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Replication and extension of a meta-analysis of antidepressants for irritable bowel syndrome: a comparison of odds ratios and risk ratios using artificial intelligence-powered tools

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We read with great interest the recent article by Temido *et al*, evaluating the efficacy of antidepressants in irritable bowel syndrome (IBS) through a systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials [1]. Their study represents a significant contribution to the IBS literature by applying high methodological standards and demonstrating clinically meaningful benefits across various symptom domains.

To evaluate the reproducibility and extend the generalizability of these findings, we used a novel large language model (LLM)-based tool we developed for title and abstract screening. We replicated the original study's selection process using a broad search strategy (PubMed and Scopus, total of 43,487 citations; 28,645 after deduplication) on May 27, 2025. Our tool successfully identified all 20 studies reported by Temido *et al*, plus 6 additional randomized controlled trials reporting binary outcomes suitable for inclusion in the meta-analysis [2-7]. We also identified 2 relevant studies that, like 4 in the original work, lacked extractable binary/dichotomous outcome data [8,9]. Our second LLM tool—designed to auto-generate R code for meta-analysis—was used to replicate the original meta-analytic computations and extend them.

Using the original dataset of 16 trials (n=1,428), we replicated the meta-analysis in R using the {meta} package. The model used was: effect measure: odds ratio (OR); model: Mantel-Haenszel (MH); between-study variance estimator:

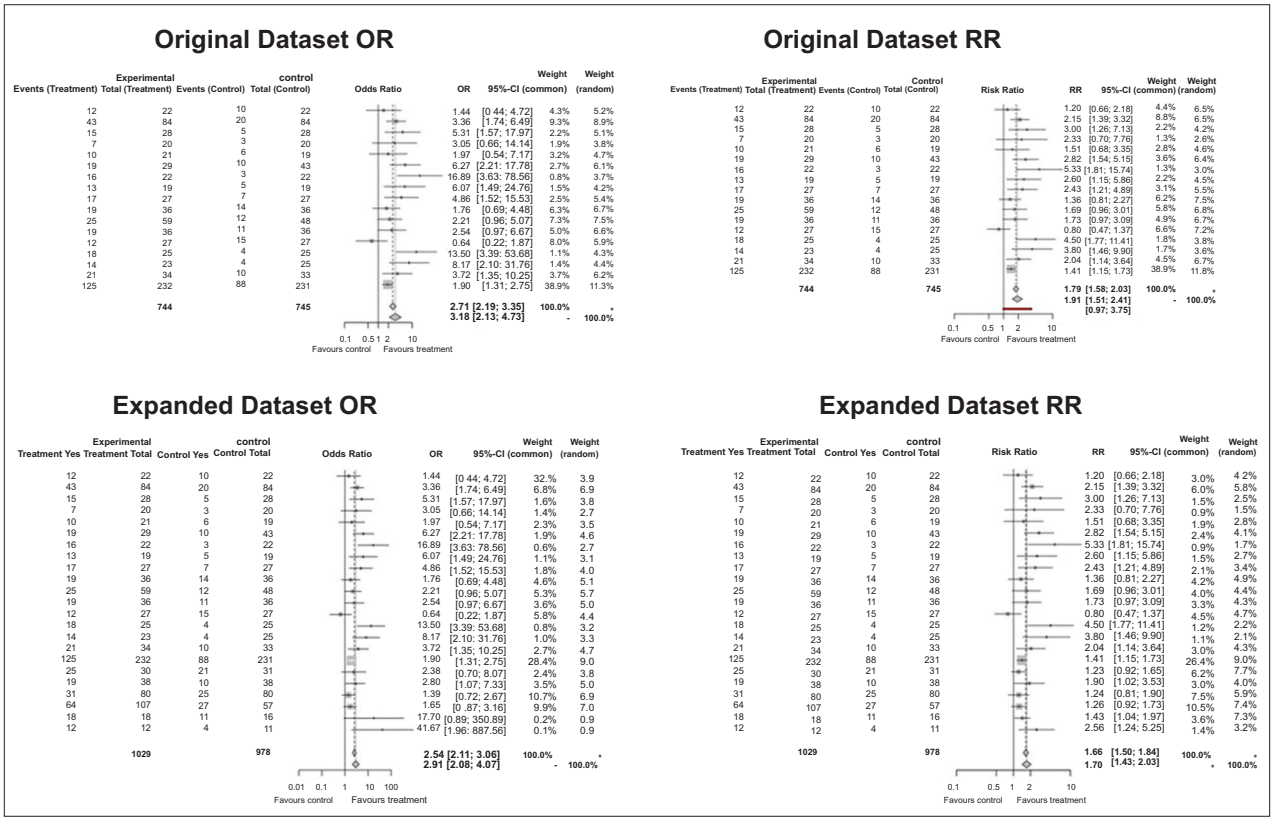

Figure 1 Composite figure showing 4 forest plots—odds ratio (OR) and risk ratio (RR) meta-analyses for both the original (16-study) and updated (22-study) datasets
CI, confidence interval

restricted maximum likelihood (REML); and confidence interval method: Hartung-Knapp. These align closely with the methodology reported by Temido *et al*, who also used a random-effects model, REML, and conducted intention-to-treat analyses via Stata v16.

The resulting pooled effect size using our script was slightly higher than that of Temido *et al* (OR 3.18 vs. 3.02), with a broader confidence interval (95%CI 2.13-4.73 vs. 2.16-4.2). This numerical difference was probably due to software-specific implementation differences, including continuity corrections and default tau^2 estimators. Despite these minor discrepancies, both analyses confirmed the significant benefit of antidepressants in improving IBS symptoms.

We also conducted a parallel analysis using risk ratio (RR) as the effect measure—an approach often considered more clinically intuitive for interpreting data from randomized controlled trials. We then repeated both OR and RR meta-analyses after incorporating 6 newly identified studies, expanding the dataset to 22 trials (n=1946). Across all 4 analyses, the findings consistently supported the clinical efficacy of antidepressants (Fig. 1).

We commend the authors for their rigorous study and suggest that future publications consider including both OR and RR metrics to broaden interpretability across audiences. We also highlight the value of integrating artificial intelligence-based review pipelines to complement traditional evidence synthesis.

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Conflict of Interest: Lefteris Teperikidis is co-founder of Synthesa, Inc., the company that develops the tools used in this validation study. Lefteris Teperikidis has consulted for SCRIPPS Research, Callibr BV, Parexel, Bruker GmbH, IVDeology, Pharmassist, Accuscript, Remedica and PARI GmbH, outside the present work. The other authors have no conflict of interest to declare

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