

INPLASY

INPLASY202670122

doi: 10.37766/inplasy2026.7.0122

Received: 30 July 2026

Published: 30 July 2026

Corresponding author:

Felipe Claudino

felipeaclaudino@gmail.com

Author Affiliation:

Universidade Federal do Rio Grande do Sul.

Review-level concordance in systematic reviews of psychotherapy-associated functional neuroimaging in major depressive disorder: A meta-epidemiological umbrella review

Claudino, FCA; Martins, HRS; Rocha, NS.

ADMINISTRATIVE INFORMATION

Support - No support.**Review Stage at time of this submission** - Data extraction.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202670122**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 July 2026 and was last updated on 30 July 2026.

INTRODUCTION

Study aim To investigate why systematic reviews synthesizing substantially overlapping functional neuroimaging evidence of psychotherapy for major depressive disorder (MDD) reach concordant or discordant conclusions. Specifically, this meta-epidemiological umbrella review evaluates review-level concordance across five predefined inferential levels, quantifies overlap of the underlying evidence, and identifies methodological and inferential factors associated with variation in review conclusions.

Background Functional magnetic resonance imaging (fMRI) has become the principal method for investigating brain changes associated with psychotherapy in major depressive disorder. Multiple systematic reviews have synthesized this evidence and consistently report measurable neuroimaging changes, yet they frequently reach different functional, neurobiological, and clinical interpretations despite evaluating substantially

overlapping primary studies. Whether these differences arise from variation in the underlying evidence or from methodological and inferential processes during evidence synthesis remains uncertain. Meta-epidemiological umbrella reviews provide an appropriate framework to investigate review-level reproducibility and identify determinants of concordance and discordance across evidence syntheses.

Rationale Although systematic reviews represent the highest level of evidence synthesis, substantial overlap of primary studies does not necessarily result in concordant conclusions. Existing umbrella reviews generally evaluate methodological quality and evidence overlap but treat review conclusions as a single homogeneous outcome. This study introduces review-level concordance across predefined inferential levels as a structured framework to distinguish reproducible empirical findings from variability arising during functional, neurobiological, and clinical interpretation. The findings may improve understanding of reproducibility across evidence syntheses and

inform future neuroimaging research and umbrella review methodology.

METHODS

Search strategy Electronic searches will be conducted in PubMed/MEDLINE, Embase, and Scopus from database inception through 22 July 2026. Database-specific search strategies will combine controlled vocabulary (MeSH and Emtree, where applicable) and free-text terms related to major depressive disorder, psychotherapy, functional magnetic resonance imaging, systematic reviews, and meta-analyses. Search syntax will be adapted for each database while preserving conceptual equivalence. Reference lists of eligible systematic reviews will also be screened manually. No restrictions on publication language, publication date, or publication status will be applied. Complete electronic search strategies are provided in Supplementary Appendix S1.

Eligibility criteria Eligible studies are systematic reviews, with or without meta-analysis, that: (1) report a systematic literature search; (2) synthesize evidence from human studies evaluating psychotherapy for major depressive disorder; (3) report functional neuroimaging outcomes; and (4) provide qualitative synthesis, quantitative meta-analysis, or both. Reviews including broader psychiatric populations will be eligible if depression-specific functional neuroimaging findings can be identified separately. Reviews of structural neuroimaging alone, narrative reviews, editorials, conference abstracts, methodological papers, protocols, pharmacological reviews without an identifiable psychotherapy component, and animal studies will be excluded. No restrictions will be imposed regarding psychotherapy modality, neuroimaging paradigm, analytical method, or synthesis strategy.

Data extraction Two reviewers will independently extract data using standardized forms. Extracted variables will include publication year, review objectives, databases searched, search end date, clinical population, psychotherapeutic interventions, neuroimaging scope, number of included primary studies, quantitative synthesis, methodological characteristics, evidence coverage, primary-study overlap, methodological confidence, risk of bias, interpretative framework, inferential levels represented in review conclusions, and principal conclusions. Disagreements will be resolved by consensus or consultation with a third reviewer.

Outcome definitions The primary outcome is review-level concordance across five predefined inferential levels: (1) empirical neuroimaging observations; (2) anatomical localization; (3) functional interpretation; (4) neurobiological mechanisms; and (5) clinical implications. Secondary outcomes include methodological confidence assessed with AMSTAR 2, risk of bias assessed with ROBIS, primary-study overlap quantified using the Corrected Covered Area (CCA), evidence coverage, methodological characteristics, and potential determinants of review-level variation.

Strategy of data synthesis / Statistical analysis

Analyses will be conducted at the review level. Methodological confidence will be assessed using AMSTAR 2, risk of bias using ROBIS, and primary-study overlap using the Corrected Covered Area (CCA) at publication and cohort levels. Comparative analyses will be descriptive and will summarize methodological characteristics, evidence coverage, overlap patterns, review-level concordance, and sources of variation using structured comparative matrices. Formal quantitative meta-epidemiological modelling will not be performed because of the limited number of eligible systematic reviews.

Country(ies) involved Brazil.

Other relevant information This review is designed as a meta-epidemiological umbrella review in which systematic reviews, rather than primary neuroimaging studies, constitute the unit of analysis. The protocol was prospectively registered in INPLASY and the review follows the PRISMA 2020 Statement. Review-level concordance across predefined inferential levels represents the primary analytical framework.

Keywords Major depressive disorder; Psychotherapy; Functional magnetic resonance imaging; Meta-epidemiology; Umbrella review; Review concordance.

Dissemination plans The findings will be disseminated through publication in a peer-reviewed scientific journal and presentation at national and international scientific conferences. Supplementary materials, including search strategies, coding manuals, overlap matrices, and methodological audit tables, will accompany the published article. Data generated during the review will be made available through the publication and its supplementary material, with additional review-level materials available from the corresponding author upon reasonable request.

Contributions of each author

Author 1 - Felipe Cesar de Almeida Claudino - Conceptualization, methodology, literature search, study selection, data extraction, formal analysis, interpretation of findings, manuscript drafting, and critical revision.

Email: felipeaclaudino@gmail.com

Author 2 - Hugo Roberto Sampaio Martins - Conceptualization, methodology, literature search, study selection, data extraction, formal analysis, interpretation of findings, manuscript drafting, and critical revision.

Author 3 - Neusa Sica da Rocha - Conceptualization, methodology, literature search, study selection, data extraction, formal analysis, interpretation of findings, manuscript drafting, and critical revision.