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Recommendations to Improve Quality of Probiotic Systematic Reviews With Meta-Analyses

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Abstract

IMPORTANCE Systematic reviews and meta-analyses often report conflicting results when assessing evidence for probiotic efficacy, partially because of the lack of understanding of the unique features of probiotic trials. As a consequence, clinical decisions on the use of probiotics have been confusing.

OBJECTIVE To provide recommendations to improve the quality and consistency of systematic reviews with meta-analyses on probiotics, so evidence-based clinical decisions can be made with more clarity.

EVIDENCE REVIEW For this consensus statement, an updated literature review was conducted (January 1, 2020, to June 30, 2022) to supplement a previously published 2018 literature search to identify areas where probiotic systematic reviews with meta-analyses might be improved. An expert panel of 21 scientists and physicians with experience on writing and reviewing probiotic reviews and meta-analyses was convened and used a modified Delphi method to develop recommendations for future probiotic reviews.

FINDINGS A total of 206 systematic reviews with meta-analysis components on probiotics were screened and representative examples discussed to determine areas for improvement. The expert panel initially identified 36 items that were inconsistently reported or were considered important to consider in probiotic meta-analyses. Of these, a consensus was reached for 9 recommendations to improve the quality of future probiotic meta-analyses.

CONCLUSIONS AND RELEVANCE In this study, the expert panel reached a consensus on 9 recommendations that should promote improved reporting of probiotic systematic reviews with meta-analyses and, thereby, assist in clinical decisions regarding the use of probiotics.

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Key Points

Question How can probiotic meta-analyses be improved so more consistent guidance is available for clinicians?

Findings For this consensus statement, an expert panel reviewed more than 206 probiotic meta-analyses and determined 3 general areas that were inconsistent and needed improvement: extrapolation of probiotic efficacy for probiotics not included in the review, incomplete descriptions of probiotic nomenclature, and inappropriate pooling of different types of probiotics within the meta-analysis. A consensus was reached for 9 specific recommendations to improve future meta-analyses.

Meaning These findings suggest methods to improve the reporting of probiotic systematic reviews and meta-analyses that may assist in clinical decisions regarding probiotic use.

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Introduction

Although the range of probiotic products has expanded in recent years, a knowledge gap exists on how to best use them.[1-3] Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host."[4] The health benefit may be related to efficacy for a specific disease indication based on randomized clinical trials (RCTs) or a structure-function claim (often based on mechanism-of-action studies), depending on for which regulatory category the probiotic is being considered (eg, live biotherapeutic product, dietary supplement, or medicinal food).[5-9]

Sources of information on probiotic use have included practical guides, online applications, or systematic reviews (SRs) with or without a meta-analysis (MA) component, but these sources often disagree on which probiotics should be recommended for different uses.[2,10-17] Guidelines published by large organizations have also provided conflicting recommendations for probiotics because of differences in methods.[18-22] These issues have led to confusion for the general public and health care professionals when attempting to choose a probiotic for clinical use.[23-26]

Systematic reviews with meta-analyses (SRMAs) have also differed in their recommendations on which probiotics are more effective in specific clinical scenarios. These differences arise from how the analyses are conducted, which trials were included, and the lack of a standardized guideline on how probiotic SRMAs should be conducted.[20,27] Standards exist for reporting clinical trials (Consolidated Standards of Reporting Trials [CONSORT])[28] and for other types of SRMAs (Preferred Reporting Items for Systematic Reviews and Meta-analyses [PRISMA]),[29] but they have not addressed issues that are unique to probiotics. Although SRMAs are tools to provide evidence-based guidance for clinical decisions, no current standard guidelines exist for reporting probiotic-specific SRMAs. This article aims to provide guidance on addressing probiotic-specific issues and to develop a consensus on recommendations that should be included when conducting future SRMAs on probiotics.

