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Relationship between Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome and the Efficacy of Rifaximin Intervention: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 March 2026 and was last updated on 1 March 2026.

INTRODUCTION

Review question / Objective To formulate a review question using the PICOS framework (Population, Intervention, Comparison, Outcome, Study design), you can focus on the key elements of the study based on your data. The study investigates the relationship between Small Intestinal Bacterial Overgrowth (SIBO) and Irritable Bowel Syndrome (IBS) and evaluates the efficacy of rifaximin in treating SIBO in IBS patients.
Here's an example of a PICOS-based review question:
Review Question:
In patients with Irritable Bowel Syndrome (IBS) (Population), how does treatment with rifaximin (Intervention) compare to a placebo or other antibiotics (Comparison) in terms of SIBO eradication and symptom improvement (Outcome) across observational and interventional studies (Study design)?
This question addresses the essential components as follows:
Population: Patients with IBS.
Intervention: Rifaximin as a treatment for IBS with concomitant SIBO.
Comparison: Placebo or alternative antibiotics.
Outcome: SIBO eradication rate and symptom improvement.
Study Design: Observational and interventional studies.

Condition being studied Irritable Bowel Syndrome (IBS) is a common functional gastrointestinal disorder that affects the large intestine, characterized by symptoms such as abdominal pain or discomfort, bloating, and altered bowel movements, including diarrhea (IBS-D), constipation (IBS-C), or a mixed pattern (IBS-M). It is a chronic condition, meaning it can persist for years, and while it significantly impacts quality of life, it does not cause structural damage to the intestines. The exact cause of IBS remains unclear, but factors such as dysregulated gut-brain interactions, altered motility, and visceral hypersensitivity are considered contributors. Environmental and genetic factors, stress, and diet can exacerbate the condition.

Small Intestinal Bacterial Overgrowth (SIBO) is a condition in which excessive bacteria grow in the small intestine, where they are normally present in much lower quantities than in the large intestine. The small intestine typically maintains a relatively low bacterial load to facilitate proper digestion and nutrient absorption. In SIBO, however, the bacterial count exceeds the normal threshold (typically over 10^3 colony-forming units per milliliter), leading to a disruption of digestive processes. This overgrowth can cause symptoms like bloating, abdominal discomfort, diarrhea, and malabsorption of nutrients. Common causes of SIBO include impaired intestinal motility, reduced stomach acid, and damage to the intestinal lining.

A significant overlap exists between IBS and SIBO, with studies suggesting that a large proportion of IBS patients may also have SIBO. In fact, IBS patients, especially those with diarrhea-predominant IBS (IBS-D), are at a higher risk of developing SIBO compared to the general population. The symptoms of both conditions often overlap, which complicates diagnosis and treatment. While both conditions are treated symptomatically, identifying and treating SIBO in IBS patients is critical, as addressing the bacterial overgrowth can lead to significant improvement in IBS symptoms.

The treatment of SIBO often involves antibiotics that specifically target the overgrowth of bacteria in the small intestine, with rifaximin being one of the most commonly used and studied options. This non-absorbable antibiotic has been shown to effectively reduce SIBO in IBS patients, providing symptomatic relief.

METHODS

Participant or population The review will address participants who are diagnosed with Irritable Bowel Syndrome (IBS), including both adults and specific pediatric or adolescent cohorts in some cases, depending on the studies included. The types of participants are outlined as follows:

Diagnosis of IBS:

Participants must be diagnosed with IBS according to established clinical criteria, such as the Rome III or Rome IV criteria. In certain studies, symptom-based diagnoses or earlier diagnostic frameworks, like Rome I or Rome II, may also be included to capture a broader range of studies.

IBS subtypes will be considered, including:

IBS-D (Diarrhea-predominant IBS): Patients primarily experience frequent diarrhea.

IBS-C (Constipation-predominant IBS): Patients primarily experience constipation.

IBS-M (Mixed IBS): Patients experience both diarrhea and constipation intermittently.

Presence of SIBO:

Participants must have Small Intestinal Bacterial Overgrowth (SIBO) diagnosed through validated methods such as the lactulose breath test (LBT) or glucose breath test (GBT). SIBO diagnosis could also be confirmed through jejunal aspirate culture, though breath tests are more commonly used in clinical practice.

