https://repository.uaeh.edu.mx/revistas/index.php/jbapr/issue/archive

Journal of Basic and Applied Psychology Research

Biannual Publication, Vol.7, No. 14 (2026) 14-24

JOURNAL OF BASIC AND APPLIED PSYCHOLOGY RESEARCH

ISSN: 2683-2267

Effectiveness of psicobiotics use in mental illness: literature review

Efectividad del uso de psicobióticos en las enfermedades mentales: Revisión bibliográfica

Yosmery González-Vázquez[a], Rubén García-Cruz[b], Verónica Rodríguez-Contreras[c] & María del Refugio Acuña-Gurrola[d]

Abstract:

Empirical evidence in recent years has shown that the use of prebiotics and probiotics has an impact on the mental state of the individual. Mental disorders such as anxiety, depression, stress are pathologies that affect the adult population and the use of psychobiotics can modify these symptoms, through homeostasis and balance of the intestinal microbiome and the modulation of the gut-brain axis. Despite this, recent studies evidence shows contradictions. The purpose of this study is to summarize the evidence on the effectiveness of probiotic use in mental illness. A bibliographic review of randomized clinical trials extracted from PubMed, Web of Science, Scielo from January 2019 to November 2024 is designed. The main results of 19 studies with 1085 participants showed that the administration of probiotics modified depressive symptomatology, anxiety, stress, cognitive impairment and insomnia in patients from the Eurasian continent, with doses higher than 1 x 10 ^{9} CFU daily and a duration of the intervention equal to or higher than 8 weeks. There is a need for intervention studies with probiotics in the elderly population, being a vulnerable age group. As well as longitudinal research to demonstrate the time of intestinal eubiosis maintained after the intervention in order to estimate the frequency of probiotic use and its impact on mental illnesses.

Keywords:

Older, probiotics, prebiotics, mental illnesses, microbiota, mental health, control case trial.

Resumen:

La evidencia empírica de los últimos años ha demostrado que el uso de prebióticos y probióticos tiene un impacto en el estado mental del individuo. Los trastornos mentales como la ansiedad, depresión, el estrés son patologías que afectan la población adulta y el uso de psicobióticos puede modificar estas sintomatologías, mediante la homeostasis y equilibrio del microbioma intestinal y la modulación del eje intestino-cerebro. A pesar de ello, estudios recientes muestran contradicciones. El motivo del presente estudio consiste en resumir la evidencia sobre la efectividad del uso de probióticos en las enfermedades mentales. Se diseña una revisión bibliográfica de ensayos clínicos aleatorios extraídos de PubMed, Web of Science, Scielo de enero de 2019 hasta noviembre de 2024. Los principales resultados de 19 estudios con 1085 participantes mostraron que la administración de probióticos modificó la sintomatología depresiva, la ansiedad, el estrés, el deterioro cognitivo y el insomnio en pacientes del continente euroasiático, con dosis superior a 1 x 10 9 UFC diarias y una duración de la intervención igual o superior a 8 semanas. Se necesita la realización de estudios de intervención con probióticos en la población adulta mayor, siendo un grupo etario vulnerable. Así como investigaciones longitudinales para evidenciar el *tiempo* de eubiosis intestinal mantenida posterior a la intervención en aras de estimar la frecuencia de uso de probióticos y su repercusión en enfermedades mentales.

***Palabras Clave**:*

Adulto mayor, probióticos, prebióticos, enfermedades mentales, microbiota, salud mental, estudio de caso control

[a] Instituto de Ciencias de la Salud (ICSa) | Pachuca de Soto | Hidalgo | México, https://orcid.org/0009-0007-7951-0909, Email: go490066@uaeh.edu.mx

[b] Instituto de Ciencias de la Salud (ICSa) | Pachuca de Soto | Hidalgo | México, https://orcid.org/0000-0001-7348-8113, Email: rubengarciacruz2014@uaeh.edu.mx

[c] Instituto de Ciencias de la Salud (ICSa) | Pachuca de Soto | Hidalgo | México, https://orcid.org/0000-0002-7116-8658, Email: veroroguez@gmail.com

d Instituto de Ciencias de la Salud (ICSa) | Pachuca de Soto | Hidalgo | México, https://orcid.org/0000-0003-3194-5392, Email: maria_acuna@uaeh.edu.mx

Received: 16/05/2025, Accepted: 26/11/2025, Published: 05/01/2026

DOI: https://doi.org/10.29057/jbapr.v7i14.14442

INTRODUCTION

The intestinal microbiota (IM) is composed of microorganisms and bacterial species that inhabit the intestine. Its diversity and ability to withstand physiological stress are related to the individual's health parameters, being the main regulator of the gut–microbiota–brain axis (GMB). Consequently, the microbiome has been studied as a genetic expression through DNA sequencing of these bacteria (Galland, 2021). The gut–microbiota–brain axis and mental health are biologically represented by a bidirectional communication network that includes the hypothalamic–pituitary–adrenal (HPA) axis, the autonomic nervous system (ANS), the immune system, and the central nervous system (CNS). This network preserves not only gastrointestinal homeostasis but also the balance of emotional and behavioral states, emitting efferent signals from the brain through sympathetic and parasympathetic branches, and afferent signals via neuronal projections, neuroendocrine mechanisms, and immune activation (Fernández, 2022).

In recent years, research related to the GMB axis has highlighted that inflammation may be a common underlying response mechanism in chronic diseases, both psychological—such as depressive disorders—and physiological, evidencing the bidirectional communication among the nervous, immune, and endocrine systems (Jiménez-Badilla & Acuña-Amador, 2021).

Although empirical support for the idea that certain bacteria in the body can positively influence the brain is recent, increasing evidence shows that the billions of microbes inhabiting the intestine substantially contribute to mental health and, likewise, to the progression of neuropsychiatric disorders, making them

sary to study the state of balance (eubiosis) of the latter. When balance is lost and beneficial bacteria are no longer able to control pathogenic ones, this is referred to as a state of imbalance or dysbiosis (Jiménez-Badilla & Acuña-Amador, 2021).

It remains unclear whether this dysbiosis, which favors the translocation or passage of neurotransmitters and interleukins, occurs secondarily to systemic inflammation or is a primary cause of depression onset in vulnerable individuals. Various studies reinforce that prebiotic and probiotic interventions constitute a "psychobiotic" strategy that favorably influences several psychiatric and neurological diseases, serving as a treatment without side effects unlike anxiolytics and antidepressants (Jiménez-Badilla & Acuña-Amador, 2021; Ansari et al., 2020; Noonan et al., 2020; Hofmeister et al., 2021; Vaghef-Mehrabany et al., 2020; Smith et al., 2021).

In this regard, better outcomes have been reported with probiotic interventions in mental disorders such as autism, Alzheimer's disease, schizophrenia, anxiety, and depression. Other studies emphasize lifestyle changes, highlighting physical activity, environment, and dietary awareness as important aspects in maintaining mental health through an integral strategy (Jiménez-Badilla & Acuña-Amador, 2021).

