BMC Psychiatry

SYSTEMATIC REVIEW Open Access

The efficacy of probiotics, prebiotics, and synbiotics on anxiety, depression, and sleep: a systematic review and meta-analysis of randomized controlled trials

Jialin Zhang[1], Linqing Zhu[1], Qing Meng[1], Zuxing Wang[2*] and Hongru Zhu[1*]

Abstract

Background With the growing recognition of the limitations associated with conventional treatments for anxiety and depression, there has been increasing interest in alternative and adjunct therapies, particularly probiotics, prebiotics, and synbiotics. However, current research results regarding their efficacy in treating anxiety, depression, and sleep have been inconsistent.

Methods A systematic literature search for randomized controlled trials (RCTs) was conducted in PubMed, Web of Science, and Embase from inception to October 2023, updated in March 2025. The included studies involved individuals with anxiety and depression disorders, or chronic disease patients/healthy populations presenting with depressive or anxiety symptoms. Two researchers independently screened and extracted data. The Cochrane risk of bias tool was used to evaluate the quality of the included studies. Data synthesis and subgroup analyses were performed in Review Manager 5.3 and Stata 15.0 software. The anxiety, depression, and sleep scores were calculated by the standard mean difference (*SMD*) and 95% confidence intervals (*CI*s).

Results A total of 72 RCTs were included (3,319 intervention and 2,778 control participants). Among these, researchers examined depression in 63 studies (2,880 and 2,493 participants) and anxiety in 49 studies (2,124 and 1,788 participants) using probiotics/prebiotics/synbiotics interventions, while 12 studies (411 and 378 participants) examined sleep using probiotic interventions. The meta-analysis demonstrated significant reductions compared to placebo in depression ($SMD = -0.53$, 95% *CI*: −0.67 to −0.39, $Z = 7.33$, $P < 0.001$) and anxiety ($SMD = -0.44$, 95% *CI*: −0.59 to −0.28, $P < 0.001$). Additionally, probiotics were shown to improve sleep quality ($SMD = -0.39$, 95% *CI*: −0.53 to −0.25, $P < 0.001$). Subgroup analyses indicated that both probiotics, prebiotics, and synbiotics independently alleviated anxiety and depression. The impact of probiotics varied by population, intervention duration, and probiotic types.

*Correspondence:
Zuxing Wang
zuxingwang7090@163.com
Hongru Zhu
zhuhongru@wchscu.cn

Full list of author information is available at the end of the article

Conclusion These findings suggest that probiotics, prebiotics, and synbiotics offer promising adjunctive treatments for anxiety, depression, and sleep disturbances. However, given the high heterogeneity and limited methodological quality of the included studies, further large-scale and high-quality RCTs with long-term follow-up are needed to further validate these outcomes.

Registration The protocol was registered on PROSPERO (Registration number: CRD42024563862).

Clinical trial number Not applicable.

Keywords Prebiotics, Probiotics, Synbiotics, Depression, Anxiety, Sleep, Systematic review, Meta-analysis

Introduction

Anxiety disorders and depression are among the most common mental health conditions worldwide. According to a 2021 report by the World Health Organization, approximately 359 million individuals were affected by anxiety disorders and 332 million by depression in the same year [1, 2]. These conditions impose a substantial personal and socioeconomic burden, resulting in an estimated global productivity loss of up to one trillion dollars annually, with projections indicating a further increase in the future [3].

Traditional pharmacological treatments for anxiety and depression are often accompanied by adverse effects, including nausea, vomiting, sexual dysfunction, weight gain, and daytime fatigue [4, 5]. These side effects can impact patient adherence, leading to early discontinuation and disruption of treatment. In addition, cognitive behavioral therapy (CBT) is often considered complex and demanding, and its relatively brief intervention duration may limit its therapeutic effectiveness [6]. Consequently, the search for more tolerable and effective therapeutic approaches has become a major focus in psychiatry. Recent advances in nutritional psychiatry have highlighted the bidirectional communication between the gut microbiota and the central nervous system. Besides, increasing evidence suggests that microorganisms can influence human behavior, thought processes, and mental health [7]. According to the gut microbiota-gut-brain axis theory, probiotics, prebiotics, and synbiotics have emerged as promising adjunctive interventions for mental health. These approaches are well-tolerated and safe, without the cognitive side effects or addictive potential associated with some psychotropic medications [8]. In detail, probiotics are live microorganisms, prebiotics are substrates selectively utilized by host microorganisms, and synbiotics are a combination of live microorganisms and substrates that confer health benefits to the host [9–11]. These microorganisms and non-digestible carbohydrates play vital regulatory roles in the gut and are believed to have potential positive effects on mental health [12].

As research in this field has advanced, several meta-analyses have reported that probiotics are effective in alleviating depressive symptoms [13, 14]. However, findings regarding their effects on anxiety remain inconsistent. While one meta-analysis demonstrated that probiotics can reduce anxiety symptoms [15], another meta-analysis reported that the efficacy in treating anxiety among adolescents is negligible [16]. Moreover, although previous reviews have examined the effects of probiotics and prebiotics on anxiety and depression, several important moderating factors remain unclear, including the characteristics of study populations, intervention duration, and probiotic types. In addition, evidence regarding the effects of probiotics on sleep remains limited [17]. Therefore, to address such research gap, our meta-analysis aimed to: (1) systematically evaluate the effects of probiotics/prebiotics/synbiotics on anxiety and depression, and further explore the effects of probiotics on sleep; and (2) conduct subgroup analyses to examine the influence of target population, intervention duration, and probiotics type on anxiety and depression.

Methods

Search strategy

Computerized searches were conducted on PubMed, Web of Science, and Embase from inception to October 2023, updated in March 2025. The study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) (registration ID: CRD42024563862). As this research was based on previously published studies, ethical approval and informed consent were not required.