Methods

Literature Review

A updated literature search was performed by the lead author (L.V.M.) using PubMed and Google Scholar databases for recent SRMAs pertaining to probiotics (January 1, 2020, to June 30, 2022). Search terms included '*Probiotic(s)*' AND '*meta-analysis*' OR '*systematic review*' AND '*since 2020*'. These articles were added to a 2018 literature search that used more extensive databases (PubMed, Google Scholar, Cochrane Database of Systematic Reviews, ISI Web of Science, EMBASE, and 2 trial registries).[2] The expert panel also provided examples of articles on probiotic issues. Inclusion criteria were an SRMA in which living probiotics were assessed. Exclusion criteria were an MA of prebiotics or synbiotics and reviews or SRs with no MA. Because probiotic efficacy is not only strain specific but also disease specific,[30] we sampled SRMAs from different diseases. When different conclusions of probiotic efficacy were reached within a disease category, representative examples were chosen for discussion. We followed relevant areas suggested in the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline[31] and assessed probiotic-specific areas not covered in the 2020 PRISMA guidelines.[29]

Expert Panel

A diverse group of experts was gathered to define recommendations for conducting probiotic SRMAs. The interdisciplinary panel consisted of experienced probiotic experts, and additional members were invited using snowball recruitment (gathering experts from known contacts in the probiotic field), as were those who had published probiotic reviews or organizational guidelines or had experience on other consensus panels. Panel members may not have worked together in the past. Areas of expertise for the 21 expert panel members included probiotics, MAs (conduct, writing, and reviewing), clinical infectious disease, gastroenterology, biostatistics, pharmacology, pediatrics, and microbiology. Panel members came from across the US, Canada, Ireland, Finland, France, and Poland.

Delphi Voting

The initial list of items was reviewed, revised, and voted on using a modified Delphi consensus method[32] (**Figure 1**). The threshold for consensus was defined as 75% or higher agreement on each item (≥16 of 21 members in agreement).

Results

Literature Review of Issues

A total of 778 articles were identified by the literature search and 183 probiotic SRMAs were pulled for screening, along with 23 additional studies provided by panel members (total of 206 SRMAs) (**Figure 2**). A total of 42 representative examples for 11 disease conditions were selected: prevention of antibiotic-associated diarrhea (AAD) (n = 7),[33-39] treatment of irritable bowel syndrome (n = 9),[40-48] treatment of pediatric acute gastroenteritis (n = 10),[49-58] prevention of postsurgical infections (n = 3),[59-61] treatment of atopic dermatitis (n = 3),[62-64] prevention of respiratory tract infections (n = 2),[65,66] prevention of neonatal infections (n = 2),[67,68] and mechanistic studies for diabetic metabolism (n = 3),[69-71] immune regulation (n = 1),[72] mental health (n = 1),[73] or weight loss (n = 1).[74]

Identification of Important Factors for Probiotic SRMAs

More than 10 separate discussions (via online conference calls or emails to individual experts) identified 36 issues important to include in probiotic SRMAs not already included in the 2020 PRISMA guidelines (**Table 1**). A consensus was reached for 23 items, which fell into 3 major areas: (1) overgeneralized conclusions on probiotic efficacy, (2) incomplete or missing strain designations or use of outdated nomenclature of the probiotic interventions, and (3) different levels of pooled subgroups (multigenus level, genus level, species level, or strain level).

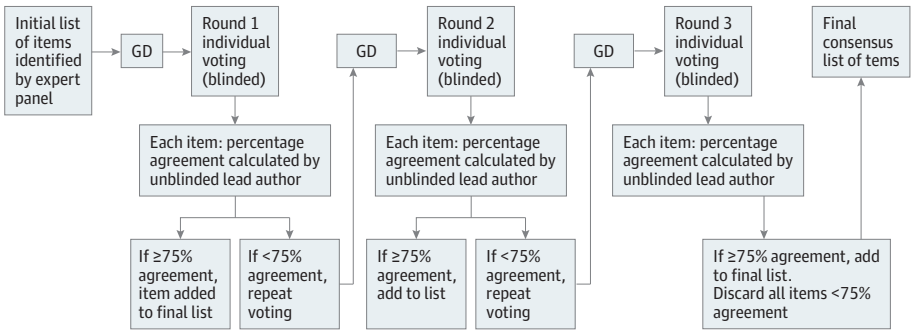
Generalized Conclusions of Efficacy

Some SRMAs within the same clinical condition reached different conclusions on probiotic efficacy. Examples of 4 such conditions are provided in **Table 2**. Some SRMAs came to a general conclusion that any type of probiotic was effective,[37,41,48,51,55,60,61] any probiotic within the same genus was effective,[33,42-45,49] or any probiotic within the same species was effective,[34,38] whereas some concluded only specific probiotic strains were effective.[35,39,47,50,52-54,56,57] Inappropriate extrapolation of efficacy to any type of probiotic was common, and the conclusion was not necessarily restricted to the strain(s) included in the SRMA.