Considering the above, there arises the need to conduct studies that summarize evidence on the effectiveness of prebiotics and probiotics in adults through a literature review of clinical studies with patients diagnosed with mental illnesses, with sufficient statistical power to draw conclusions about the the subject of intense scientific scrutiny. Furthermore, specific evidence suggests that, in individuals sensitive to depression, inflammation is the direct result of intestinal bacterial signaling (Agranyoni et al., 2021).

It is estimated that approximately one in eight people worldwide has experienced a mental disorder (WHO, 2022). Thus, the use of probiotics and prebiotics is being studied as a therapeutic option, particularly in neuropsychological and autoimmune diseases, specifically multiple sclerosis (MS), major depressive disorder (MDD), generalized anxiety disorder (GAD), and autism spectrum disorder (ASD), where the GMB axis plays an important role in maintaining homeostasis, understood as the state of balance among these systems (Armengol et al., 2023).

An adequate and coordinated physiological response, such as an immune or stress response, is necessary for survival. However, long-term disturbances of this homeostatic environment may contribute to the progression of disorders by altering physiological processes such as immune activation due to increased intestinal barrier permeability and the passage of pro-inflammatory cytokines into the bloodstream and across the blood–brain barrier, leading to neuroinflammation. Additionally, activation of the hypothalamic–pituitary–adrenal axis, with predominance of kynurenine, favors the production of depressive symptoms, conditions hyperactivity of the HPA axis and the immune system, and, together with decreased nervous system (NS) activity, promotes bodily adaptation to stress and behavioral changes characteristic of depressive illness (Ramírez et al., 2018; Alessi & Bennett, 2020; Rea et al., 2020; Tao et al., 2020).

To understand communication between the nervous system and the intestinal microbiota, it is neces

results. The following research question was formulated: What is the effect of psychobiotics in adults with mental disorders?

METHODS

General Objective:

- Summarize the evidence on the effectiveness of psychobiotics in mental illnesses.

Specific Objectives:

1. Identify the dosage in CFU and the appropriate duration of probiotic administration for modifying these diseases.
2. Evaluate whether the effect of probiotics varies in relation to food intake.

Study Design: This study is descriptive and observational, based on a literature review of the topic.

Search Methods and Data Sources: An advanced electronic search was conducted in Google Scholar, PubMed, and Scielo databases using filters for randomized clinical trials, case–control studies, English or Spanish language, and publication period from February 2019 to October 2024. General search terms included: depression, dysbiosis, affective disorder, mental illness, psychiatric disorder, probiotics treatment, psychobiotics treatment, prebiotics treatment, prebiotics, probiotics, psychobiotics, effectiveness, anxiety reduction, and

depression reduction. In PubMed: (depression OR dysbiosis) AND (probiotics treatment OR psychobiotic). In Scielo: the same terms were applied.

Sample: Composed of 24 studies.

Inclusion Criteria:

- Randomized controlled trials (RCTs).
- Clinical cohorts with controls, with intervention involving probiotic and prebiotic consumption.
- Reports using similar methods and scientific rating scales for depression.
- Selection of the most recent articles within the last six years, complete, to avoid overlap.
- Participants aged 19 years or older, diagnosed with a mental illness or disorder.

Exclusion Criteria:

- Systematic reviews and literature reviews.
- Meta-analyses.
- Case reports.
- Case series.

Study Selection:

The initial search yielded 1,586 articles. Filters were applied for publication time, limiting to those published in the last six years, reducing the search to 1177 articles. Subsequently, meta-analyses, systematic reviews, and case reports were excluded, considering only clinical trials and randomized controlled trials, resulting in 136 articles.

A database was created in Microsoft Excel, duplicates were removed, and titles and abstracts were evaluated, leaving 24 articles selected as the most relevant for the research. Studies not focused on patients with neuropsychological disorders, those measuring probiotic effectiveness in populations under 19 years of age, and those not using psychological instruments to measure changes were excluded (Figure 1). Full texts of the selected studies were then analyzed for confirmation.

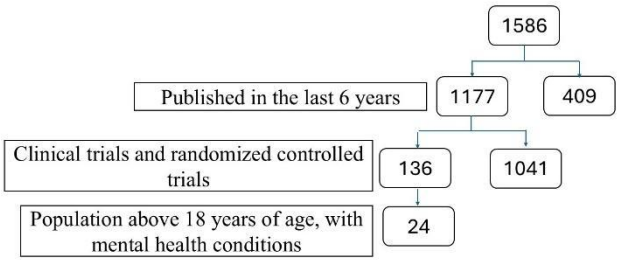

Figure 1. Flow diagram

This process was carried out using a matrix developed in Microsoft Excel 2010. The information included: author, year of publication, study design, title, participants, psychobiotic, dosage, duration, timing of probiotic administration, results, and citation.

Ethical Aspects of the Study

In this literature review, no personal data were handled, and no interventions were conducted on human subjects. Based on this study, an intervention with probiotics was carried out in older Mexican adults.

RESULTS

Description of the included studies

The search for information related to randomized clinical trials in patients with mental illnesses who received probiotic and prebiotics as interventions showed that, after applying inclusion and exclusion criteria, 24 articles presented adequate statistical power for the proposed analysis.

Patients with depressive symptoms were studied in 45.8% of the trials (Reininghaus et al., 2020; Schaub et al., 2022; Chahwan, 2019; Tian et al., 2022; Karakula-Juchnowicz et al., 2019; Kazemi et al., 2019; Saccarello et al., 2020; Ullah et al., 2022; Nikolova et al., 2023; Komorniak et al., 2023; Baião et al., 2023), Table 1. Two studies focused on patients with anxiety and depression (Ho et al., 2021; Zhu et al., 2023), three on participants with mild cognitive impairment (Fei et al., 2023; Hsu et al., 2023; Asaoka et al., 2022), and two on depression with coronary artery disease (Moludi et al., 2019; Moludi et al., 2022).

The remaining studies addressed individuals with anxiety, depression, and insomnia (Lee et al., 2021), cognitive performance and depression (Rudzki et al., 2019), insomnia (Lan et al., 2023), cognitive function in healthy older adults (Shi et al., 2022), sexual function (Hashemi-Mohammadabad et al., 2024), and well-being (Morales-Torres et al., 2023).

Table 1.
Frequency of mental and neurological disorders by study.

	Frequency(N)	%
Depression	11	45.8
Anxiety and depression	2	8.3
Depression and sexual function	1	4.2
Anxiety, depression, and insomnia	1	4.2
Depression and cognitive performance	1	4.2
Depression and coronary artery disease	2	8.3
Insomnia	1	4.2
Well-being	1	4.2
Cognitive functions in healthy adults	1	4.2
Mild cognitive impairment	3	8.3
Total studies	24	100

The reviewed studies were conducted in 13 countries. Of these, 20.8% were carried out in China, three in Poland, two in Taiwan, and two in Iran. The remaining investigations took place in Italy, the United Kingdom, Austria, Switzerland, Australia, Japan, Scotland, Korea, and the United States between 2019 and 2024 (Table 2).