The search strategy included the following terms: (dysbiosis OR metagenom* OR microbiome* OR microbiota OR prebiotic* OR probiotic* OR synbiotic* OR "bacterial translocation" OR "colon flora" OR "fecal flora" OR "gut flora" OR "intestinal flora" OR "enteric bacteria" OR "fecal bacteria" OR "gut bacteria" OR "intestinal bacteria" OR "fecal microflora" OR "gut microflora" OR "intestinal microflora" OR "gut microbial" OR bifidobacter* OR lactobacill*) And (depress* OR "af-fective disorder" OR "affective illness" OR "mood disorder" OR anxi* OR internalizing OR "mental health" OR "mental illness" OR "psy-chiatric disorder" OR "psychiatric illness"). The detailed search strategy for each database is provided in the supplementary materials.

Inclusion and exclusion criteria

Inclusion Criteria: (1) randomized controlled trials (RCTs) investigating the effects of probiotics, prebiotics, and/or synbiotics on depression and/or anxiety in humans, with additional analyses conducted on the effects of probiotics on sleep based on eligible studies; (2) studies involving participants diagnosed with anxiety or depressive disorders, as well as chronic disease patients/healthy populations presenting with depressive or anxiety symptoms; (3) for healthy individuals, probiotics, prebiotics, and/or synbiotics were required to be the only intervention, (4) depression and anxiety outcomes need to be evaluated separately.

Exclusion criteria for this study include: (1) unavailability or incompleteness of full-text original data; (2) non-English publications; (3) absence of relevant outcome measures; (4) lack of standardized assessment scales or use of self-made evaluation tools; (5) duplicate studies; (6) studies focusing on psychiatric disorders other than anxiety and depression; (7) naturalistic investigations of self-reported consumption.

Literature screening and data extraction

Data extraction was performed independently and in duplicate by two reviewers, and any discrepancies were resolved through discussion or consultation with a third reviewer. The extracted data included author, publication year, country, age, percentage of female participants, duration of probiotics/prebiotics/synbiotics administration, follow-up period, sample size, intervention measures, outcome indicators, and the types, doses, and formulations of microbial strains.

Literature quality assessment

Following the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions by Higgins et al. [18], two researchers independently assessed the quality of the included studies to ensure assessment accuracy. The evaluation encompassed the following criteria: random sequence generation, allocation concealment, blinding of participants, researchers, and outcome assessment, completeness of outcome data, selective reporting, and other potential sources of bias. Each criterion was rated as having a "low risk of bias", "unclear risk of bias", or "high risk of bias".

Statistical analysis

Meta-analyses were conducted using Review Manager 5.3 and Stata 15.0 software. Heterogeneity among studies was assessed through the Q test and I^2 statistic. A fixed-effects model was utilized if the Q test revealed $P \geq 0.05$ and $I^2 \leq 50\%$, indicating low heterogeneity. Conversely, a random-effects model was applied if the Q test resulted in $P < 0.05$ and $I^2 > 50\%$, suggesting substantial heterogeneity. Sensitivity analysis was employed to ensure the stability and reliability of the study. If specific studies were found to introduce instability, they were excluded, and the meta-analysis was repeated to compare results. Given that the anxiety, depression, and sleep scores included in our analysis were all continuous variables with different assessment tools, the standardized mean difference (*SMD*) was employed as the effect size, accompanied by 95% confidence intervals (*CI*s). Among those, anxiety and depression were defined as the primary outcomes, while sleep outcomes were analyzed as an exploratory secondary outcome using data from studies included for anxiety and depression, to provide further insights into the potential effects of the probiotics on sleep. For any included multi-arm study, the shared control group was divided into subgroups of approximately equal size for each experimental group [19, 20]. Additionally, more than ten studies were available, publication bias was assessed using Egger's test, with the "trim and fill" method applied if bias was detected [21, 22]. According to the methodological characteristics of previous similar studies and the distribution rule of the included literature, subgroup analyses were performed based on the type of microecological preparations, target population, intervention duration and probiotics type, to explore potential moderating factors of such interventions on anxiety and depression [12, 23–25].

Results

Literature search results

The results of the literature search are summarized in Fig. 1A. A total of 6,394 studies were initially retrieved from PubMed, Web of Science, and Embase. After removing 1,098 duplicates, 42 eligible articles were identified through title and abstract screening, followed by full-text review. Subsequently, we updated the literature from October 2023 to March 2025 across the same databases according to the predefined eligibility criteria. After rigorous screening, 138 RCTs were identified, of which 25 studies met the inclusion criteria for final analysis. The additional five original studies were incorporated based on references from two prior meta-analyses [13, 24]. In total, 72 studies were included in the analysis: 50 probiotic trials [26–75], 11 prebiotic trials [76–86], 5 synbiotic trials [87–91], 3 three-arm studies comparing probiotics, prebiotics, and placebo [92–94], 1 three-arm study comparing probiotics, synbiotics, and placebo [95], and 2 four-arm studies comparing probiotics, prebiotics, synbiotics, and placebo [96, 97]. Among these studies, researchers from 63 studies examined the effects of probiotics/prebiotics/synbiotics on depression and anxiety, which were defined as the primary outcomes, whereas researchers from 12 studies assessed the impact of probiotics on sleep quality, considered a secondary outcome.