Insufficient Description of Probiotic Interventions

Many SRMAs failed to completely identify the probiotic by genus, species, subspecies (if appropriate), and strain. Another challenge is that updates in bacterial nomenclature have resulted in name changes for several bacterial genera, making it difficult to recover literature using historical designations.[75-77] For example, the former genus *Lactobacillus* is currently composed of 25 genera.[75] In addition, multiple designations can be used for the same strain. Thus, *Lacticaseibacillus rhamnosus* GG (ATCC 53103) has been identified as *Lactobacillus rhamnosus* GG or even simply LGG in different SRMAs.

Figure 1. Delphi Consensus Flowchart



Individual panel members were blinded to voting results of other panel members.

GD indicates group discussion.

Pooling Data From Identical or Different Probiotic Strains

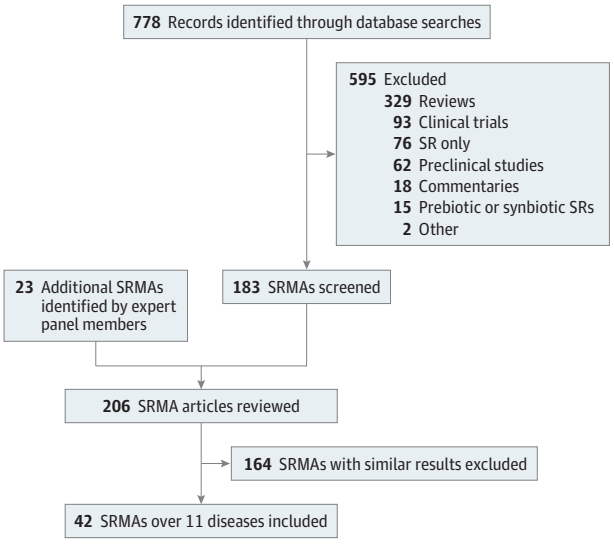
Conclusions of SRMAs may be biased or misleading if heterogeneous interventions are pooled. In the probiotic field, current research supports the importance of considering individual strain differences when pooling studies.[3,31,78] The main strength of using a strain-specific approach to assess efficacy is that clear conclusions on specific probiotic strains can be drawn, particularly when delivered in the same vehicle and dose.[47,67]

We identified MAs that based their efficacy conclusions on pooled data from different taxonomic levels (Table 2). Several MAs pooled probiotics at the genus level, for example, all *Lactobacillus* (now *Lacticaseibacillus*) or all *Bacillus* or all *Bifidobacterium*, yet different species or strains within the same genus showed differences in efficacy.[33,36,42-45,62,63] One study reported pooled efficacy of any *Lactobacillus* and concluded that "any *Lactobacillus* probiotic effectively treated atopic dermatitis."[63] In fact, 6 RCTs were pooled, of which 3 involved *L rhamnosus* GG, 1 used *Limosilactobacillus* (formerly *Lactobacillus*) *fermentum* VRI003, 1 used *Lacticaseibacillus* (formerly *Lactobacillus*) *paracaseii,* and 1 used a mix of *L rhamnosus* GG and *Bifidobacterium animalis* subsp *lactis,* whereas another subgroup of studies containing *Bifidobacterium* pooled 3 RCTs, each testing a different probiotic (*B animalis* subsp *lactis* or *B bifidum* or a mix of *L rhamnosus* GG and *B animalis* subsp *lactis*). The authors did not determine whether the various strains had different efficacies.

