

Charting the Gut–Brain Axis: A Scoping Review of Clinical Trials on Probiotic Supplements for Depression and Anxiety

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ADMINISTRATIVE INFORMATION

Support - dicentra.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - The author is employed at Dicentra Inc., a contract research organization (CRO) providing services to the dietary supplement industry. While this may be perceived as a potential conflict, the review will be conducted with strict adherence to methodological rigor, transparency, and scientific neutrality. No probiotic manufacturer is funding this work.

INPLASY registration number: INPLASY202580048

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 August 2025 and was last updated on 14 August 2025.

INTRODUCTION

Review question / Objective Using the PCC framework: Population: Adults diagnosed with depression or anxiety, based on standardized diagnostic criteria or validated self-report scales. Concept: Oral probiotic supplementation as a dietary supplement, assessed for effects on depression and/or anxiety symptoms. Context: Clinical trials (randomized controlled, non-randomized controlled), cohort studies, and case-control studies conducted in any setting, published between 2011–2025.

The objective is to map and summarize the available clinical evidence on the use of probiotic supplements for depression and anxiety, including study designs, probiotic strains/formulations, outcome measures, and reported efficacy.

Background Depression and anxiety are highly prevalent mental health conditions that affect quality of life and global productivity. Emerging evidence suggests that the gut–brain axis plays a role in mood regulation, with probiotics—live microorganisms conferring health benefits when administered in adequate amounts—being investigated for potential psychobiotic effects. The dietary supplement industry has shown increasing interest in probiotics for mood health. This review will systematically map the available clinical evidence in this field to identify research trends, gaps, and implications for dietary supplement development.

Rationale Although numerous preclinical studies have investigated probiotics for mood disorders, clinical evidence remains scattered across heterogeneous study designs. No recent scoping review has comprehensively summarized clinical

trial and observational data in this area with a dietary supplement focus. A scoping review is justified to:

Collate and describe the range of clinical research conducted between 2011–2025.

Identify evidence gaps and strain-specific effects.

Support the supplement industry in making evidence-based product and regulatory decisions.

METHODS

Strategy of data synthesis • Databases: PubMed/MEDLINE, Embase, Web of Science, CENTRAL, PsycINFO.

• Search Concepts: (probiotic* OR psychobiotic*) AND (supplement OR capsule OR powder) AND (depression OR anxiety) AND (clinical trial OR controlled trial OR randomized OR nonrandomized OR quasi-experimental).

• Timeframe: January 2011 to August 2025.

Electronic databases: PubMed, Embase, Web of Science, PsycINFO, Cochrane CENTRAL, and Scopus.

Search terms: combinations of “probiotic”, “psychobiotic”, “dietary supplement” with “depression”, “anxiety”, “mood disorder”, and specific probiotic strain names.

Data will be extracted into standardized forms and synthesized narratively, with descriptive statistics and frequency tables summarizing study characteristics, probiotic strains, dosages, and outcome measures.

Eligibility criteria • Population: Adults and children with clinically diagnosed depression or anxiety, or elevated stress symptoms.

• Intervention: Oral probiotic supplements (capsules or powders), single or multi-strain.

• Comparator: Placebo, standard care, or baseline measures.

• Outcomes: Depression and anxiety symptom scales (e.g., BDI, HAM-D, STAI), quality-of-life indices, neuroinflammatory or neurotrophic biomarkers (e.g., IL-6, BDNF, cortisol).

• Study designs: Randomized controlled trials (RCTs), non-randomized controlled trials (non-RCTs) with defined comparator groups.

• Language: English, peer-reviewed publications.

• Timeframe: Publications from January 2011 through August 2025.

• Exclusions: Animal studies, in vitro studies, fermented foods, synbiotics lacking isolated probiotic components, observational studies (cohort, case-control), and grey literature.

Source of evidence screening and selection

Two independent reviewers will screen titles/abstracts, then full texts, against the eligibility

criteria. Discrepancies will be resolved by discussion or by a third reviewer.

Data management References will be managed using EndNote. Screening and data extraction will be conducted using Covidence. Data will be stored securely in password-protected files.

Reporting results / Analysis of the evidence

Data will be summarized narratively and in tables. Analysis will focus on mapping the type, scope, and characteristics of studies, rather than meta-analysis.

Presentation of the results Results will be presented in: Tables summarizing study characteristics and findings. Figures showing the number of publications over time and study design distribution. Flow diagram (PRISMA-ScR format).

Language restriction English only.

Country(ies) involved Canada.

Other relevant information This review will position probiotics strictly as dietary supplements, not as pharmaceutical treatments.

This review intentionally excludes preclinical, in vitro, and observational studies to maintain strict relevance to clinical interventions using oral probiotic supplements in human populations with depression and anxiety.

Keywords probiotics; dietary supplements; depression; anxiety; mood disorder; psychobiotics; gut-brain axis.

Dissemination plans The review will be submitted to a peer-reviewed journal relevant to dietary supplements and functional foods. Findings will also be shared internally at Dicentra to inform client advisories and industry presentations.

Contributions of each author

Author 1 - Moustafa Kardjadj - Lead author; design, analysis, charting & mapping.

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Author 2 - Karol Wojewnik - Design & validation.

Author 3 - Lauren Park - Screening, data extraction & validation.

Author 4 - Dylan Fronda - Screening, data extraction & validation.

Author 5 - Dejan Spasic - Resources & validation.

Author 6 - Peter Wojewnik - Funding, resources & validation.

Author 7 - Alicia Wojewnik - Funding, resources & validation.