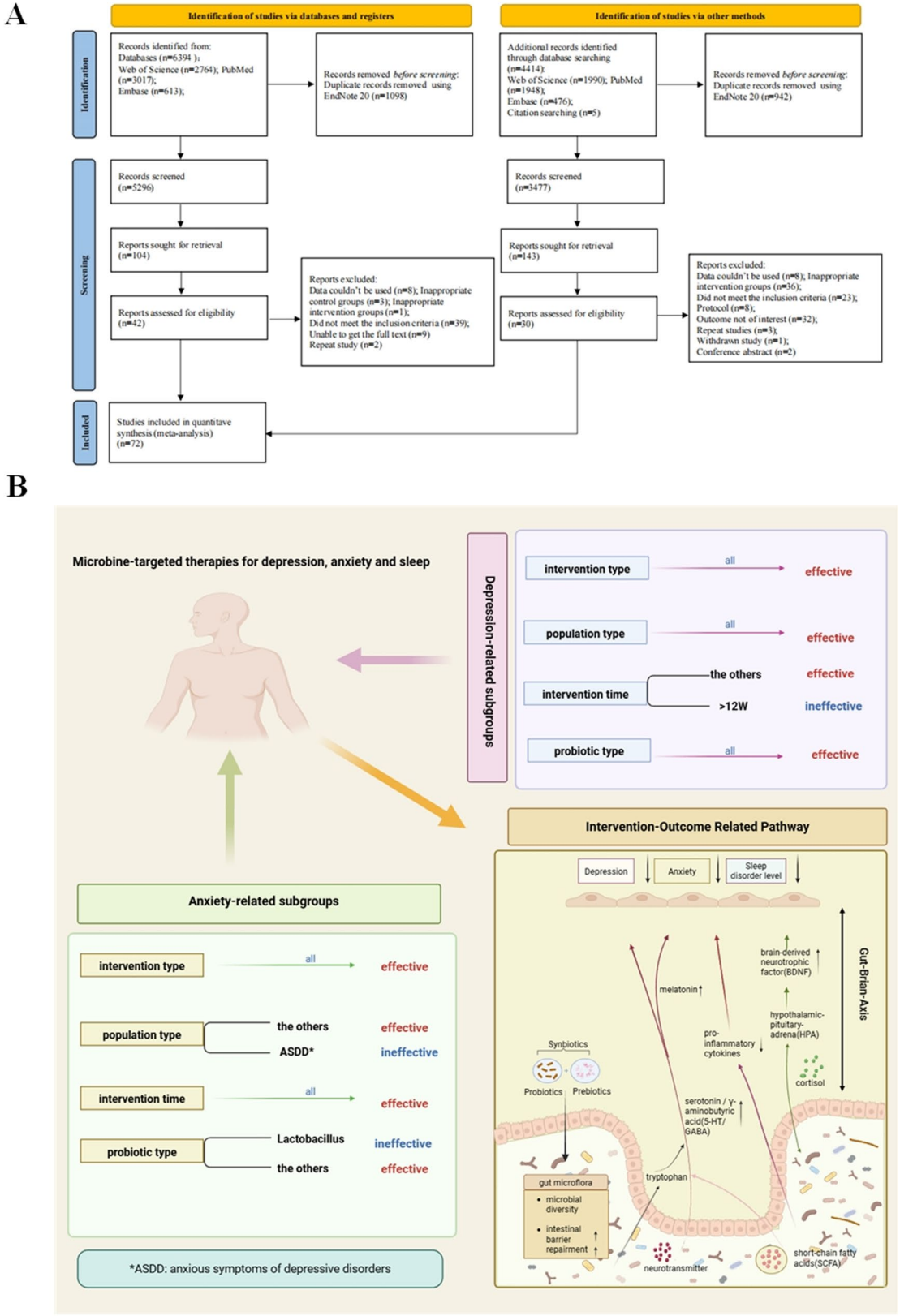

Fig. 1 **A**: PRISMA flow chart of literature search; **B**: Proposed mechanisms and subgroup findings on how probiotics, prebiotics, and synbiotics alleviate anxiety, depression, and improve sleep quality

Characteristics and quality assessment of included studies

A total of 72 studies, comprising 3,319 participants in intervention groups and 2,778 in control groups, were included in the analysis. Among them, 63 studies assessed the effects of probiotics/prebiotics/synbiotics on depression (2,880 intervention and 2,493 control participants), and 49 studies evaluated their effects on anxiety (2,124 and 1,788 participants, respectively). Additionally, 12 studies investigated the impact of probiotics on sleep (411 intervention and 378 control participants), and the sample size of each RCT ranged from 16 [39] to 400 [72]. The mean age of all participants was between 19.4 [71] and 77.2 [90], while eight studies simply reported the age range (18–23) [45, 52, 54, 57, 78, 82–84]. The characteristics of the included studies and details of the microbial agents are shown in Tables S1 and S2, respectively.

Two researchers independently evaluated the quality of the studies according to the Cochrane Handbook. Specifically, 60 studies (83.3%) adequately described the generation of the random sequence, and 52 studies (72.2%) explicitly reported the allocation concealment procedure. Blinding of participants and personnel was described in 61 studies (84.7%). Most studies (55.6%) did not report blinding of outcome measures but used self-report questionnaires to measure outcomes, so blinded outcome assessment is not applicable in these studies. Attrition bias and reporting bias were addressed in all studies. Finally, only 29 studies (40.3%) adequately addressed "other bias". Overall, only 14 studies (19.4%) showed low risk of bias across all seven criteria, which may lead to overestimation of the overall effect of the intervention. The quality assessment chart and risk of bias, generated using Review Manager 5.3, can be accessed in the supplementary materials Figure S1.