The same issue has arisen with other SRMAs that pooled probiotic strains at a species level. For example, in the study by Huang et al,[64] all *L acidophilus* trials were pooled, discounting any strain effects. Di et al[55] compared trials with *L rhamnosus* GG against a pooled group of 11 different non-LGG strains. Goodman et al[38] reviewed 42 RCTs of 26 different probiotics, concluding that *L casei* probiotics were "effective to prevent AAD," but a closer examination of their data revealed that, of 5 different strains of *Lacticaseibacillus* (formerly *Lactobacillus*) *casei* studied, only 1 (a 3-strain blend of *L acidophilus* CL1285, *L casei* LBC80R, and *L rhamnosus* CLR2) prevented AAD, whereas the other 4 were ineffective. This type of imprecision continues to occur in the published literature, despite being firmly discouraged.[25,31]

When MAs were limited to 1 probiotic strain or used subgroups comprising identical strains (or the same strains in multistrain blends), it was possible to discern which strains might be effective for a given disorder.[35,39,47,50,52-54,56,65] For example, Farahmandi et al[66] reviewed 13 RCTs for allergic rhinitis and found that conclusions could only be drawn on 2 of the 9 strains eligible for analysis (ie,

Figure 2. PRISMA Literature Search Flowchart



PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SR systematic review; SRMA, systematic review with meta-analysis.

Table 1. Items Initially Identified as Important to Consider in Probiotic Systematic Reviews and Meta-Analyses and Final Voting Results

Domain and item	Specifics	Panelists agreeing to add as a recommendation, No. (%) (N = 21)
Title		
Description of study	Provide aim of meta-analysis as probiotic efficacy and safety (treat or prevent disease) or exploratory (mechanism of action)	18 (86)
Identify which probiotics are included in the review	Provide current complete nomenclature and strain designations (as space allows)	17 (81)
Abstract	Include current complete nomenclature and strain designations, as space allows	17 (81)
Introduction		
Background rationale	Justification for choice of strains; optional: kinetic studies, mechanism of action, prior preclinical studies	10 (48)
Objective/aim	Aim of study listing primary and secondary outcomes (strain-specific efficacy or exploratory or mechanistic)	18 (86)
Methods: probiotic description		
Strains fit standard probiotic definition	Confirm probiotic criteria fulfilled (strains are living not dead or prebiotic, adequate dose, evidence of health benefit)	16 (76)
Current nomenclature and strain designations	Current genus, species, subspecies if applicable and strain designations (with older synonyms found in literature) for each strain	18 (86)
Genetic identity	Genomic sequence of each strain, if known	5 (24)
Delivery vehicle and matrix	Powder, sachet, liquid, food product	11 (52)
Formulation	Specify any added ingredients and added concentrations	11 (52)
Total daily dose of each strain	Colony-forming units per day (not milligrams per day) total or by colony-forming units per dose and number of doses per day	18 (86)
Viability and potency	Colony-forming units per gram at start and end of study or live to dead ratio at start and end of study	5 (24)
No. of strains in intervention	Single strain or list strains in multistrain blend	20 (95)
Initiation	Time (hours or days) intervention started (at admission, with antibiotic onset)	9 (43)
Manufacturer	Brand name, manufacturer, country	10 (48)
Methods: study design		
Comparators	For example: open control, placebo, standard treatment, other probiotic	12 (57)
Outcomes	Primary, secondary, and tertiary outcomes well defined	8 (38)
Minimum No. of trials	At least 2 trials per probiotic strain or multistrain blend	16 (76)
Exclusion and inclusion	Exclude trials with incomplete probiotic nomenclature or strain designations	16 (76)
Duration	Length of intervention administration	9 (43)
Follow-up	Length of follow-up after intervention (days or weeks)	9 (43)
Run-in and washout periods	For probiotics, run-in duration (exclude if any probiotics taken 4 weeks before enrollment), washout times if crossover trials	9 (43)
Statistical methods	Type of meta-analysis and software used	9 (43)
Results		
Strains included	Provide number of studies included by each probiotic strain or multistrain blend using current nomenclature and strain designations	20 (95)
Study performance	Number randomized and completed (attrition), baseline comparison, compliance, risk of bias	5 (24)
Primary outcome	Primary outcome assessed for each probiotic strain or multistrain blend and disease specific	16 (76)
Common outcome	Common primary outcome measure used	8 (38)
Secondary outcomes and subgroup analyses	Assessed for each probiotic strain or multistrain blend in secondary outcome or subgroup	15 (71)
Safety		
Safety of each strain	Compare adverse events for each strain(s) or multistrain blend	20 (95)
Adverse events and safety	Number of adverse events and serious adverse events by probiotic strain compared with control	7 (33)