It was found that 62.5% of the articles were randomized, double-blind, and placebo-controlled (Reininghaus et al., 2020; Schaub et al., 2022; Karakula-Juchnowicz et al., 2019; Saccarello et al., 2020; Ullah et al., 2022; Ho et al., 2021; Komorniak et al., 2023; Asaoka et al., 2022; Moludi et al., 2019; Moludi et al., 2022; Lan et al., 2023; Shi et al., 2022; Rudzki et al., 2019; Lee et al., 2021). Additionally, 95.8% included both male and female participants.

Table 2.
Characteristics of studies by location.

Study location	Frequency (N)	%
	24	100
Austria (Reininghaus et al., 2020)	1	4.2
Switzerland (Schaub et al., 2022)	1	4.2
Australia (Chahwan et al., 2019)	1	4.2
China (Tian et al., 2022; Zhu et al., 2023; Fei et al., 2023; Lan et al., 2023; Shi et al., 2022)	5	20.8
Japan (Asaoka et al., 2022)	1	4.2
Poland (Karakula-Juchnowicz et al., 2019; Komorniak et al., 2023; Rudzki et al., 2019)	3	12.5
Scotland (Kazemi et al., 2019)	1	4.2
Korea (Lee et al., 2021)	1	4.2
Taiwan (Ho et al., 2021; Hsu et al., 2023)	2	8.3
Iran (Moludi et al., 2019; Moludi et al., 2022; Hashemi-Mohammadabad et al., 2024)	3	12.5
Italy (Saccarello et al., 2020; Ullah et al., 2022)	2	8.3
United Kingdom (Nikolova et al., 2023; Baião et al., 2023)	2	8.3
USA (Morales-Torres et al., 2023)	1	4.2

Twelve studies did not specify sample characteristics; 25.0% involved outpatients, and 20.8% involved hospitalized participants. The age range in 58.3% of the studies was between 18 and 60 years, with a mean age of 44.4 years (Table 3).

Inclusion and exclusion criteria by study The inclusion criteria used were patients with depressive disorders, anxiety, Alzheimer-type dementia, and stress diagnosed according to ICD-10, aged over 18 years, with informed consent approval, adequate reading and comprehension of information, Stress Response Inventory (SRI) score ≥ 50 and ≤ 100, and Beck Depression Inventory-II (BDI-II) score ≥ 20 and ≤ 45.
The studies excluded patients with psychiatric disorders such as psychotic disorder, acute suicidal tendencies, lack of consent, drug addiction, diseases such as epilepsy, brain tumors, severe traumatic brain injuries or previous brain surgeries, intellectual disability, immunodeficiency, systemic lupus erythematosus, HIV, multiple sclerosis, antibiotic therapy in the last month, glucocorticoid treatment, acute infectious diarrheal disease, probiotic intake during the trial or in the last month, dietary restrictions, acute infectious diseases, and psychiatric disorders such as bipolar disorder and schizophrenia.

Instruments used
Several scales were employed to measure outcomes, generally assessing depressive symptoms and their severity, the presence of anxiety and stress, as well as other aspects such as quality of life related to the gastrointestinal system, cognitive capacity, and executive functions.
The most frequently used were the Beck Depression Inventory (BDI) and the Hamilton Depression Rating Scale (HAMD), applied in 41.6% and 37.5% of the studies, respectively. Other scales included the Symptom Checklist-90-Revised (SCL-90), the Depression Anxiety Stress Scale (DASS-21), the Beck Anxiety Inventory (BAI), the Leiden Index of Depression Sensitivity-Revised (LEIDS-R), the Stress Response Inventory (SRI), the Montgomery–Åsberg Depression Rating Scale (MADRS), the Perceived Stress Scale (PSS-10), the Pittsburgh Sleep Quality .

Table 3
Characteristics of the studies according to sampling type, gender, sample size, and mean age.

Total studies	Frequency (N)	%
	24	100
Study characteristics		
Randomized, double-blind, placebo-controlled	15	62.5
Randomized, single-blind, placebo-controlled	6	29.1
Randomized, parallel, triple-blind, placebo-controlled	1	4.2
Randomized with active control	1	4.2
Randomized, two groups (Probiotics + SSRIs vs SSRIs)	1	4.2
Gender		
Both male and female	23	95.8
Female only	1	4.2
Male only	0	0.0
Not specified	0	0.0
Sample		
Outpatients	6	25.0
Hospitalized patients	5	20.8
Non-clinical sample	2	8.3
Not specified	11	45.8
Age range		
20–40 years	2	8.3
20-66 years	1	4.2
18-60 years	14	58.3
Over 60 years	3	12.5
Not specified	4	16.6
Mean age (MA): 44.4 years	-	-

Index (PSQI), the Insomnia Severity Index (ISI), the Epworth Sleepiness Scale (ESS), the State-Trait Anxiety Inventory (STAI), the Zung Self-Rating Anxiety Scale (Z-SDS), and the Patient Health Questionnaire-9 (PHQ-9). Regarding biomarkers, the most commonly used were 16S rRNA for sequencing and microbiota data processing, IL-β3, TNF-α, serum and salivary cortisol as a stress biomarker, C-reactive protein (CRP), intestinal microbiota analysis, estimation of alpha and beta biodiversity at the genomic level, high-performance liquid chromatography (HPLC) to estimate kynurenine/tryptophan and tryptophan/branched-chain amino acids (BCAA) ratios, and kynurenine via ELISA testing. Biochemical parameters included tryptophan (TRP), kynurenine (KYN), kynurenic acid (KYNA), 3-hydroxykynurenine (3HKYN), anthranilic acid (AA), 3-hydroxyanthranilic acid (3HAA), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and plasma/urinary concentrations. Serum levels of CRP, lipopolysaccharide (LPS), TNF-α, and interleukins were also measured.

Table 4.

Scales, instruments and biomarkers used by study.