Age Group:

The review will primarily focus on adult participants (typically aged 18 years or older), as the majority of studies in this area involve adults. However, certain studies involving pediatric or adolescent populations (e.g., studies that explore IBS in children or adolescents) may be included for a more comprehensive understanding, especially if they use similar diagnostic criteria and treatment protocols.

Control Group:

For studies investigating the prevalence of SIBO in IBS, healthy individuals (age-matched, asymptomatic controls) will be included as the comparison group. These healthy individuals should not have a history of gastrointestinal disorders and should not exhibit any gastrointestinal symptoms.

These participants represent the core groups that the review will address, ensuring a focus on IBS patients with or without SIBO, and offering insights into the impact of SIBO on IBS symptoms and the efficacy of treatments like rifaximin for this patient population.

Intervention The primary intervention to be evaluated in this review is the use of rifaximin, an antibiotic, for the treatment of Small Intestinal Bacterial Overgrowth (SIBO) in patients with Irritable Bowel Syndrome (IBS).

Intervention Description:

Rifaximin is a non-absorbable, broad-spectrum antibiotic derived from the rifamycin class. It acts

locally within the gastrointestinal (GI) tract, particularly in the small intestine, and is minimally absorbed into the bloodstream, making it well-suited for targeting bacteria in the gut with minimal systemic side effects.

Dosage and Duration:

Rifaximin dosage typically ranges from 600 mg/day to 1650 mg/day, depending on the specific study protocol. The treatment duration varies, with common regimens being 10 to 14 days. Some studies may also assess different doses or treatment durations to explore their impact on outcomes.

The review will evaluate the efficacy of rifaximin in clearing bacterial overgrowth, particularly in patients with diarrhea-predominant IBS (IBS-D) and other IBS subtypes.

Objectives of Evaluating Rifaximin:

SIBO Eradication: The primary goal of rifaximin treatment is the eradication of SIBO, as measured by post-treatment negative breath tests (e.g., lactulose hydrogen breath test (LBT) or glucose breath test (GBT)).

Symptom Improvement: Secondary outcomes will include improvement in global IBS symptoms such as abdominal pain, bloating, stool consistency, and quality of life (measured using tools like the IBS Quality of Life (IBS-QOL) scale or Visual Analog Scale (VAS) scores).

Comparisons:

In addition to evaluating rifaximin, the review will also explore comparisons between rifaximin and other treatment options, including:

Placebo: In some studies, the effects of rifaximin will be compared to placebo groups to assess its effectiveness relative to no treatment.

Other Antibiotics: Rifaximin will also be compared to other systemic antibiotics, such as metronidazole or neomycin, which have been used to treat SIBO, to determine whether rifaximin offers superior outcomes in terms of safety, tolerability, and efficacy in IBS patients with concomitant SIBO.

By evaluating the efficacy of rifaximin for IBS patients with SIBO, this review aims to synthesize evidence regarding its role in symptom relief and bacterial eradication. This could provide valuable guidance for clinical decisions on managing IBS patients who also suffer from SIBO.

Comparator In this review, the comparative interventions applied to the target population (IBS patients with SIBO) will include:

Placebo Treatment:
In some studies, placebo will be used as the comparative intervention. The placebo group will serve to evaluate the efficacy of rifaximin by comparing it to an inert substance that has no therapeutic effect. This comparison helps determine whether improvements in IBS symptoms or SIBO eradication are genuinely due to rifaximin or simply the result of the placebo effect.

Other Antibiotics:
Another comparative intervention will involve other antibiotics commonly used to treat SIBO in IBS patients. These include:

Metronidazole: A broad-spectrum antibiotic often used in the treatment of SIBO. Metronidazole targets a wide range of anaerobic bacteria, including those in the small intestine.

Neomycin: An aminoglycoside antibiotic sometimes used in combination with rifaximin, especially for methane-predominant SIBO (intestinal methanogen overgrowth). Neomycin has been studied for its role in treating IBS with SIBO, though its systemic absorption can lead to more side effects than rifaximin.

