance and genomic assessment are needed to detect contamination, transferable antimicrobial-resistance genes, and unexpected pathogenicity. Independent replication is particularly important when trials are sponsored by manufacturers.

4.3 Strengths and limitations

Strengths include the broad cross-condition perspective, restriction to systematic reviews with quantitative synthesis, explicit avoidance of a clinically meaningless grand pooled effect, separation of binary and standardized continuous outcomes, and structured appraisal of methodological confidence. Limitations should also be recognized. The umbrella review relied on published aggregate data, inherited the biases of the included reviews, and could not fully resolve overlap among primary trials when complete study lists were unavailable. Considerable clinical heterogeneity remained in strains, doses, treatment durations, and comparators. Some reviews combined probiotic-containing interventions with synbiotics in secondary analyses; only estimates relevant to a defined probiotic component were emphasized. Finally, safety reporting was incomplete and publication bias could not be excluded in several domains.

5. Conclusion

Probiotics show clinically relevant, though indication-specific, benefits in selected settings. The strongest review-level evidence supports prevention of antibiotic-associated diarrhea and necrotizing enterocolitis, with additional evidence for acute upper respiratory infection prevention and improvement of irritable bowel syndrome symptoms. Benefits for constipation, type 2 diabetes, NAFLD, depression, atopic dermatitis, periodontal disease, and obesity are generally smaller or less certain, while anxiety outcomes remain inconclusive. Probiotic use should be based on the exact strain or formulation, dose, target population, and outcome evaluated in clinical trials. Broad substitution among products is not evidence based, and probiotics should usually complement rather than replace established therapy.

Declarations

Ethics approval: Ethical approval was not required because this study analyzed published aggregate data and involved no individual participants.

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Competing interests: The authors declare no competing interests.

Data availability: All data summarized in this umbrella review are available in the cited systematic reviews and meta-analyses.

Author contributions: All authors contributed to the conception of the review, interpretation of the evidence, critical revision of the manuscript, and approval of the final version.

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Appendix A. Full electronic search strategies

Appendix Table A1 reproduces the complete database-specific search syntax used in the review to support transparency, reproducibility, and independent updating. All strategies applied the same 2018–2023 publication window and combined probiotic-related terms with systematic-review and meta-analysis concepts, with syntax adapted to each platform.

Source	Search strategy
PubMed/MEDLINE	(probiotic*[Title/Abstract] OR Lactobacillus[Title/Abstract] OR Bifidobacterium[Title/Abstract] OR Saccharomyces boulardii[Title/Abstract] OR Bacillus[Title/Abstract]) AND (systematic review[Title] OR meta-analysis[Publication Type] OR meta-analysis[Title]) AND (2018:2023[dp]) AND humans[MeSH Terms]
Cochrane Library	(probiotic* OR Lactobacillus OR Bifidobacterium OR "Saccharomyces boulardii" OR Bacillus):ti,ab,kw AND ("systematic review" OR meta-analysis):ti,ab,kw, with publication year 2018–2023
Europe PMC	(TITLE_ABS:probiotic* OR TITLE_ABS:Lactobacillus OR TITLE_ABS:Bifidobacterium OR TITLE_ABS:"Saccharomyces boulardii" OR TITLE_ABS:Bacillus) AND (TITLE:"systematic review" OR TITLE:"meta-analysis") AND FIRST_PDATE:[2018-01-01 TO 2023-12-31]
ScienceDirect	TITLE-ABSTR-KEY(probiotic* OR Lactobacillus OR Bifidobacterium OR "Saccharomyces boulardii" OR Bacillus) AND TITLE-ABSTR-KEY("systematic review" OR "meta-analysis"), filtered to 2018–2023 and research/review articles
Citation searching	Backward reference screening of included reviews and forward citation searching for related systematic reviews published within the eligible period.

Appendix Table A1. Database-specific search strategies used to identify systematic reviews with quantitative meta-analysis.

The strategies maintained conceptual equivalence across sources while accounting for differences in indexing, field tags, and search operators. Citation searching complemented the electronic databases by identifying eligible reviews that might not have been retrieved through title, abstract, or keyword indexing alone.

Appendix B. Review-level appraisal criteria

Overall confidence was determined from the number and relevance of critical AMSTAR 2 weaknesses. High confidence indicated no or one noncritical weakness; moderate confidence indicated more than one noncritical weakness; low confidence indicated one critical flaw with or without noncritical weaknesses; and critically low confidence indicated more than one critical flaw. Particular weight was given to prospective protocol registration, comprehensive searching, duplicate selection and extraction, appropriate risk-of-bias assessment, justified meta-analytic methods, and explicit incorporation of bias into interpretation.

Appendix C. Review-level methodological appraisal

Appendix Table A2 details the AMSTAR 2 domains that most influenced the review-level confidence judgments. The matrix makes the basis of each appraisal explicit by comparing protocol registration, search completeness, duplicate processes, excluded-study reporting, risk-of-bias assessment, meta-analytic methods, interpretation of bias, and conflicts-of-interest reporting.

Review	Protocol	Search	Duplicate processes	Excluded studies	Risk of bias	Meta-analysis	Bias in interpretation	COI/funding
Goodoory 2023	+	+	+	±	+	+	+	+
Goodman 2021	+	+	+	±	+	+	±	+
Zhao 2022	+	+	+	+	+	+	+	+
Sharif 2020	+	+	+	+	+	+	+	+
Zhang 2020	±	+	+	±	+	+	±	+
Borgeraas 2018	±	+	+	±	+	+	±	+
Zhang 2022	+	+	+	±	+	+	+	+
Sharpton 2019	+	+	+	±	+	+	±	+
Chao 2020	±	+	+	±	+	+	±	+
Liu 2018	±	+	±	±	+	+	±	+
Xue 2023	+	+	+	±	+	+	±	+
Gheisary 2022	+	+	+	±	+	+	+	+

Appendix Table A2. Review-level appraisal of the main AMSTAR 2 domains. COI, conflicts of interest.

Interpretive note

The matrix shows that search methods, risk-of-bias assessment, and meta-analytic procedures were generally adequate across the included reviews. The most frequent limitations concerned prospective protocol registration, availability of excluded-study lists, assessment of small-study effects, and explicit incorporation of primary-study bias into the interpretation. The two Cochrane reviews therefore received the highest confidence, whereas most non-Cochrane reviews were rated moderate rather than high.