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# Placebo Response Variability in Irritable Bowel Syndrome: An Arm-Based Network Meta-Analysis

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## ADMINISTRATIVE INFORMATION

**Support -** Chengdu University of TCM for evidence-based medicine research (no. XKTD2021004).

**Review Stage at time of this submission -** Completed but not published.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY2024110111

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 November 2024 and was last updated on 26 November 2024.

## INTRODUCTION

**Review question / Objective** The impact of placebo response on health outcomes in various diseases, including IBS, is significant. To better understand the effect of different placebo administration methods on the efficacy of IBS treatment, this meta-analysis aims to explore research findings on the degree of improvement.

**Condition being studied** Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain, bloating, and altered bowel habits. It significantly affects patients' quality of life and involves a combination of genetic, epigenetic factors, gut microbiota imbalances, and inflammatory processes. Psychosocial factors also play a significant role in the onset and exacerbation of IBS symptoms.

## METHODS

**Search strategy** A systematic search was conducted across PubMed, Embase, and Web of Science databases from January 2005 to December 2023, using a combination of controlled vocabulary (e.g., MeSH terms) and keywords related to IBS, gastrointestinal symptoms, and clinical research methodology terms such as RCTs, double-blind, random, placebo, and IBS-specific treatments. Additionally, manual reviews of conference abstracts from leading gastroenterology meetings were conducted.

**Participant or population** The review focuses on patients diagnosed with Irritable Bowel Syndrome (IBS), excluding those with significant comorbidities. The studies included adults and adolescents with IBS, diagnosed according to the Rome I, II, III, and IV criteria.

**Intervention** The intervention of interest includes various placebo interventions used in the treatment of IBS, such as placebo tablets, sham acupuncture, sham moxibustion, herbal placebo, sham FMT, and sham IFC.

**Comparator** The comparator for this review is the effect of different placebo interventions on IBS symptoms, compared against each other and against no treatment or standard care.

**Study designs to be included** Randomized, double-blind, placebo-controlled clinical trials.

**Eligibility criteria** Inclusion criteria comprised RCT studies involving groups without secondary conditions or prior unsuccessful IBS treatments, adhering to established diagnostic criteria for IBS. Exclusion criteria encompassed non-RCTs, studies lacking standardized diagnostic or outcome indicators, systematic reviews/meta-analyses of case reports, RCTs lacking a placebo arm, and literature with unavailable full text.

**Information sources** Electronic databases (PubMed, Embase, Web of Science), conference abstracts from leading gastroenterology meetings, and manual review of reference lists for additional relevant studies.

**Main outcome(s)** The primary outcome is the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS). Secondary outcomes include the Irritable Bowel Syndrome Quality of Life Instrument (IBS-QoL) and the IBS Symptom Visual Analog Scale (VAS).

**Data management** Data extraction was conducted independently by two authors using Microsoft Excel data sheets with a pre-designed template. Disagreements were resolved through discussion or consultation with relevant experts.

**Quality assessment / Risk of bias analysis** Two reviewers independently assessed eligible material using Cochrane risk of bias methods, considering randomization, blinding, allocation concealment, number of participants lost to follow-up, evidence of selective reporting, and study size.

**Strategy of data synthesis** A Bayesian framework was employed for the network meta-analysis, using Markov Chain Monte Carlo (MCMC) simulations to estimate the posterior distributions. Convergence was assessed, and the relative effect of each placebo intervention was estimated using mean difference (MD) with corresponding 95% credible intervals (95%CrIs).

**Subgroup analysis** NA.

**Sensitivity analysis** Sensitivity analyses were performed by excluding RCTs with a sample size of less than 50 participants to assess the robustness of the findings.

**Country(ies) involved** China.

**Other relevant information** The study was supported by the National Natural Science Foundation of China (81873387), the National Key Talents Project of Traditional Chinese Medicine (2019), and the foundation of the Training Project for Young and Middle-aged Science and Technology Leaders in Xianyang (Major Scientific and Technological Innovation Project) (2019k01-52), among others.

**Keywords** Placebo; Irritable bowel syndrome; Arm-based; Network meta-analysis.

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