Meta-analysis results

Primary outcomes

Researchers from 63 studies reported the effects of probiotics/prebiotics/synbiotics on depression scores. Due to significant heterogeneity (I^2 = 83%), a random effects model was used. The intervention group demonstrated a significant improvement in depression scores compared with the control group (*SMD* = − 0.53, 95% *CI*: −0.67 to − 0.39, $P < 0.001$). Besides, researchers from 49 studies examined the effects of these interventions on anxiety scores. Given the significant heterogeneity (I^2 = 81%), a random effects model was used. The results revealed a statistically significant reduction in anxiety scores in the intervention group compared with controls (*SMD* = − 0.44, 95% *CI*: −0.59 to − 0.28, $P < 0.001$). Additionally, researchers from 12 studies focused on probiotics and sleep scores. Given the low heterogeneity (I^2 = 49%), a fixed-effect model was applied for the pooled analysis. The findings indicated a significant difference in sleep scale changes between the intervention and control groups, with the intervention group showing greater improvement (*SMD* = − 0.39, 95% *CI*: −0.53 to − 0.25, $P < 0.001$). Meta-regression analyses revealed no statistically significant moderating effects of age ($P = 0.57$ for depression; $P = 0.35$ for anxiety) or gender ($P = 0.64$ for depression; $P = 0.97$ for anxiety) on depressive or anxiety symptoms. The results are summarized in Figs. 2 and 3, and 4, with subgroup analysis details presented in Table 1.

Subgroup analysis

Subgroup analysis by intervention type The results indicate that probiotics, prebiotics and synbiotics interventions led to statistically significant improvements in depression scores (I^2 = 86.0%, *SMD* = − 0.56, 95% *CI*: −0.74 to − 0.38, $P < 0.001$; I^2 = 64%, *SMD* = − 0.32, 95% *CI*: −0.53 to − 0.10, $P = 0.004$; I^2 = 71%, *SMD* = − 0.53, 95% *CI*: −0.91 to − 0.16, $P = 0.005$, respectively), with intervention groups demonstrating greater improvement than controls. Similarly, all three types of interventions led to significant reductions in anxiety scores (I^2 = 84%, *SMD* = − 0.39, 95% *CI*: −0.58 to − 0.20, $P < 0.001$; I^2 = 65%, *SMD* = − 0.57, 95% *CI*: −0.83 to − 0.31, $P < 0.001$; I^2 = 68%, *SMD* = − 0.59, 95% *CI*: −1.03 to − 0.15, $P = 0.009$, respectively).

Probiotics group Probiotics for depression

A total of 49 studies examined the effects of probiotics on depression scores. Subgroup analyses based on population type showed significant improvements across all groups: individuals with depressive disorders (I^2 = 77%, *SMD* = − 0.82, 95% *CI*: −1.17 to − 0.46, $P < 0.001$), healthy individuals (I^2 = 84%, *SMD* = − 0.50, 95% *CI*: −0.76 to − 0.25, $P < 0.001$), and individuals with chronic illnesses (I^2 = 90%, *SMD* = − 0.59, 95% *CI*: −0.91 to − 0.27, $P < 0.001$). In all three populations, intervention groups demonstrated greater improvement than controls.

Subgroup analysis based on intervention duration revealed significant improvements in the following three groups: interventions lasting ≤ 4 weeks (I^2 = 86%, *SMD* = − 0.69, 95% *CI*: −1.05 to − 0.32, $P < 0.001$), interventions lasting between 4 and 8 weeks (I^2 = 87%, *SMD* = − 0.66, 95% *CI*: −0.95 to − 0.36, $P < 0.001$), and interventions lasting between 8 and 12 weeks, including 12 weeks (I^2 = 66%, *SMD* = − 0.30, 95% *CI*: −0.50 to − 0.09, $P = 0.004$). However, interventions lasting > 12 weeks did not show a significant effect (I^2 = 99%, *SMD* = − 1.31, 95% *CI*: −4.55 to 1.92, $P = 0.43$).

Analyses based on probiotic type indicated significant improvements for all groups: Lactobacillus Group (I^2 = 72%, *SMD* = − 0.31, 95% *CI*: −0.53 to − 0.09, $P = 0.005$), Bifidobacterium Group (I^2 = 89%, *SMD* = − 0.71, 95% *CI*: −1.33 to − 0.10, $P = 0.02$), Lactobacillus Combined with