Standard IBS Treatments:
In certain studies, standard IBS treatments (e.g., dietary changes, probiotics, antispasmodic medications, or laxatives) may also be used as comparative interventions. These treatments are typically aimed at managing IBS symptoms without addressing the underlying SIBO.

The purpose of these comparative interventions is to evaluate rifaximin's effectiveness in treating SIBO in IBS patients, assessing outcomes like SIBO eradication, symptom improvement, and overall quality of life, in comparison to no treatment (placebo) and other available treatments. This will help determine whether rifaximin provides superior or comparable results to other therapies commonly used in IBS patients with concomitant SIBO.

Study designs to be included The review will include the following study designs to address the objective:Observational Studies:Cohort StudiesCase-Control StudiesCross-Sectional StudiesInterventional Studies:Randomized

Controlled Trials (RCTs)Open-Label StudiesThese designs will provide both the association between SIBO and IBS, as well as the efficacy of rifaximin in treating SIBO in IBS patients, offering a comprehensive understanding of its impact.

Eligibility criteria In addition to the criteria defined in the PICOS framework, the following additional inclusion and exclusion criteria will be applied to ensure a focused and high-quality review:

Additional Inclusion Criteria:

Language: Studies published in English or those for which English translations are available.

Diagnostic Confirmation of SIBO: Only studies where SIBO is diagnosed using validated breath tests (e.g., lactulose hydrogen breath test (LBT), glucose breath test (GBT)), or jejunal aspirate culture.

Data Completeness: Studies with complete outcome data for SIBO eradication and IBS symptom improvement post-treatment.

Adult Population: Although pediatric studies may be considered, the review will prioritize studies involving adults (≥18 years) unless specific pediatric IBS/SIBO studies provide relevant data.

Follow-up Data: Studies that report post-treatment follow-up data (for at least 4 weeks) to assess the sustained effects of rifaximin.

Additional Exclusion Criteria:

Animal Studies: Studies conducted on animals will be excluded.

Studies with Incomplete Data: Studies with insufficient data on SIBO prevalence, rifaximin dosage, or clinical outcomes will be excluded.

Duplicate Publications: Studies with overlapping data (same patient population from the same center) or duplicate publications will be excluded to avoid data inflation.

Conference Abstracts and Editorials: These will be excluded due to a lack of sufficient methodological details or peer-reviewed data.

Non-SIBO IBS Studies: Studies that examine IBS without explicitly diagnosing or addressing SIBO will be excluded.

Studies Involving Comorbid Organic GI Diseases: Studies including patients with organic gastrointestinal diseases (e.g., Crohn's disease, celiac disease) will be excluded, as these conditions may confound the relationship between IBS and SIBO.
These additional criteria aim to refine the selection process, ensuring that only studies with robust, relevant, and complete data are included in the review.

Information sources
1. Electronic Databases:

PubMed: A comprehensive database of biomedical literature, including studies on IBS, SIBO, and treatment outcomes.

Embase: A database with a strong focus on pharmacology, drug therapy, and gastrointestinal disorders, ideal for finding studies on rifaximin and other related interventions.

Cochrane Central Register of Controlled Trials (CENTRAL): This source includes systematic reviews and randomized controlled trials (RCTs), making it a valuable resource for evaluating the efficacy of rifaximin.

Web of Science: A multidisciplinary database that will be searched for studies related to the intersection of IBS and SIBO, as well as rifaximin therapy.

Scopus: A comprehensive database for scientific research, which will help identify studies in gastroenterology, microbiology, and drug treatment.

2. Trial Registers:

ClinicalTrials.gov: A register of clinical trials, which will be used to identify ongoing or unpublished studies related to rifaximin treatment for IBS with SIBO.

International Clinical Trials Registry Platform (ICTRP): This will be used to access trial registries from around the world, ensuring that any relevant unpublished or ongoing studies are included.

3. Grey Literature:

Conference Abstracts: Abstracts from major gastroenterology or microbiology conferences (e.g., Digestive Disease Week, American College of Gastroenterology Annual Meeting) will be examined for studies not yet published in full.