(continued)

Table 1. Items Initially Identified as Important to Consider in Probiotic Systematic Reviews and Meta-Analyses and Final Voting Results (continued)

Domain and item	Specifics	Panelists agreeing to add as a recommendation, No. (%) (N = 21)
Discussion		
Efficacy	If >1 probiotic strain or multistrain blend, compare efficacy of each separately	17 (81)
Limitations	Explore sources of heterogeneity	10 (48)
Limitations	Effect of excluded trials	12 (57)
Conclusions		
Finding	Focused on strain or multistrain blend tested (unless aim was exploratory), not generalized to all probiotics, focused on primary outcome	16 (76)
Certainty of evidence	Strength of evidence (GRADE)	7 (33)
Other		
Registration	Meta-analysis registered with PROSPERO	8 (38)

Abbreviations: GRADE, Grading of Recommendations, Assessment, Development and Evaluation; PROSPERO, International Prospective Register of Systematic Reviews.

Table 2. Examples of Systematic Reviews and Meta-Analyses With Inconsistent Conclusions of Probiotic Efficacy Within 4 Representative Disease Conditions

Conclusion of meta-analysis by disease condition	Source
Prevention of antibiotic-associated diarrhea	
Any probiotic was effective	Ma et al,[37] 2020
Any probiotic within same genus was effective	Hempel et al,[33] 2012
Any probiotic within same species was effective	Goldenberg et al,[34] 2015
	Goodman et al,[38] 2021
Specific strain(s) effective	Szajewska et al,[35] 2015
	Kullar et al,[39] 2021
Treatment of irritable bowel syndrome	
Any probiotic was effective	Hoveyda et al,[41] 2009
	Fatahi et al,[48] 2022
Any probiotic within same genus was effective	Tiequn et al,[42] 2015
	Ford et al,[43] 2018
	Liang et al,[44] 2019
	Niu et al,[45] 2020
Specific strain(s) effective	McFarland et al,[47] 2021
Treatment of pediatric acute gastroenteritis	
Any probiotic was effective	Salari et al,[51] 2012
	Di et al,[55] 2020
Any probiotic within same genus was effective	Van Neiel et al,[49] 2002
Specific strain(s) effective	McFarland et al,[50] 2021
	Feizizaheh et al,[52] 2014
	Szajewska et al,[53] 2019
	Szajewska et al,[54] 2020
	Collinson et al,[56] 2020
	Li et al,[57] 2021
Prevention of postsurgery infections	
Any probiotic effective	Chowdhury et al,[60] 2020
	Cogo et al,[61] 2021

had at least 2 RCTs per strain and a common outcome measure). McFarland et al[47] evaluated 42 RCTs with 14 different probiotic strain(s) and found only 4 probiotics significantly reduced abdominal pain symptoms in patients with irritable bowel syndrome. Zhao et al[72] pooled 6 RCTs, including trials using 5 *Lacticaseibacillus* (formerly *Lactobacillus*) *plantarum* strains, and found significant differences

among strains for immune marker responses. To determine the efficacy for specific probiotics for the treatment of pediatric acute gastroenteritis, 1 MA was limited to trials that used only *L rhamnosus* GG,[53] and another meta-analysis assessed different strains of *Saccharomyces boulardii* in separate subgroups.[54] Clearly, to account for strain specificity, the MA can be limited to trials with the same strain (or the same multistrain blend of strains) or conduct subgroup analyses by each strain type or multistrain blend.

The scientific rationale to pool studies should be based on the aim of the SRMA. For example, if studying the efficacy and safety of a probiotic is the aim, strain-specific or subgroup analysis with blends of the same strains may be appropriate. The analysis can also be restricted to trials on only 1 strain or 1 type of multistrain blend. In contrast, pooling data more broadly may be appropriate if the aim is more exploratory, for example, investigating a common mechanism of action that might be expressed across larger taxonomic groups. Underlying characteristics may be shared among taxonomic groups at a species or genus level that drive equivalent efficacy for a shared mechanism of action.[8,69-74]

Recommendations for Improving Probiotic SRMAs

The expert panel agreed on 9 recommendations to improve the quality and consistency of probiotic SRMAs (to supplement PRISMA guidelines) (**Table 3**). The specific areas where these recommendations should be addressed within separate sections of a probiotic SRMA are described here.