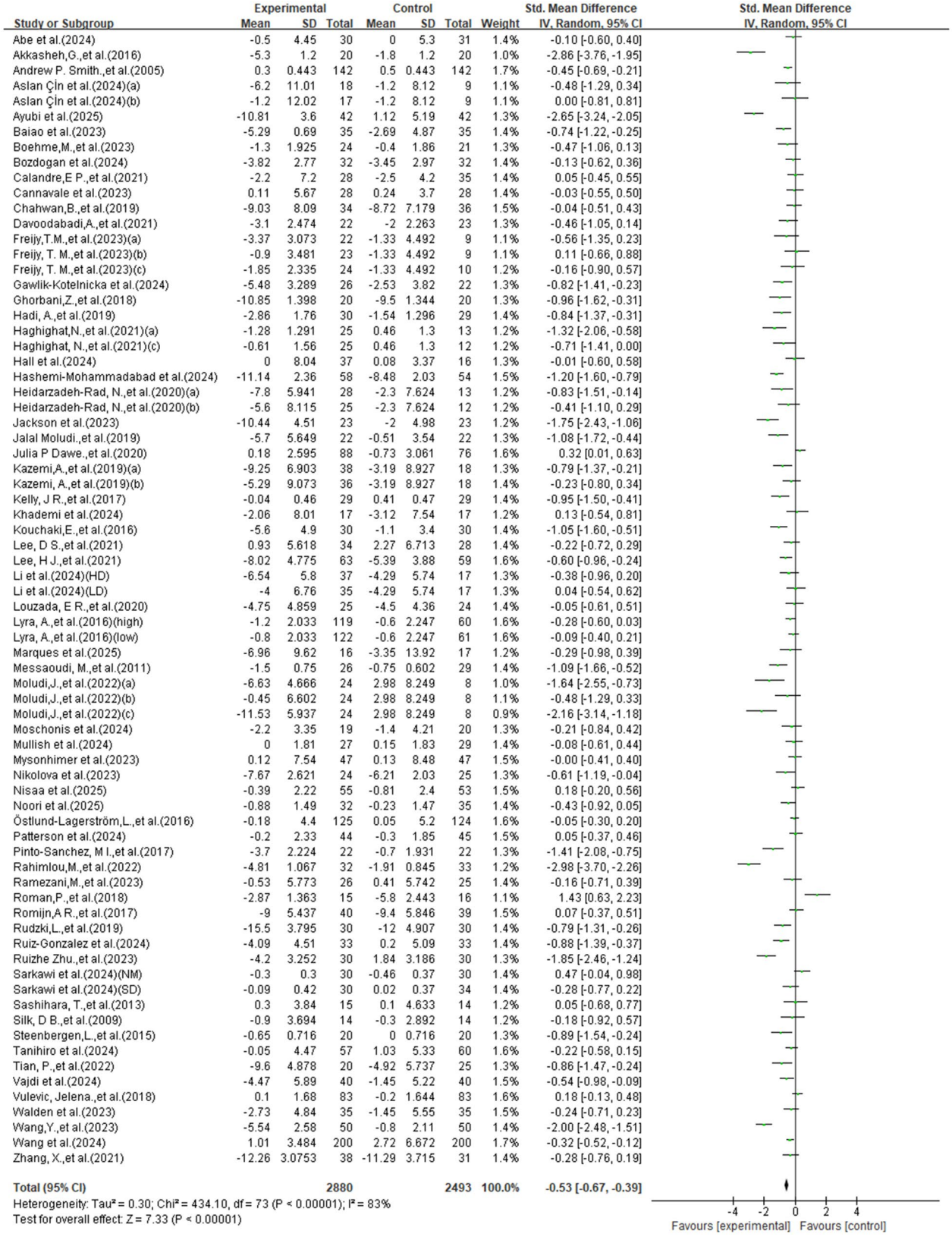

Fig. 2 Overall analysis of probiotics, prebiotics, synbiotics to alleviate depressive symptoms. Note: (**a**) = probiotic; (**b**) = prebiotic; (**c**) = synbiotic; low = low dose probiotics; high = high dose probiotics; SD = Irritable bowel syndrome (IBS) patients had subthreshold depression; NM = IBS patients with normal mood

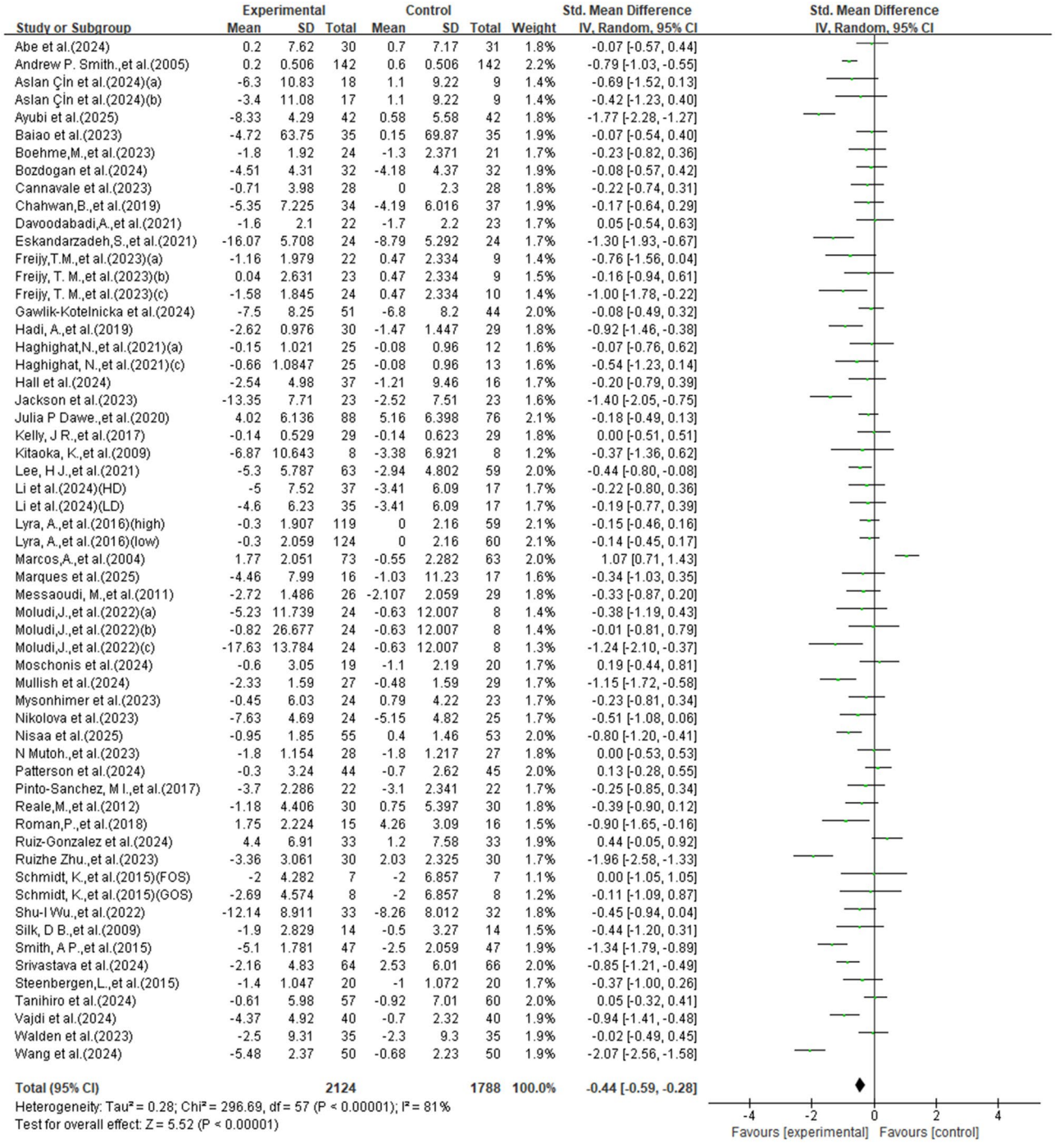

Fig. 3 Overall analysis of probiotics, prebiotics, synbiotics to alleviate anxiety symptoms. Note: (**a**) = probiotic; (**b**) = prebiotic; (**c**) = synbiotic; low = low dose probiotics; high = high dose probiotics; FOS = fructooligosaccharides; GOS = galactooligosaccharides