Government and Institutional Reports: Relevant government or institutional reports on IBS and SIBO treatment guidelines may also be reviewed if available.

Theses and Dissertations: University repositories may be searched for grey literature studies related to IBS and SIBO treatment.

Medical Society Websites: Websites of professional organizations such as the American Gastroenterological Association (AGA) may provide access to guidelines, unpublished studies, or ongoing research.

4. Contacting Authors:

Corresponding Authors of Relevant Studies: If necessary, corresponding authors of included studies will be contacted to request additional data, unpublished results, or clarifications about methodology and outcomes that are relevant to the review.

5. Bibliographic Search:

Reference Lists: The reference lists of selected articles, including systematic reviews and meta-analyses on IBS and SIBO, will be manually checked for additional studies that meet the inclusion criteria.

These sources will ensure a comprehensive and up-to-date inclusion of all relevant studies, maximizing the potential for identifying high-quality evidence regarding the relationship between IBS and SIBO and the efficacy of rifaximin as a treatment.

Main outcome(s)

1. Primary Outcomes:
SIBO Eradication Rate:
Measured by the negative follow-up breath test (Lactulose or Glucose Hydrogen Breath Test) after rifaximin treatment. This will be assessed across studies reporting pre- and post-treatment SIBO status.

Effect Measure: Pooled event rate (ER), which is the percentage of patients who achieve SIBO clearance.

Timing: Post-treatment assessment, typically between 1-2 weeks after the end of the rifaximin regimen.

2. Secondary Outcomes:

Global IBS Symptom Improvement:

Assessed using tools like the IBS Severity Scoring System (IBS-SSS) or Visual Analog Scale (VAS) for symptoms such as abdominal pain, bloating, stool consistency, and overall quality of life.

Effect Measure: Pooled symptom improvement rate (percentage of patients with significant reduction in IBS symptoms).

Timing: Symptom assessment at baseline and post-treatment, with follow-up at 4-6 weeks for sustained improvement.

Quality of Life Improvement:

Measured by IBS-QOL or similar scales assessing the impact of IBS symptoms on daily functioning.

Effect Measure: Mean difference in scores before and after treatment.

Timing: Post-treatment, with follow-up as above.

3. Exploratory Outcomes:

Adverse Effects:

Any side effects or adverse reactions to rifaximin, such as gastrointestinal disturbances or allergic reactions.

Effect Measure: Incidence rate of adverse events.

Timing: During and immediately after treatment.

These outcomes will help evaluate the efficacy of rifaximin in both clearing SIBO and improving IBS symptoms and patient quality of life.

Quality assessment / Risk of bias analysis

1. Observational Studies (Cohort, Case-Control, and Cross-Sectional Studies):

Newcastle-Ottawa Scale (NOS):
The NOS will be used to assess the quality of observational studies. This tool evaluates studies based on three main domains:

Selection: The representativeness of the study population, the selection of controls, and the ascertainment of exposure.

Comparability: The comparability of the groups (e.g., adjustment for confounding factors).

Outcome: The method of outcome assessment, such as the accuracy and reliability of SIBO diagnosis and symptom measurement.

Each domain is scored, and studies are given a total score based on the number of criteria met. A study with a score of 7 or higher out of a possible 9 points is considered high quality, while scores below 7 indicate moderate to low quality.

2. Randomized Controlled Trials (RCTs) and Interventional Studies:

Cochrane Risk of Bias Tool (RoB 2):
For RCTs, the RoB 2 tool will be used to assess the risk of bias across five domains:

Randomization process: Was the randomization method adequately implemented?

Deviations from intended interventions: Were there any deviations from the planned intervention protocol?

Missing outcome data: Were there any missing data, and how were they handled?

Measurement of outcomes: Were the outcomes measured in a consistent and valid manner?

Selection of the reported result: Was the analysis pre-specified, and were there any selective reporting biases?

Each domain will be rated as low risk, some concerns, or high risk. The overall risk of bias for each study will be determined by the domains with the highest risk.

3. Grey Literature and Non-Randomized Studies:

Specific Criteria:
Studies from grey literature (e.g., conference abstracts or unpublished trials) will be evaluated based on methodological rigor, reporting completeness, and transparency. These studies will be assessed for their sample size, diagnostic clarity (e.g., SIBO testing methods), and outcome measures.