Measurement Scales	**Freq. (N)**	**%**	**References**
HAMD: Hamilton Depression Rating Scale	9	37.5	Reininghaus et al., 2020; Schaub et al., 2022; Tian et al., 2022; Ullah et al., 2022; Nikolova et al., 2023; Komorniak et al., 2023; Zhu et al., 2023; Rudzki et al., 2019; Hashemi-Mohammadabad et al., 2024.
GSRS: Gastrointestinal Symptom Rating Scale	4	16.6	Schaub et al., 2022; Tian et al., 2022; Karakula-Juchnowicz et at., 2019; Fei et al., 2023
MADRS: Montgomery–Åsberg Depression Rating Scale	2	8.3	Tian et al., 2022; Karakula-Juchnowicz et at., 2019
Measurement Scales	**Freq. (N)**	**%**	**References**
PSS-10: Perceived Stress Scale	2	8.3	Karakula-Juchnowicz et al., 2019; Rudzki et al., 2019
DASS-21: Depression Anxiety Stress Scale	1	4.2	Chahwan et al., 2019
ESS: Epworth Sleepiness Scale	1	4.2	Ho et al., 2021
Z-SDS: Zung Self-Rating Anxiety Scale	1	4.2	Saccarello et al., 2020
BPRS: Brief Psychiatric Rating Scale	1	4.2	Tian et al., 2022
PANAS: Positive and Negative Affect Scale	1	4.2	Baião et al., 2023
AIS: Athens Insomnia Scale	2	12.5	Komorniak et al., 2023; Lan et al., 2023
HAMA: Hamilton Anxiety Scale (Chinese version)	2	8.3	Nikolova et al., 2023; Zu et al., 2023
GAD-7: Generalized Anxiety Disorder Scale	1	4.2	Nikolova et al., 2023
RYFF: Psychological Well-Being Scale	1	4.2	Morales-Torres et al., 2023
SWLS: Satisfaction with Life Scale	1	4.2	Morales-Torres et al., 2023
DERS: Difficulties in Emotion Regulation Scale	1	4.2	Morales-Torres et al., 2023
ADL: Activities of Daily Living Scale	1	4.2	Hsu et al., 2023;
MoCa: Montreal Cognitive Assessment	2	8.3	Fei et al., 2023; Shi et al., 2022
Measurement instruments	**Freq. (N)**	**%**	**References**
PHQ-9: Patient Health Questionnaire-9	2	8.3	Ullah et al., 2022; Baião et al., 2023
MINI: Mini International Neuropsychiatric Interview	1	4.2	Chahwan et al., 2019
LEIDS-R: Leiden Index of Depression Sensitivity-Revised	1	4.2	Chahwan et al., 2019
APT: Prueba de Atención y Percepción	1	4.2	Rudzki et al., 2019
B-IBS: Cuestionario de síntomas del SII de Birmingham	1	4.2	Saccarello et al., 2020
PSQI: Pittsburgh Sleep Quality Index	3	12.5	Ho et al.,2021; Fei et al., 2023; Lan et al., 2023
Measurement instruments	**Freq. (N)**	**%**	**References**
BDI: Beck Depression Inventory	10	41.6	Reininghaus et al., 2020; Schaub et al., 2022; Chahwan et al., 2019; Karakula-Juchnowicz et al., 2019; Kazemi et al., 2019; Komorniak et al., 2023; Ho et al., 2021; Moludi et al., 2019; Moludi et al., 2022
BAI: Beck Anxiety Inventory	3	12.5	Chahwan et al., 2019; Ho et al.,2021; Lee et al., 2021
ISI: Índice de gravedad del insomnio	2	8.3	Saccarello et al., 2020; Ho et al., 2021
IDS: Inventory of Depressive Symptomatology	1	4.2	Nikolova et al., 2023; Zhu et al., 2023
SRI: Stress Response Inventory	1	4.2	Lee et al., 2021
SF-36: Health Survey	1	4.2	Morales-Torres et al., 2023
STAI: State-Trait Anxiety Inventory	4	16.6	Schaub et al., 2022; Baião et al., 2023; Moludi et al., 2019; Morales-Torres et al., 2023
SCL-90: Symptom Checklist-90	3	12.5	Reininghaus et al., 2020; Karakula-Juchnowicz et at., 2019; Rudzki et al., 2019
MAIA: Multimensional Assessment of Interoceptive Awareness	1	4.2	Morales-Torres et al., 2023
FFMQ: Five Facet Mindfulnes Questionnaire	1	4.2	Morales-Torres et al., 2023
MMSE: Mini-Mental State Examination	3	12.5	Fei et al., 2023
ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale	2	8.3	Hsu et al., 2023; Asaoka eta la., 2022
VSRAD: Voxel-Based Specific Regional Analysis System for Alzheimer's Disease	1	4.2	Asaoka eta la., 2022
CDR: Clinical Dementia Rating	1	4.2	Hsu et al., 2023;
RBANS: Repeatable Battery for the Assessment of Neuropsychological Status	1	4.2	Shi et al., 2022
FSFI: Female Sexual Function Index	1	4.2	Hashemi-Mohammadabad et al., 2024
Biomarkers	**Freq.(N)**	**%**	**References**
ARNr 16S: 16S ribosomal ribonucleic acid	2	12.5	Reininghaus et al., 2020; Chahwan et al., 2019
IL- β3: Interleukin β3	3	12.5	Tian et al., 2022; Karakula-Juchnowicz et at., 2019; Rudzki et al., 2019
-Cortisol	2	8.3	Tian et al., 2022; Lan et al., 2023
TNF- α: Tumor Necrosis Factor α	4	16.6	Tian et al., 2022; Karakula-Juchnowicz et at., 2019; Moludi et al., 2019; Rudzki et al., 2019
ACTH: Adrenocorticotropic Hormone	1	4.2	Lan et al., 2023
PCR: Polymerase Chain Reaction	3	12.5	Karakula-Juchnowicz et at., 2019; Moludi et al., 2019; Moludi et al., 2022
BDNF: Brain-Derived Neurotrophic Factor	1	4.2	Fei et al., 2023
TRP: Tryptophan	1	4.2	Kazemi et al., 2019
ELISA: Enzyme-Linked Immunosorbent Assay	1	4.2	Kazemi et al., 2019
-Microbiota study	3	12.5	Zhu et al., 2023; Fei et al., 2023; Asaoka et al., 2022
NGS: Next-Generation Sequencing	1	4.2	Hsu et al., 2023
- Alpha biodiversity	1	4.2	Zhu et al., 2023
-Beta diversity	1	4.2	Zhu et al., 2023

Intervention used

The intervention period ranged from 28 days to 12 months. The use of multi-strain probiotics was applied in 19 studies, while the remaining studies used a single strain. In two studies, both probiotics and prebiotics were administered, and in one trial, co-supplementation of both showed better results compared to placebo. Administration was provided in various forms such as capsules, tablets, and powder.

The most commonly used strains were: Bifidobacterium breve CCFM1025, Bifidobacterium longum, Bifidobacterium adolescentis NK98, Bifidobacterium longum Rosell-175, Lactobacillus rhamnosus, Lactobacillus helveticus, and Lactobacillus reuteri NK33. The administered doses varied across studies, ranging from 1×10^9 colony-forming units (CFU) to 9×10^{12} CFU.

Prebiotics such as galactooligosaccharides, inulin, and S-adenosyl methionine were also used. Placebos included biotin, maltose, lyophilized corn starch, maltodextrin, and cellulose, with identical characteristics in smell, taste, and external appearance to those administered in the experimental group.