Title

Two recommendations regarding the title were agreed on. First, an indication of the aim (efficacy or safety, for example "treatment" or "prevention") or a more exploratory aim (mechanism of action) should be stated (86% agreement [n = 18 of 21]). Second, the identification of each probiotic strain should be listed in the title as completely as space allows (genus, species, and strain designation). However, if the SRMA includes multiple types of probiotics, the use of *probiotics* in the title may be appropriate (81% agreement [n = 17 of 21]).

The complete description of the probiotic strain(s) should also be provided in the abstract (81% agreement [n = 17 of 21]), methods section (86% agreement [n = 18 of 21]), and results and discussion sections (81% agreement [n = 17 of 21]). In addition, SRMAs should use the most current nomenclature for each probiotic strain, even if these were not used in the product label or clinical study (86% agreement [n = 18 of 21]).

Introduction

The aim of the SRMA should be clearly stated, as the degree to which the data can be pooled depends on the aim of the review. For example, if the goal is to determine which probiotic strain(s) are clinically effective for a specific disease indication, efficacy should be based on separate studies or subgroup analysis with the same strain or multistrain blend composed of the same strains. In contrast, if a more mechanistic or exploratory aim is planned (eg, "Do all lactobacilli probiotics share a specific mechanism to treat lactose intolerance?"), then pooling different species and/or strains of a genus may be scientifically justified, albeit given the caveat that some strains or species within the same genus may not be clinically effective. If the aim of the SRMA is to evaluate probiotic safety, this should be stated. Thus, we recommend the primary aim of the SRMA be clearly stated in the introduction (86% agreement [n = 18 of 21]).

Methods: Defining the Probiotic Interventions

A cornerstone of a strong SRMA is the proper identification and characterization of the intervention. We recommend that the probiotic product or probiotic strains tested fulfill the standard definition of a *probiotic* (live microorganisms that, when administered in adequate amounts, confer a health benefit on the host).[4] Some SRMAs have drawn inappropriate conclusions based on pooling data

Table 3. Recommendations to Improve Quality and Consistency of Probiotic Systematic Reviews and Meta-Analyses

Recommendation No.	Recommendation
1	Clearly state if the aim is for efficacy, safety, or exploratory or mechanistic
2	Provide the number of strains in the intervention (single strain or blend of several strains) and complete strain(s) designations (genus, species, subspecies [if appropriate], and strain)
3	Provide both current nomenclature and older names used if different
4	Provide daily dose (colony-forming units or milligrams per day) and duration for each probiotic strain
5	Only pool data if at least 2 randomized clinical trials of strain or blend are included
6	Provide the number of included randomized clinical trials per strain(s)
7	Provide pooled outcome measure by each strain(s)
8	Describe adverse reactions reported for each strain or blend of strains
9	Make a conclusion of efficacy only for those strains included in the systematic review and meta-analysis by type of strain and not generalized to any or all types of probiotics in general

from studies using probiotics, prebiotics, and synbiotics.[79] Because prebiotics and synbiotics may have different mechanisms and effects compared with probiotics, we recommend excluding trials that used prebiotics or synbiotics[80,81] (76% agreement [n = 16 of 21]). Some SRMAs have tried to determine whether multistrain blends were more effective than single-strain probiotics, but they pooled different strains in these 2 groups.[69] Other SRMAs combined single strains and multistrain blends. We do not recommend these approaches. Clearly stating in both the methods and the results sections whether a single strain or multistrain blend is being assessed is recommended[82] (100% agreement [n = 21 of 21]).

Methods: Probiotic Dose

An SRMA should include an efficacy assessment for the dose used for each probiotic strain(s). It is difficult to compare the results of different studies when different units are used to describe the dose used.[83,84] For example, one study found *Clostridium butyricum* MIYAIRI 588 significantly reduced *Clostridioides difficile* infections at a dose of 3 g/d,[85] yet another study found the same strain was not effective at a dose of 1 to 4 × 10^7 CFU/d.[86] This issue makes it difficult to determine whether a difference in efficacy was due to dosage. Another difficulty arises with multistrain blends; often just the total dose is reported. A clear description of the intervention should include the dose for each strain in the blend (86% agreement [n = 18 of 21]).