Bifidobacterium Group (I^2 = 86%, *SMD* = − 0.60, 95% *CI*: −0.90 to − 0.31, $P < 0.001$), and Mixed Strains of Three or More Types (I^2 = 92%, *SMD* = − 0.82, 95% *CI*: −1.36 to − 0.29, $P = 0.003$). Across all probiotic types, intervention groups showed statistically significant improvements in depression scores compared with controls.

Probiotics for anxiety

A total of 38 studies examined the effects of probiotics on anxiety scores. When grouped by population type, the pooled results revealed that individuals with chronic illnesses (I^2 = 83%, *SMD* = − 0.49, 95% *CI*: −0.79 to − 0.20, $P = 0.001$) and healthy individuals (I^2 = 86%, *SMD* = − 0.31, 95% *CI*: −0.59 to − 0.02, $P = 0.04$) demonstrated a

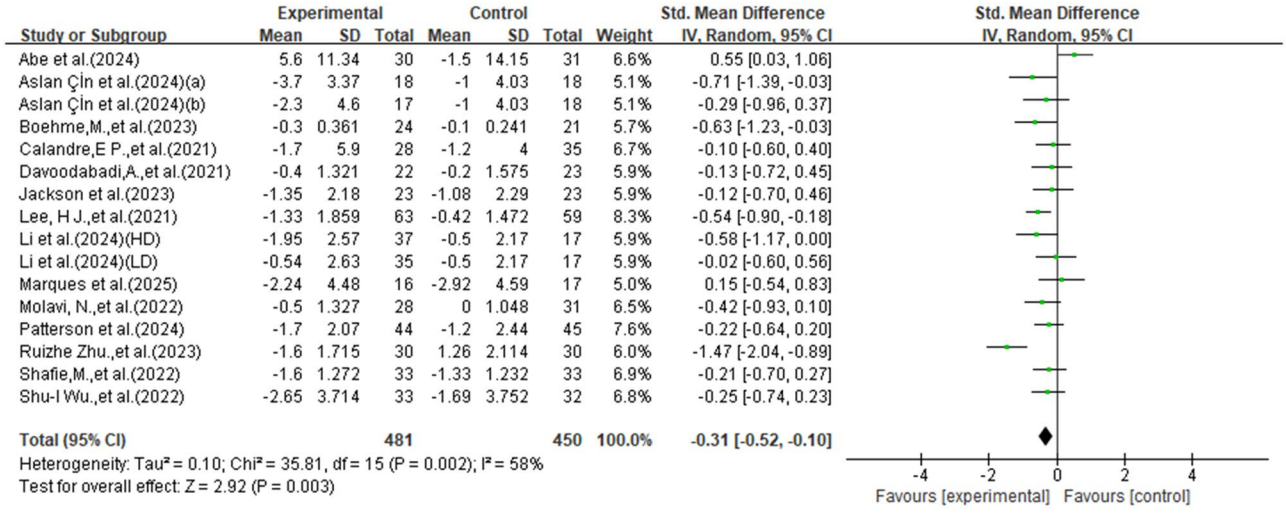

Fig. 4 Overall analysis of probiotics for sleep relief

significant reduction in anxiety scores compared with the control group, while individuals with depressive disorders did not exhibit a significant reduction (I^2 = 73%, *SMD* = − 0.48, 95% *CI*: −0.97 to 0.01, *P* = 0.06).

Subgroup analysis based on intervention duration revealed consistent beneficial effects across all groups: interventions lasting ≤ 4 weeks (I^2 = 86%, *SMD* = − 0.51, 95% *CI*: −0.93 to − 0.09, *P* = 0.02), interventions lasting between 4 and 8 weeks, including 8 weeks (I^2 = 86%, *SMD* = − 0.39, 95% *CI*: −0.72 to − 0.06, *P* = 0.02), and interventions lasting > 8 weeks (I^2 = 75%, *SMD* = − 0.28, 95% *CI*: −0.54 to − 0.02, *P* = 0.03). Overall, all three intervention durations resulted in statistically significant improvements in anxiety scores compared with the control group.

The results of subgroup analysis based on the types of probiotics are as follows: Lactobacillus Group (I^2 = 86%, *SMD* = − 0.14, 95% *CI*: −0.57 to 0.30, *P* = 0.54), Bifidobacterium Group (I^2 = 88%, *SMD* = − 0.43, 95% *CI*: −0.84 to − 0.02, *P* = 0.04), Lactobacillus Combined with Bifidobacterium Group (I^2 = 61%, *SMD* = − 0.25, 95% *CI*: −0.47 to − 0.03, *P* = 0.02), and Mixed Strains of Three or More Types (I^2 = 86%, *SMD* = − 0.72, 95% *CI*: −1.23 to − 0.20, *P* = 0.006). The pooled results revealed that the Lactobacillus group exhibited no statistically significant improvement in anxiety scale scores, whereas the other three intervention groups demonstrated significant reductions compared with the control group.

Sensitivity analysis

Sensitivity analyses were conducted using Stata 15.0 by systematically removing each included study and repeating the meta-analysis. The results remained consistent across all analyses, indicating the robustness and stability of the findings (Supplementary Materials Figure S2, S3, and S4).