RESULTS

Results by studies

It was evidenced that, out of the total studies analyzed, 21 (85.5%) showed satisfactory results following probiotic administration (Chahwan et al., 2019; Tian et al., 2022; Karakula-Juchnowicz et al., 2019; Kazemi et al., 2019; Saccarello et al., 2020; Baião et al., 2023; Nikolova et al., 2023; Komorniak et al., 2023; Zhu et al., 2023; Fei et al., 2023; Hsu et al., 2023; Asaoka et al., 2022; Moludi et al., 2019; Moludi et al., 2022; Lee et al., 2021; Rudzki et al., 2019; Lan et al., 2023; Shi et al., 2022; Hashemi-Mohammadabad et al., 2024; Morales-Torres et al., 2023).

Of these, 8 studies used multi-strain probiotics containing Bifidobacterium and Lactobacillus (Chahwan et al., 2019; Tian et al., 2022; Karakula-Juchnowicz et al., 2019; Baião et al., 2023; Nikolova et al., 2023; Komorniak et al., 2023; Fei et al., 2023; Hsu et al., 2023; Hashemi-Mohammadabad et al., 2024). Four studies applied two strains, most frequently Lactobacillus helveticus and Bifidobacterium longum. Nine investigations used a single probiotic strain, with Bifidobacterium breve, Lactobacillus plantarum, and Lactobacillus rhamnosus being the most common.

The dosage that yielded the best outcomes was greater than 1×10^9 CFU once daily. The most frequently employed intervention period, which also showed the most favorable results, was 8 weeks or longer, used in 14 trials (66.6%). Half of the studies (50.0%) did not specify whether probiotic administration was associated with food intake; four indicated administration with water, five reported probiotics taken with food, and three prior to meals. It is not possible to determine whether combining probiotics with food influenced the outcomes, as most studies did not describe the specifics of administration timing. However, other studies have demonstrated that spontaneously fermented foods such as yogurt, milk kefir, and vegetables serve as valuable sources of prebiotic strains potentially beneficial to overall health (Marco et al., 2021).

Statistically significant improvements were obtained in scale scores and biomarkers related to probiotic administration in 21 studies. Nineteen of these showed a marked reduction in depressive symptoms (Table 5). In five studies, anxiety improved; others reported better sleep quality, significant effects on stress and cognitive functioning, one study modified the severity of depressive symptoms and improved sexual function, and improvements in healthy behavior were also observed.

Results by Pathologies

Cognition and Cognitive Impairment

Asaoka et al. (2022): *Bifidobacterium breve* improved cognitive function and prevented brain atrophy in older patients with suspected mild cognitive impairment.

Fei et al. (2023): Probiotic intervention benefited multiple neuronal behaviors in older adults with mild cognitive impairment.

Hsu et al. (2023): In patients with Alzheimer's disease, probiotics improved inflammatory biomarkers, oxidative stress, and cognitive function.

Shi et al. (2022): *Bifidobacterium longum* BB68S enhanced cognitive functions in healthy older adults.

Rudzki et al. (2019): In patients with major depression, *Lactobacillus plantarum* 299v reduced kynurenine concentration and improved cognitive functions.

Major Depression and Depressive Symptoms

Baião et al. (2023): Multispecies probiotics reduced emotional salience and improved mood in moderate depression.

Chahwan et al. (2019): Triple-blind trial; probiotics showed partial reduction of depressive symptoms, although with high dropout rates.

Kazemi et al. (2019): Probiotics and prebiotics improved psychological outcomes in patients with major depression compared to placebo.

Komorniak et al. (2023): In post-bariatric surgery patients, short-term probiotic intervention reduced depressive symptoms.

Moludi et al. (2019): In post-myocardial infarction patients, probiotics improved depressive symptoms and quality of life.

Moludi et al. (2022): In coronary artery disease, probiotics + prebiotics reduced chronic inflammation and depressive symptoms.

Nikolova et al. (2023): Probiotics as adjunctive treatment in depression were well tolerated and showed positive effects.

Reininghaus et al. (2020, PROVIT): Probiotics + vitamin B7 improved depressive symptoms in hospitalized patients.

Saccarello et al. (2020): SAMe + Lactobacillus plantarum HEAL9 improved mild to moderate depressive symptoms.

Schaub et al. (2022): Complementary probiotics showed positive clinical, microbial, and neural effects in depression.

Tian et al. (2022): Bifidobacterium breve CCFM1025 attenuated major depression by regulating the gut microbiota and tryptophan metabolism.

Ullah et al. (2022): SAMe + probiotics improved symptoms in subthreshold and mild to moderate depression. Karakula-Juchnowicz et al. (2019, protocol): Designed a trial to evaluate probiotics + gluten-free diet in major depression; results not yet published.

Anxiety

Morales-Torres et al. (2023): In healthy adults, lifestyle-modulated psychobiotics reduced anxiety.

Zhu et al. (2023): *Lactobacillus plantarum* JYLP-326 alleviated anxiety, depression, and insomnia in university students.

Insomnia and sleep

Ho et al. (2021): *Lactobacillus plantarum* PS128 improved depressive symptoms and sleep quality in self-reported insomniacs.

Lan et al. (2023): *Bifidobacterium breve* CCFM1025 improved sleep quality by regulating the HPA axis.

Lee et al. (2021): Probiotic NVP-1704 improved mental health and sleep in healthy adults.

Zhu et al. (2023): In addition to anxiety and depression, showed benefits in university insomnia.

Cardiovascular Diseases

Moludi et al. (2019): Post-myocardial infarction, probiotics improved depression and quality of life.

Moludi et al. (2022): In coronary artery disease, probiotics + prebiotics reduced inflammation and depression.

Other Pathologies

Hashemi-Mohammadabad et al. (2024): Probiotics as adjunctive therapy improved sexual function in women with depression treated with SSRIs.

Risk of Bias Assessment

Regarding studies on psychobiotics and depression, Baião et al. (2023) showed low risk in randomization, blinding, and data management, but unclear risk in allocation concealment and selective reporting due to lack of public trial registration. Chahwan et al. (2019), despite being declared triple-blind, did not detail the method of randomization or allocation concealment and presented a high dropout rate without clear statistical handling, which implies high risk of attrition bias and unclear risk in other domains. Rudzki et al. (2019) adequately described randomization, blinding, and intention-to-treat analysis, but lacked verifiable registration, raising concerns about selective reporting. Tian et al. (2022) reported computerized randomization and appropriate blinding, but did not specify allocation concealment or handling of losses and lacked public registration, thus classified as unclear risk in several domains; whereas Schaub et al. (2022) met all methodological criteria—randomization and allocation concealment described, double blinding, blinded assessors, minimal losses, and public registration with prespecified outcomes positioning it as the only trial with low risk across all domains (Table 5).

In the set of clinical trials on psychobiotics and cognitive function in older adults, Asaoka et al. (2022) stands out for its methodological robustness, with computerized randomization, adequate blinding, and minimal losses, although with limited information on public registration, placing it at overall low risk. Fei et al. (2023) and Shi et al. (2022) show good quality in randomization, blinding, and data management, but present unclear risk in allocation concealment and selective reporting due to lack of methodological details and absence of verifiable registration; similarly, Lan et al. (2023) and Hsu et al. (2023) meet the basic criteria of randomization and blinding, as well as adequate handling of losses, but are also classified as unclear risk in allocation concealment and selective reporting.