4. Overall Quality:

After individual assessments using NOS and RoB 2, the studies will be categorized into high, moderate, or low quality based on the total score and risk of bias.

Studies that exhibit high methodological rigor and low risk of bias will be prioritized in the analysis, ensuring that the conclusions of the review are based on reliable and valid evidence.

This systematic approach to quality assessment will help minimize the impact of biases and ensure that the findings of the review are robust and credible.

Strategy of data synthesis The data analysis for this systematic review and meta-analysis will involve several steps to ensure the accurate synthesis of the results across studies. Both quantitative and qualitative data will be analyzed depending on the nature of the outcome measures reported in the included studies.
1. Data Extraction:
Study Characteristics: Data will be extracted independently by two reviewers using a standardized form. The information collected will include:
Study design (e.g., cohort, case-control, RCT)
Sample size
Diagnostic criteria for IBS and SIBO
Rifaximin dosage, duration, and method of administration
Outcome measures (SIBO eradication rates, symptom improvement, adverse events)
Follow-up duration
Disagreements between reviewers will be resolved through discussion or consultation with a third reviewer.
2. Quantitative Data Analysis:
Meta-Analysis:
A random-effects model will be used for the meta-analysis to account for variability across studies due to differences in study designs, participant characteristics, and measurement methods.
For outcomes such as SIBO eradication rate, the pooled event rate (ER) will be calculated to estimate the proportion of patients who experience SIBO clearance after rifaximin treatment. The 95% confidence intervals (CIs) will be reported.
For outcomes like global IBS symptom improvement, the mean difference (MD) or standardized mean difference (SMD) will be calculated when the studies report continuous data on symptom scales (e.g., IBS-SSS, VAS).
If there is sufficient data, subgroup analyses will be conducted based on:
Rifaximin dosage (e.g., low-dose vs. high-dose)
Treatment duration (e.g., 10-day vs. 14-day regimens)
Diagnostic method for SIBO (e.g., LBT vs. GBT)
IBS subtype (e.g., IBS-D, IBS-C, IBS-M)
3. Assessment of Heterogeneity:
I^2 statistic:

The I^2 statistic will be used to assess the level of statistical heterogeneity across studies. An I^2 value of:

0-40% indicates low heterogeneity,

30-60% suggests moderate heterogeneity, and

>60% indicates high heterogeneity.

Studies with high heterogeneity will be explored in subgroup analyses to identify potential sources.

4. Sensitivity and Subgroup Analyses:

Sensitivity analysis:
This will be performed by sequentially removing each study to assess the influence of individual studies on the overall results. If the results change substantially when a single study is excluded, it may indicate that the study has a disproportionate impact on the findings.

Subgroup analysis:
For example, stratification by the type of breath test (LBT vs. GBT) or treatment duration (10 days vs. 14 days) will help understand the potential effect modifiers.

5. Publication Bias:

Funnel plots:
Funnel plots will be visually inspected to assess the symmetry, which may indicate the presence of publication bias. Asymmetry in the funnel plot suggests that smaller studies with null results may be underrepresented.

Egger's Test:
For meta-analyses with 10 or more studies, Egger's regression test will be used to provide a statistical test for funnel plot asymmetry, further assessing publication bias.

6. Qualitative Data Synthesis:

If necessary, a narrative synthesis will be performed for patient-centered outcomes like quality of life and adverse effects, particularly if these outcomes are reported using various measurement tools that do not allow for meta-analysis.

7. Software:

All statistical analyses will be performed using R software (Version 4.3.0), with the.

Subgroup analysis Subgroup analysis will be conducted to explore potential sources of heterogeneity and to better understand the factors that may influence the effectiveness of rifaximin in treating SIBO in IBS patients. The following subgroups will be analyzed based on relevant clinical, methodological, and demographic factors:

Rifaximin Dosage:

Studies will be categorized into low-dose (600–800 mg/day) and medium-to-high-dose (≥1200 mg/day) groups. This will help assess if the higher doses of rifaximin result in better efficacy in SIBO eradication and symptom improvement.

