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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

Lefteris Teperikidis[a,b,c], Christos Mademlis[d], Georgios Hatzinakos[e], Nikolaos Lazaridis[f]

Synthesa, Inc, NY, USA; School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; Medical School, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; St. Luke's Hospital, Thessaloniki, Greece; The Royal Free Hospital, University College London Institute for Liver and Digestive Health, London, United Kingdom

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: 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

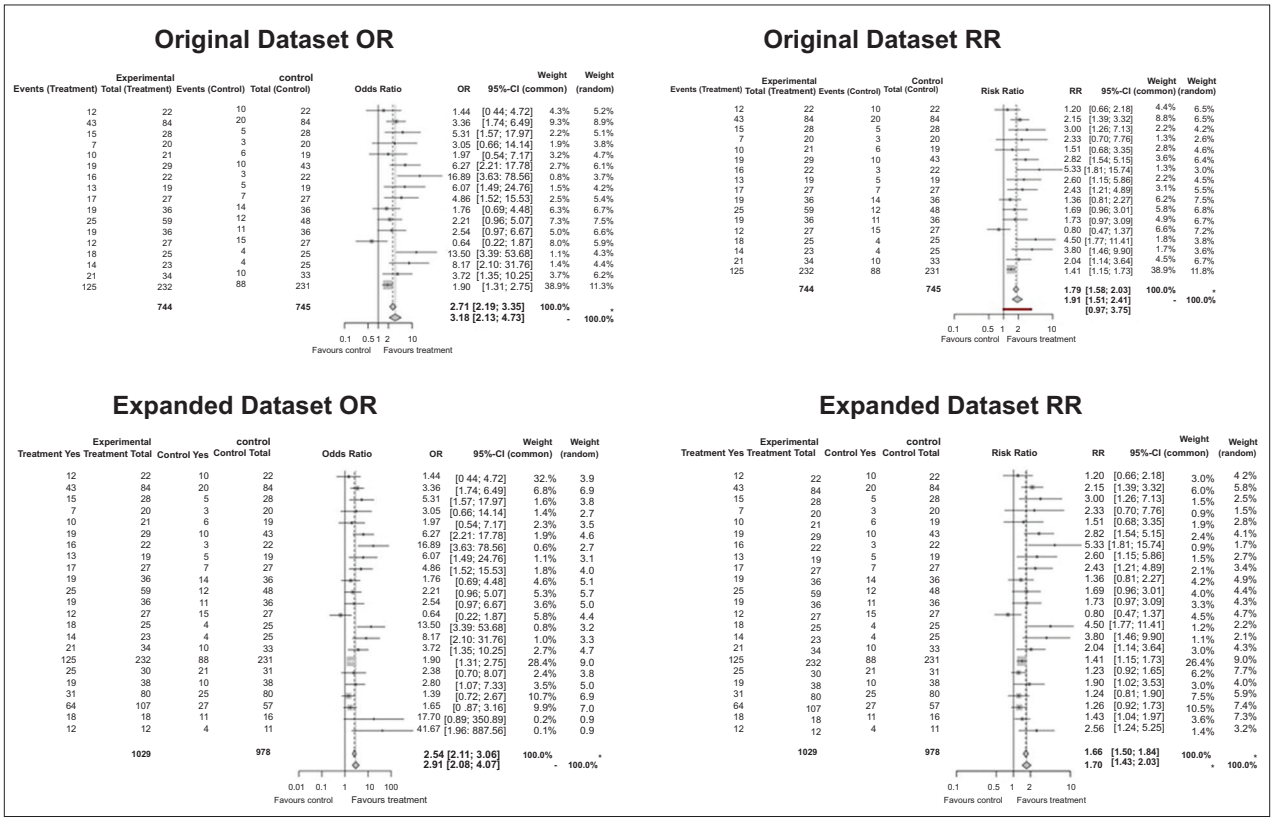

Figure 1 Composite figure showing 4 forest plots—odds ratio (OR) and risk ratio (RR) meta-analyses for both the original (16-study) and updated (22-study) datasets