In the set of more recent clinical trials on psychobiotics in depression and comorbidities, methodological quality appears variable: Hashemi-Mohammadabad et al. (2024) reported adequate randomization and allocation concealment, but the comparator without placebo broke practical blinding and generated high risk of performance bias, in addition to doubts about selective reporting; Ho et al. (2021) stands out for its solid design, with computerized randomization, indistinguishable placebo, blinded assessors, and public registration, being classified as low risk across all domains; Kazemi et al. (2019) showed a double-blind design with placebo, but lacked verifiable details on sequence generation, allocation concealment, and registration, placing it at unclear risk in several domains (Table 5).

In articles evaluating the use of probiotics in depression and specific medical conditions, methodological quality was heterogeneous. Komorniak et al. (2023), although designed as a double-blind pilot study with indistinguishable placebo, presents limitations in the description of randomization, allocation concealment, and handling of losses, which requires classifying several domains as unclear risk. In contrast, Lee et al. (2021) stands out for its methodological robustness, with computerized randomization, adequate allocation concealment, double blinding, and public registration, placing it at overall low risk. Moludi et al. (2019) shows a correct design in randomization and participant blinding, but lacks details on allocation concealment and blinding of outcome assessors, maintaining unclear risk in those domains despite minimal losses and complete outcome reporting. Moludi et al. (2022), in patients with coronary artery disease, confirms adequate randomization and blinding and proper data management, but the absence of information on allocation concealment and blinding of assessors raises methodological concerns. Morales-Torres et al. (2023), although double-blind with placebo, maintains several domains as unclear due to lack of methodological details; Nikolova et al. (2023) provides solid results with overall low risk thanks to transparency in randomization, blinding, and registration. Reininghaus et al. (2020) presents a robust design with low risk in most domains, although with some uncertainty regarding attrition.

Table 5

Risk of bias assessment according to Cochrane indicators for systematic reviews

	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias
	Random sequence generation	Allocation concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting
Baião et al. (2023)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Chahwan et al. (2019)	Unclear risk	Unclear risk	Low risk	Low risk	Alto riesgo	Unclear risk
Rudzki et al. (2019)	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Tian et al. (2022)	Low risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Schaub et al. (2022)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias
	Random sequence generation	Allocation concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting
Asaoka et al. (2022)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Fei et al. (2023)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Shi et al. (2022)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Lan et al. (2023)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Hsu et al. (2023)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Hashemi-Mohammadabad et al. (2024)	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear risk
Ho et al. (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Karakula-Juchnowicz et al. (2019)	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Kazemi et al. (2019)	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk
Komorniak et al. (2023)	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk
Moludi et al. (2019)	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk
Lee et al. (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Moludi et al. (2022)	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk
Morales-Torres et al. (2023)	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk
Nikolova et al. (2023)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias
	Random sequence generation	Allocation concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting
Reininghaus et al. (2020)	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk
Saccarello et al, (2020)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Shi et al. (2022)	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk
Ullah et al. (2022)	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk
Zhu et al. (2023)	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk

Saccarello et al. (2020) stands out for its rigor, with block randomization, adequate allocation concealment, double blinding, and public registration, placing it at overall low risk. In contrast, Shi et al. (2022), Ullah et al. (2022), and Zhu et al. (2023), although declaring randomized designs and double blinding with indistinguishable placebo, lack verifiable details on sequence generation, allocation concealment, and blinding of assessors, in addition to limitations in handling losses or absence of prospective registration, which classifies them as unclear risk in several domains (Table 5). In general, studies can be classified according to risk of bias.

Trials with unclear risk: Baião et al. (2023), Rudzki et al. (2019), Tian et al. (2022), Kazemi et al. (2019), Komorniak et al. (2023), Moludi et al. (2019), Morales-Torres et al. (2023), Fei et al. (2023), Shi et al. (2022), Lan et al. (2023), Hsu et al. (2023), Ullah et al. (2022), and Zhu et al. (2023) meet the basic criteria of randomization and blinding but lack verifiable details on allocation concealment, assessor blinding, and prospective registration. In some cases, the handling of losses or the absence of clear protocols generates additional uncertainty.

Trials with high risk in specific domains: Chahwan et al. (2019) presents a high risk of attrition bias due to its elevated dropout rate without adequate statistical management, and Hashemi-Mohammadabad et al. (2024) shows high risk of performance bias by using a comparator without placebo, breaking practical blinding.

CONCLUSIONS

The use of probiotics has shown promising results in patients with neuropsychological disorders, specifically depressive disorders, anxiety, stress, cognitive impairment, insomnia, Alzheimer's disease, among others. Improvements were greater when multi-strain probiotics including Lactobacillus and Bifidobacterium were used at doses above 1×10^9 CFU, with a daily intervention lasting 8 weeks or more. Probiotics could be ingested with food or water, and reductions were observed in BDI and HAMD scores, as well as in inflammatory biomarkers.

Regarding the risk of bias in the analyzed studies, current evidence supports the potential of psychobiotics as adjuncts in depression, anxiety, and cognitive impairment, but methodological variability requires cautious interpretation of the results. Trials with registered protocols and clearly described procedures provide greater credibility, whereas pilot studies or those with incomplete information should be considered exploratory. To consolidate the clinical validity of psychobiotics, large-scale, multicenter trials with complete methodological transparency are needed.

This study synthesized the most recent information on the use of psychobiotics and highlights the need for further research in the older adult population, given the comorbidities in this age group. Their use appears promising as a new treatment to achieve homeostasis in the body and improve mental disorders.

REFERENCES

Agranyoni, O., Meninger-Mordechay, S., Uzan, A., Ziv, O., Salmon-Divon, M., Rodin, D., Raz, O., Koman, I., Koren, O., Pinhasov, A., & Navon-Venezia, S. (2021). Gut microbiota determines the social behavior of mice and induces metabolic and inflammatory changes in their adipose tissue. npj biofilms and microbiomes, 7(1). https://doi.org/10.1038/s41522-021-00193-9

Alessi, M. & Bennett, M. (2020). Mental health is the health of the whole body: How psychoneuroimmunology & health psychology can inform & improve treatment. Journal of Evaluation in Clinical Practice, 26(5), 1539–1547. https://doi.org/10.1111/jep.13386

Almendros, L. (2021). Repository of Final Degree Projects of the European University (Madrid). The microbiota–gut–brain axis in anxiety [Thesis]. http://hdl.handle.net/20.500.12880/812

Ansari, F., Pourjafar, H., Tabrizi, A., & Aghebati-Maleki, L. (2020). The Effects of Probiotics and Prebiotics on Mental Disorders: A Review on Depression, Anxiety, Alzheimer, and Autism Spectrum Disorders. Current Pharmaceutical Biotechnology, 21(7), 555-565. https://doi.org/10.2174/1389201021666200107113812

Armengol, M., Martínez, A., Martí, E., Valls, G., & Montañá, T. (2023). How does the gut microbiota influence our mental health? Ceuic.Es. https://ceuic.es/campus/MICROBIOTA.pdf.