Publication bias

Among the 63 studies assessing the effects of probiotics/prebiotics/synbiotics on depression outcomes, Egger's regression test indicated significant publication bias (t = − 3.30, *P* = 0.002). Trim-and-fill analysis using Stata 15.0 software identified 13 studies as potential sources of bias, but even after adjustment, the results remained statistically significant (*P* < 0.001). For the 49 studies examining anxiety outcomes, Egger's test showed no evidence of publication bias (t = − 0.91, *P* = 0.366). Additional details on the trim-and-fill results can be found in the supplementary materials Figure S5.

Discussion

In our meta-analysis, probiotics/prebiotics/synbiotics significantly improved both anxiety and depression compared with the control groups. Notably, the pooled effect on depressive symptoms (*SMD* = − 0.53; 95% *CI*: −0.67 to − 0.39) was slightly greater than that observed for anxiety scores (*SMD* = − 0.44; 95% *CI*: −0.59 to − 0.28). This difference may partly reflect disparities in data availability, as depressive symptoms were evaluated in more studies covering a broader range of intervention types (50 probiotic, 14 prebiotic, and 8 synbiotic studies), whereas anxiety outcomes were informed by fewer eligible studies (38 probiotic, 12 prebiotic, and 5 synbiotic studies). Moreover, depression outcomes included more multi-arm trials (7 three-arm and 4 four-arm trails), which probably provide richer comparative information and more stable pooled estimate. In addition, probiotic interventions also produced modest but significant improvements in sleep outcomes (*SMD* = − 0.39; 95%*CI*: −0.53, − 0.25). To further elucidate potential sources of heterogeneity, subgroup analyses and meta-regression models were performed, followed by pathophysiological interpretations of the identified moderators (Fig. 1B).

Table 1 Meta-analysis main results and subgroup analysis results

	Study number	Patient/control number	Effect sizes (95%CI)	Effect size *P* value	Heterogeneity I^2(%)
1. Main analysis					
1.1. Probiotics, Prebiotics, and synbiotics on depression	63	2880/2493	−0.53(−0.67, −0.39)	0.000***	83%
1.2. Probiotics, Prebiotics, and synbiotics on anxiety	49	2124/1788	−0.44(−0.59, −0.28)	0.000***	81%
1.3. Probiotics on sleep	12	411/378	−0.39(−0.53, −0.25)	0.000***	49%
2. Subgroup: different interventions on depression					
2.1. Groups by probiotics	50	2141/1972	−0.56(−0.74, −0.38)	0.000***	86%
2.2. Groups by prebiotics	14	558/544	−0.32(−0.53, −0.10)	0.004**	64%
2.3. Groups by synbiotics	8	205/202	−0.53(−0.91, −0.16)	0.005**	71%
3. Subgroup: probiotics on depression					
3.1. Groups by demographic characteristics					
3.1.1. Depressive symptoms of depressive disorders	10	316/304	−0.74(−1.17, −0.46)	0.000***	77%
3.1.2. Depressive symptoms of healthy people	21	823/781	−0.5(−0.76, −0.25)	0.000***	84%
3.1.3. Depressive symptoms of people with chronic illnesses	18	977/865	−0.59(−0.91, −0.27)	0.000***	90%
3.2. Groups by intervention time					
3.2.1. Time ≤ 4 W	11	553/525	−0.69(−1.05, −0.32)	0.000***	86%
3.2.2. 4 W< Time ≤ 8 W	23	754/740	−0.66(−0.95, −0.36)	0.000***	87%
3.2.3. 8 W< Time ≤ 12 W	13	714/598	−0.34(−0.50, −0.09)	0.004**	66%
3.2.4. Time > 12 W	2	120/109	−1.31(−4.55, 1.92)	0.43	99%
3.3. Groups by probiotic type					
3.3.1. Lactobacillus	12	730/600	−0.31(−0.53, −0.09)	0.005**	72%
3.3.2. Bifidobacteria	6	232/197	−0.71(−1.33, −0.10)	0.02*	89%
3.3.3. Lactobacillus + Bifidobacteria	21	718/703	−0.60(−0.90, −0.31)	0.000***	86%
3.3.4. Mixed Strains of Three or More Types	10	461/472	−0.82(−1.36, −0.29)	0.003**	92%
4. Subgroup: different interventions on anxiety					
4.1. Probiotics – Anxiety	38	1553/1376	−0.39(−0.58, −0.20)	0.000***	84%
4.2. Prebiotics – Anxiety	12	436/421	−0.57(−0.83, −0.31)	0.000***	65%
4.3. Synbiotics – Anxiety	5	135/128	−0.59(−1.03, −0.15)	0.009**	68%
5. Subgroup: probiotics on anxiety					
5.1. Groups by demographic characteristics					
5.1.1. Anxious symptoms of depressive disorders[1]	4	133/130	−0.48(−0.97, 0.01)	0.06	73%
5.1.2. Anxious symptoms of healthy people	21	749/701	−0.31(−0.59, −0.02)	0.04*	86%
5.1.3. Anxious symptoms of people with chronic illnesses	13	671/545	−0.49(−0.79, −0.20)	0.000***	83%
5.2. Groups by intervention time					
5.2.1. Time ≤ 4 W	11	384/351	−0.51(−0.93, −0.09)	0.02*	86%
5.2.2. 4 W< Time ≤ 8 W	17	577/564	−0.39(−0.72, −0.06)	0.02*	86%
5.2.3. Time > 8 W	10	592/461	−0.28(−0.54, −0.02)	0.03*	75%
5.3. Groups by probiotic type					
5.3.1. Lactobacillus	9	330/316	−0.14(−0.57, 0.30)	0.54	86%
5.3.2. Bifidobacteria	7	526/367	−0.43(−0.84, −0.02)	0.04*	88%
5.3.3. Lactobacillus + Bifidobacteria	14	466/458	−0.25(−0.47, −0.03)	0.02*	61%
5.3.4. Mixed Strains of Three or More Types	8	231/235	−0.72(−1.23, −0.20)	0.006**	86%

Note: *<0.05, **<0.01, ***<0.001; literature marked with a "1" in the upper right corner includes one article on depressive disorders co – morbid with anxiety disorders

Depression-related outcomes remained statistically significant regardless of intervention type (probiotics, prebiotics, or synbiotics), target population, or probiotic strain. Similarly, anxiety-related consistently demonstrated therapeutic benefits across different intervention types and assessment time points, supporting the robustness of these findings. However, some differential moderation patterns emerged. For depression, intervention duration was the only significant moderator, whereas for anxiety, both target population and probiotic strain significantly influenced treatment effects.