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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[a]Synthesa, Inc., 19 West 24th St., New York, NY 10010, USA (Lefteris Teperikidis); [b]Clinical Research Unit, Special Unit for Biomedical Research and Education (SUBRE), School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece (Lefteris Teperikidis); [c]Third Department of Cardiology, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece (Lefteris Teperikidis); [d]Second Propedeutic Department of Internal Medicine, Medical School, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece (Christos Mademlis); [e]Department of Gastroenterology, St. Luke's Hospital, Thessaloniki, Greece (Georgios Hatzinakos); [f]Royal Free Unit for Endoscopy, The Royal Free Hospital, University College London Institute for Liver and Digestive Health, London, United Kingdom (Nikolaos Lazaridis)

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Lefteris Teperikidis, Synthesa, Inc, NY, USA, 19 West 24th St., 1000 NY, USA, e-mail: lefteris@synthesa.ai

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Authors' reply

Maria José Temido[a], Margarida Cristiano[a], Carolina Gouveia[b,c], Bárbara Mesquita[d], Pedro Figueiredo[a,c], Francisco Portela[a,c]

Hospitais da Universidade de Coimbra, Unidade Local Saúde de Coimbra; Hospital de Cascais; University de Coimba, Portugal

We sincerely thank Teperikidis L, *et al* for their insightful commentary on our recent publication evaluating the efficacy of antidepressants in irritable bowel syndrome (IBS) [1]. We are pleased that our systematic review and meta-analysis were received with interest and that our methodological approach was acknowledged as rigorous and clinically meaningful.

We read with great interest the authors' description of how they used a novel large language model (LLM)-based tool to replicate and extend our study. The successful identification of all 20 studies included in our meta-analysis, as well as 6 additional randomized controlled trials reporting binary outcomes, is a valuable contribution. This reinforces the strength of their artificial intelligence (AI)-assisted screening process and reflects the growing utility of AI in streamlining the review process. It is particularly encouraging that their broad

search strategy yielded additional data while maintaining high sensitivity, which is essential for the reliability of systematic reviews.

The fact that their second LLM tool was able to automatically generate R code for meta-analytic computations is also noteworthy. The reproducibility of our original findings using this automated pipeline strengthens the overall robustness of the conclusions, and demonstrates how AI can complement traditional approaches, especially in complex evidence synthesis tasks. These developments are promising for the future of systematic reviews, particularly in areas where the literature is extensive and heterogeneous.

We also appreciate Teperikidis L, *et al*'s identification of additional studies without extractable binary outcome data, similar to some included in our original analysis. This highlights an ongoing challenge in meta-research—the variability in outcome reporting across trials—which future guidelines should continue to address.

Importantly, we agree with the authors' suggestion regarding the inclusion of both odds ratios (OR) and risk ratios (RR) in future analyses. This dual reporting can improve clarity and enhance the interpretability of findings for clinicians, researchers, and other stakeholders. We will certainly consider this approach in upcoming work, and we believe it could become a standard practice in quantitative syntheses going forward.

Overall, we commend the Teperikidis L, *et al*'s initiative and the creative integration of LLM tools to assess and build upon our work. Their efforts not only contribute to methodological transparency and reproducibility, but also open new pathways for collaboration between traditional and AI-enhanced systematic reviewing practices.

We thank the authors once again for their constructive feedback and for contributing to the advancement of research methodology in this field. We look forward to future discussions and potential collaborations as we continue to refine how we evaluate and synthesize clinical evidence.

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[a]Serviço de Gastrenterologia, Hospitais da Universidade de Coimbra, Unidade Local Saúde de Coimbra (Maria José Temido, Margarida Cristiano, Pedro Figueiredo, Francisco Portela); [b]Serviço de Psiquiatria, Hospitais da Universidade de Coimbra, Unidade Local Saúde de Coimbra (Carolina Gouveia); [c]Faculdade de Medicina, Universidade de Coimbra (Carolina Gouveia, Pedro Figueiredo, Francisco Portela); [d]Departamento de Saúde Mental do Hospital de Cascais (Bárbara Mesquita), Portugal

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Correspondence to: Maria José Temido, MD, Serviço de Gastrenterologia, Hospitais da Universidade de Coimbra, Unidade Local Saúde de Coimbra, Coimbra, Portugal, e-mail: mariajosetemido@gmail.com

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