Asaoka, D., Xiao, J., Takeda, T., Yanagisawa, N., Yamazaki, T., Matsubara, Y., Sugiyama, H., Endo, N., Higa, M., Kasanuki, K., Ichimiya, Y., Koido, S., Ohno, K., Bernier, F., Katsumata, N., Nagahara, A., Arai, H., Ohkusa, T., & Sato, N. (2022). Effect of the probiotic Bifidobacterium breve on improving cognitive function and preventing brain atrophy in elderly patients with suspected mild cognitive impairment: Results of a 24-week randomized, double-blind, placebo-controlled trial. Journal of Alzheimer's Disease (JAD), 88(1), 75–95. https://doi.org/10.3233/JAD-220148

Baião, R., Capitão, P., Higgins, C., Browning, M., Harmer, J., & Burnet, J. (2023). Multispecies probiotic administration reduces emotional salience and improves mood in subjects with moderate depression: A randomized, double-blind, placebo-controlled study. Psychological Medicine, 53(8), 3437–3447. https://doi.org/10.1017/S003329172100550X

Chahwan, B., Kwan, S., Isik, A., van Hemert, S., Burke, C., & Roberts, L. (2019). Gut feelings: A randomized, triple-blind, placebo-controlled trial of probiotics for depressive symptoms. Journal of Affective Disorders, 253, 317–326. https://pubmed.ncbi.nlm.nih.gov/

Fei, Y., Wang, R., Lu, J., Peng, S., Yang, S., Wang, Y., Zheng, K., Li, R., Lin, L., & Li, M. (2023). Probiotic intervention benefits multiple neural behaviors in older adults with mild cognitive impairment. Geriatric Nursing, 51, 167–175. https://doi.org/10.1016/j.gerinurse.2023.03.006

Hashemi-Mohammadabad, N., Taghavi, S., Lambert, N., Moshtaghi, R., Bazarganipour, F., & Sharifi, M.

(2024). Adjunctive probiotic effects on sexual function in depressed women undergoing SSRI treatment: A double-blind randomized controlled trial. BMC Psychiatry, 24(1), 44. https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-023-05429-w

Ho, Y., Tsai, Y., Kuo, T., & Yang, C. (2021). Effects of Lactobacillus plantarum PS128 on depressive symptoms and sleep quality in self-reported insomniacs: A randomized, double-blind, placebo-controlled pilot trial. Nutrients, 13(8), 2820. https://doi.org/10.3390/nu13082820

Hofmeister, M., Clement, F., Patten, S., Li, J., Dowsett, L., Farkas, B., Mastikhina, L., Egunsola, O., Diaz, R., Cooke, N. & Taylor, V. (2021). The effect of interventions targeting gut microbiota on depressive symptoms: a systematic review and meta-analysis. Canadian Mediacal Association Journal OPEN, 9(4), E1195-E1204. https://doi.org/10.9778/cmajo.20200283

Hsu, Y., Huang, Y., Tsai, S., Kuo, Y., Lin, J., Ho, H., Chen, J., Hsia, K., & Sun, Y. (2023). Efficacy of probiotic supplements on brain-derived neurotrophic factor, inflammatory biomarkers, oxidative stress, and cognitive function in patients with Alzheimer's dementia: A 12-week randomized, double-blind, active-controlled study. Nutrients, 16(1), 16. https://doi.org/10.3390/nu16010016

Jimenez-Badilla, I., & Acuña-Amador, L. (2021). Clinical evidence on the use of gut microbiota modulators for the treatment of mental disorders: A systematic literature review. Biological Psychiatry

Karakula-Juchnowicz, H., Rog, J., Juchnowicz, D., Łoniewski, I., Skonieczna-Żydecka, K., Krukow, P., Futyma-Jedrzejewska, M. & Kaczmarczyk, M. (2019). The study evaluating the effect of probiotic supplementation on the mental status, inflammation, and intestinal barrier in major depressive disorder patients using gluten-free or gluten-containing diet (SANGUT study): a 12-week, randomized, double-blind, and placebo-controlled clinical study protocol. Nutrition journal, 18(1), 50. https://doi.org/10.1186/s12937-019-0475-x

Kazemi, A., Noorbala, A., Azam, K., Eskandari, M., & Djafarian, K. (2019). Effect of probiotics and prebiotics versus placebo on psychological outcomes in patients with major depressive disorder: A randomized clinical trial. Clinical Nutrition, 38(2), 522–528. https://doi.org/10.1016/j.clnu.2018.04.010

Komorniak, N., Kaczmarczyk, M., Łoniewski, I., Martynova-Van Kley, A., Nalian, A., Wroński, M., Kaseja, K., Kowalewski, B., Folwarski, M., & Stachowska, E. (2023). Analysis of the efficacy of diet and short-term probiotic intervention on depressive symptoms in patients after bariatric surgery: A randomized, double-blind, placebo-controlled pilot study. Nutrients, 15(23), 4905. https://doi.org/10.3390/nu15234905

Lan, Y., Lu, J., Qiao, G., Mao, X., Zhao, J., Wang, G., Tian, P., & Chen, W. (2023). Bifidobacterium breve CCFM1025 improves sleep quality through regulation of HPA axis activity: A randomized clinical trial. Nutrients, 15(21), 4700. https://doi.org/10.3390/nu15214700

Lee, H., Hong, J., Kim, J., Kim, D., Jang, S., Han, S., & Yoon, I. (2021). Effects of the probiotic NVP-1704 on mental health and sleep in healthy adults: An 8-week randomized, double-blind, placebo-controlled trial. Nutrients, 13(8), 2660. http://dx.doi.org/10.3390/nu13082660

MacQueen, G., Surette, M. & Moayyedi, P. (2017). The gut microbiota and psychiatric illness. Journal of Psychiatry & Neuroscience, 42(2), 75-77. https://doi.org/10.1503/jpn.170028

Marco, M. L., Sanders, M. E., Gänzle, M., Arrieta, M. C., Cotter, P. D., De Vuyst, L., Hill, C., Holzapfel, W., Lebeer, S., Merenstein, D., Reid, G., Wolfe, B. E., & Hutkins, R. (2021). International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods. Nature Reviews Gastroenterology & Hepatology, 18(3), 196–208. https://doi.org/10.1038/s41575-020-00390-5

Moludi, J., Alizadeh, M., Mohammadzad, M., & Davari, M. (2019). The effect of probiotic supplementation on depressive symptoms and quality of life in patients after myocardial infarction: Results of a preliminary double-blind clinical trial. Psychosomatic Medicine, 81(9), 770–777. https://doi.org/10.1097/PSY.0000000000000749