Treatment Duration:

Subgroups will be based on treatment duration (e.g., 10 days vs. 14 days) to determine whether the length of treatment impacts the success rates for SIBO eradication and IBS symptom relief. We hypothesize that a longer duration may lead to better outcomes, but this will be tested through subgroup comparison.

Diagnostic Method for SIBO:

Studies will be stratified by the method of diagnosing SIBO, specifically:

Lactulose Breath Test (LBT)

Glucose Breath Test (GBT)
This will help assess the sensitivity and specificity of each diagnostic method and whether it affects the effectiveness of rifaximin.

IBS Subtypes:

Subgroup analyses will be conducted based on IBS subtype:

IBS-D (Diarrhea-predominant IBS)

IBS-C (Constipation-predominant IBS)

IBS-M (Mixed IBS)
Understanding the effects of rifaximin on different IBS subtypes is important because SIBO prevalence and IBS symptom profiles vary by subtype.

Geographical Region:

Subgroup analysis will also be performed based on the geographical region of the study, as environmental, dietary, and genetic factors may

contribute to differences in study outcomes. This will help determine if the efficacy of rifaximin varies across populations from different regions.

Study Quality:

Studies will be grouped based on their methodological quality (as assessed by Newcastle-Ottawa Scale (NOS) for observational studies and Cochrane Risk of Bias (RoB 2) for RCTs). This will allow us to explore whether studies with higher quality provide more reliable estimates of treatment effects.

These subgroup analyses will help provide a more nuanced understanding of factors that may influence the outcomes of rifaximin treatment for SIBO in IBS patients, aiding clinicians in making more informed treatment decisions.

Sensitivity analysis Sensitivity analysis will be conducted to assess the robustness of the results and determine whether the findings are significantly affected by any individual study or methodological choices. The goal is to ensure that the results are consistent and not disproportionately influenced by a single study, data anomalies, or high-risk studies.

The following methods will be employed:

Exclusion of Individual Studies:

A leave-one-out approach will be used, where each study will be iteratively excluded from the meta-analysis to examine whether any particular study has an undue influence on the overall effect estimate. If the exclusion of a study leads to a significant change in the results, it may indicate that the study is an outlier or of low quality, and its inclusion might be distorting the findings.

Impact of Study Quality:

Sensitivity analysis will be conducted by stratifying the studies based on their quality. Studies with a high risk of bias or low methodological quality (as assessed using the Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for observational studies) will be excluded to evaluate how much the results change when considering only studies of high quality. This will help determine if low-quality studies are skewing the overall outcomes.

Assessment of Heterogeneity:

The I^2 statistic will be calculated across studies after exclusion of studies with high heterogeneity ($I^2 > 50\%$) to check if removing those studies leads to a more homogeneous set of studies, improving the confidence in the pooled effect size.

Sensitivity analysis will also be conducted separately for studies with high vs. low heterogeneity to explore the effect of heterogeneity on pooled results.

Evaluation of Subgroup Effect:

The results of subgroup analyses (e.g., by rifaximin dosage, treatment duration, diagnostic method) will be tested through sensitivity analysis to ensure that the subgroup findings remain consistent when different study characteristics are considered. If the results change significantly when analyzing specific subgroups, this may suggest that certain factors are influencing treatment outcomes.

Impact of Publication Bias:

Sensitivity analysis will also consider the possibility of publication bias. If significant asymmetry is observed in the funnel plots or statistical tests (e.g., Egger's test), sensitivity analysis will help determine whether excluding small studies or studies with negative results affects the overall findings.

Purpose of Sensitivity Analysis:

Sensitivity analysis will provide confidence in the stability of the review's conclusions, ensuring that the results are not unduly influenced by individual studies, methodological flaws, or study biases. By testing different assumptions and exclusions, this analysis will strengthen the reliability and generalizability of the review's findings regarding rifaximin's effectiveness in treating SIBO in IBS patients.

Country(ies) involved China - Department of Gastroenterology, Children's Hospital of Soochow University.

Keywords Small Intestinal Bacterial Overgrowth; Irritable Bowel Syndrome; Rifaximin; Meta-Analysis.

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