Methods: Number of Trials Needed

By definition, an MA pools data from more than 1 study. We recommend pooling data from at least 2 RCTs for each strain or multistrain blend if the aim is to assess the efficacy of a specific strain(s). Although some SRMAs have included subgroups with only 1 trial,[33,34,38,43,62] we do not recommend including subgroups with fewer than 2 trials. Exploratory SRMAs may provide results from a single RCT but should recognize this as a limitation (76% agreement [n = 16 of 21]).

Results: Primary Outcome

Because probiotic efficacy is both strain and disease specific, we recommend assessing 1 disease indication or using subgroups for different disease indications. For example, *L rhamnosus* GG was effective for the prevention of AAD in children but not in adults.[31] We also recommend clearly presenting efficacy data for subgroups of identical strains or by multistrain blends composed of the same strains (76% agreement [n = 16 of 21]).

Results: Secondary Outcomes and Subgroup Analysis

We could not reach a consensus on the subject of efficacy analyses using other types of subgroup analysis or meta-regression models for factors that impact efficacy (eg, by country, ethnicity, gender, immunization status, dose of probiotic, or formulation or manufacturer).[58,87-89] Several studies have reported differences in probiotic efficacy by ethnicity (eg, Asian vs White study population), although the reasons are not always apparent.[55,64,90] Many of the SRMAs have not addressed heterogeneity by assessing factors related to PICOS (population, intervention, comparator, outcomes, and safety) characteristics used in the individual study. However, the paucity of this type of data in multiple trials is too limited to permit a general recommendation at this time.

Results: Safety

We recommend that a description of adverse events or safety data be provided for each probiotic strain or multistrain blend[91,92] (95% agreement [n = 20 of 21]). Reporting adverse events or safety data is often overlooked in SRMAs but is an important clinical consideration.

Conclusions

The conclusion of an SRMA should focus on the efficacy and safety related to only those strain(s) studied. Extrapolation of the results to other strains, doses, or populations should be avoided

without a scientific rationale (eg, if the aim was a common mechanism or in support of a hypothesis to be tested) (76% agreement [n = 16 of 21]).

Discussion

The importance of a valid SRMA cannot be overstated. Clinical decisions and guideline recommendations are often based on SRMAs published in the literature. However, the inconsistency of the findings and conclusions often leads to confusion. Even recent MAs continue to inappropriately pool data from different probiotic strains.[8,72] The expert panel had extensive discussions on these inconsistencies and agreed on 9 recommendations to improve future probiotic MAs.

Strengths and Limitations

This study has 2 main strengths. The first is that the recommendations arose from iterative discussions with expert panel members who had a broad range of expertise and specializations. The second is that an extensive literature search was performed. However, the study also has some limitations. One limitation was that the recommendations were based on consensus agreements, which may be biased by viewpoints of the panel members. However, the wide range of expertise and the iterative development of the recommendations using the Delphi method may have minimized this bias. Another limitation is that some items did not reach a consensus (eg, formulation, shelf-life, adherence, and initiation times) and were not included in our recommendations. Another limitation is that we did not include a review of every probiotic SRMA found in the literature, but an effort was made to include representative SRMAs for each type of disease condition. Because this study focused on probiotic SRMAs, it did not include reviews on prebiotics or synbiotics, which may have their own unique issues.

The power of an SRMA depends on the inclusion of as many individual RCTs as possible. However, many trials were excluded from published SRMAs because of deficiencies in the original study, including heterogeneity of outcome measures, failure to provide complete identification of the probiotic, insufficient study description, and incomplete data reporting. We recommend that future RCTs with probiotics address these issues and provide a complete description of the tested probiotic to be considered in future SRMAs.

Conclusions

Our expert panel reached consensus on 9 important probiotic-specific recommendations for items that should be included in SRMAs assessing probiotics. Implementation of these 9 recommendations should improve the quality and consistency of reported probiotic reviews and, we hope, improve clinical practices relating to the appropriate use of probiotics.

ARTICLE INFORMATION

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