Moludi, J., Khedmatgozar, H., Nachvak, S., Abdollahzad, H., Moradinazar, M., & Sadeghpour, A. (2022). The effects of combined probiotic and prebiotic administration on chronic inflammation and depressive symptoms in patients with coronary artery disease: A randomized clinical trial. Nutritional Neuroscience, 25(8), 1659–1668. https://doi.org/10.1080/1028415X.2021.1889451

Morales-Torres, R., Carrasco-Gubernatis, C., Grasso-Cladera, A., Cosmelli, D., Parada, F., & Palacios-García, I. (2023). Psychobiotic effects on anxiety are mediated by lifestyle behaviors: A randomized placebo-controlled trial in healthy adults. Nutrients, 15(7), 1706. https://doi.org/10.3390/nu15071704

Nikolova, V., Cleare, A., Young, A., & Stone, J. (2023). Acceptability, tolerability, and estimates of putative effects of probiotic treatment as an adjunctive therapy in patients with depression: A randomized clinical trial. JAMA Psychiatry, 80(8), 842–847. https://doi.org/10.1001/jamapsychiatry.2023.1817

Noonan, S., Zaveri, M., Macaninch, E. & Martyn, K. (2020). Food & mood: a review of supplementary prebiotic and probiotic interventions in the treatment of anxiety and depression in adults. BMJ nutrition, prevention & health, 3(2), 351-362. https://doi.org/10.1136/bmjnph-2019-000053

World Health Organization. (June 8, 2022). Mental disorders. https://www.who.int/news-room/fact-sheets/detail/mental-disorders

Panamerican Health Organization. (October 16, 2023). Mental health. https://www.paho.org/en/topics/mental-health

Rea, K., Dinan, T. & Cryan, J. (2020). Gut Microbiota: A Perspective for Psychiatrists. Neuropsychobiology, 79(1), 50-62. https://doi.org/10.1159/000504495

Reininghaus, E., Platzer, M., Kohlhammer-Dohr, A., Hamm, C., Mörkl, S., Bengesser, S., Fellendorf, F., Lahousen-Luxenberger, T., Leitner-Afschar, B., Schöggl, H., Amberger-Otti, D., Wurm, W., Queissner, R., Birner,

A., Falzberger, V., Painold, A., Fitz, W., Wagner-Skacel, J., Brunnmayr, M., Rieger, A., ... Dalkner, N. (2020). PROVIT: Supplementary probiotic treatment and vitamin B7 in depression: A randomized controlled trial. Nutrients, 12(11), 3422. https://doi.org/10.3390/nu12113422

Rudzki, L., Ostrowska, L., Pawlak, D., Małus, A., Pawlak, K., Waszkiewicz, N., & Szulc, A. (2019). Probiotic Lactobacillus Plantarum 299v decreases kynurenine concentration and improves cognitive functions in patients with major depression: A double-blind, randomized, placebo controlled study. Psychoneuroendocrinology, 100, 213–222. https://doi.org/10.1016/j.psyneuen.2018.10.010

Saccarello, A., Montarsolo, P., Massardo, I., Picciotto, R., Pedemonte, A., Castagnaro, R., Brasesco, P. C., Guida, V., Picco, P., Fioravanti, P., Montisci, R., Schiavetti, I., & Vanelli, A. (2020). Oral administration of S-adenosylmethionine (SAMe) and Lactobacillus plantarum HEAL9 improves mild to moderate depressive symptoms: A randomized, double-blind, placebo-controlled study. Primary Care Companion for CNS Disorders, 22(4), 19m02578. https://doi.org/10.4088/PCC.19m02578

Schaub, A., Schneider, E., Vázquez-Castellanos, J., Schweinfurth, N., Kettelhack, C., Doll, J., Yamanbaeva, G., Mählmann, L., Brand, S., Beglinger, C., Borgwardt, S., Raes, J., Schmidt, A., & Lang, U. (2022). Clinical, gut microbial, and neural effects of adjunctive probiotic therapy in depressed patients: A randomized controlled trial. Translational Psychiatry, 12(1), 227. https://doi.org/10.1038/s41398-022-01977-z

Shi, S., Zhang, Q., Sang, Y., Ge, S., Wang, Q., Wang, R., & He, J. (2022). The probiotic Bifidobacterium longum BB68S improves cognitive functions in healthy older adults: A randomized, double-blind, placebo-controlled trial. Nutrients, 15(1), 51. https://doi.org/10.3390/nu15010051

Smith, K., Greene, M. F., Babu, J. R., & Frugé, A. D. (2021). Psychobiotics as treatment for anxiety, depression, and related symptoms: a systematic review.Nutritional Neuroscience, 24(12), 963-977. https://doi.org/10.1080/1028415x.2019.1701220

Tao, H., Wang, L., Guo, J. & Guo, M. (2020). Research Progress on the Relationship between Intestinal Flora and Mental and Psychological Diseases. Advances in microbiology, 10(06), 295-305. https://doi.org/10.4236/aim.2020.106021

Tian, P., Chen, Y., Zhu, H., Wang, L., Qian, X., Zou, R., Zhao, J., Zhang, H., Qian, L., Wang, Q., Wang, G. & Chen, W. (2022). Bifidobacterium breve CCFM1025 attenuates major depression disorder via regulating gut microbiome and tryptophan metabolism: A randomized clinical trial. Brain, behavior, and immunity, 100, 233– 241. https://doi.org/10.1016/j.bbi.2021.11.023

Ullah, H., Di Minno, A., Esposito, C., El-Seedi, H., Khalifa, S., Baldi, A., Greco, A., Santonastaso, S., Cioffi, V., Sperandeo, R., Sacchi, R. & Daglia, M. (2022). Efficacy of a food supplement based on S-adenosyl methionine and probiotic strains in subjects with subthreshold depression and mild-to-moderate depression: A monocentric, randomized, cross-over, double-blind, placebo-controlled clinical trial. Biomedicine & pharmacotherapy, 156, 113930. https://doi.org/10.1016/j.biopha.2022.113930

Vaghef-Mehrabany, E., Asbaghi, O., Behrooz, M., Ranjbar, F., & Ebrahimi-Mameghani, M. (2020). Can psychobiotics “mood” ify gut? An update systematic review of randomized controlled trials in healthy and clinical subjects, on anti-depressant effects of probiotics, prebiotics, and synbiotics. Clinical Nutrition, 39(5), 1395-1410. https://doi.org/10.1016/j.clnu.2019.06.004

Zhu, R., Fang, Y., Li, H., Liu, Y., Wei, J., Zhang, S., Wang, L., Fan, R., Wang, L., Li, S., & Chen, T. (2023). The psychobiotic Lactobacillus plantarum JYLP-326 alleviates symptoms of anxiety, depression, and insomnia in college students through modulation of gut microbiota and its metabolism. Frontiers in Immunology, 14, 1158137. https://doi.org/10.3389/fimmu.2023.1158137