Quality of methodology

Overall, the methodological quality of the included studies was moderate but showed certain limitations. Only 14 studies (19.4%) were judged to have a low risk of bias,

while the remaining studies were rated as having "some concerns" or "high risk", mainly due to selection bias, performance bias, and detection bias, the results may be overestimated. Except for sleep outcomes, substantial heterogeneity was observed across analyses. This suggests that the pooled effect sizes likely represent an average of true effects rather than a single consistent effect. Such variability may arise from differences in study design, participant characteristics, intervention protocols, outcome measures, and contextual factors. Therefore, these findings should be interpreted with caution.

Principal findings

We found that probiotics/prebiotics/synbiotics can alleviate symptoms of anxiety and depression. Specifically, the gut microbiota can modulate brain function and behavior through the microbiota–gut–brain axis, thereby influencing mental health [7]. This axis serves as a bidirectional communication system between the gut and the brain, involving various microorganisms such as commensal, probiotic, and pathogenic bacteria [16, 98, 99]. As substrates for probiotics, prebiotics are indigestible to humans but can selectively promote the growth of beneficial bacteria, thereby improving intestinal microecological balance [100–102]. Synbiotics, combining probiotics and prebiotics, further enhance this regulatory effect on gut microbiota composition and activity [103–105]. Consequently, modulation of the gut microbiota through these interventions may influence the microbiota–gut–brain axis and contribute to the prevention or alleviation of anxiety and depression [106]. In addition, patients with depression often exhibit elevated levels of proinflammatory cytokines, and inflammatory responses may accelerate the metabolism of neurotransmitters such as serotonin (5-HT), thereby increasing the risk of depression [107–109]. Probiotics, prebiotics, and synbiotics can indirectly improve emotional symptoms by reducing proinflammatory cytokines and enhancing anti-inflammatory cytokine levels, which may be particularly beneficial for individuals with chronic inflammatory conditions [109–112]. Moreover, these supplements may promote the expression of brain-derived neurotrophic factor (BDNF) and enhance the synthesis of neurotransmitters such as γ-aminobutyric acid (GABA) and 5-HT, all of which play essential roles in the regulation of anxiety and depression [113–117].

Our findings that probiotics improve sleep quality align with previous narrative reviews [118]. This may be because probiotics can promote central serotonin and melatonin synthesis by increasing plasma levels of free tryptophan, thus ultimately improving mood and sleep rhythms simultaneously [119].

Subgroup analysis

Subgroup analysis of different intervention types on anxiety and depression

Our findings indicate that probiotics, prebiotics, and synbiotics, when administered alone, effectively alleviated symptoms of anxiety and depression. These results are consistent with previous studies reporting the beneficial effects of probiotics on mental health outcomes [8, 14, 15]. In addition, our meta-analysis showed that prebiotic supplementation improved both depressive and anxiety symptoms, in agreement with the findings of Zandifar et al., who conducted a similar meta-analysis on prebiotics and probiotics [17]. Evidence from other meta-analyses also supports the efficacy of synbiotics in reducing anxiety levels [15]. Although research on synbiotics for depression remains limited, a meta-analysis has suggested that synbiotics may enhance the expression of BDNF, thereby offering potential benefits in alleviating anxiety and depression [120].

Subgroup analysis of probiotics on anxiety and depression symptoms in different populations

The subgroup analyses indicate that probiotics may alleviate depressive symptoms across diverse population types, including depressed patients, healthy individuals, and those with chronic diseases experiencing anxiety and depression. This effect is believed to be mediated through probiotics' ability to modulate the gut-brain axis, influence neurotransmitter production, reduce inflammation, and regulate immune function, ultimately leading to a reduction in depressive symptoms. In particular, depressed individuals, who typically present with more severe symptoms at baseline, may experience more significant improvements with probiotic intervention. A systematic review of clinical trials has also reported that psychobiotic interventions significantly improved immunological and inflammatory biomarkers in patients with major depressive disorder, supporting the biological plausibility of these findings, particularly among individuals with comorbid inflammatory conditions [121]. For example, for our inclusion of patients with comorbid chronic diseases, such as patients on long-term hemodialysis who may have a microinflammatory state [122], as well as patients with diarrhea, patients with irritable bowel syndrome, and the obese population itself, can lead to altered gut flora [123–125]. By restoring microbial balance and reducing inflammation, probiotics may contribute to the alleviation of anxiety and depressive symptoms in these populations. Meanwhile, healthy individuals may benefit from probiotics by modestly modulating the gut-brain axis and neurotransmitter production, thereby alleviating depressive symptoms.

In the subgroup analysis of probiotic intervention on anxiety scores, pooled results from three studies

involving participants with depressive disorders and one study including an anxiety disorder population revealed no statistically significant difference in anxiety score changes between intervention and control groups. This lack of significance may be attributed to low baseline anxiety levels in certain studies, particularly those involving depressed patients with only mild anxiety symptoms [32, 52]. These findings suggest that the anxiolytic effects of probiotics may depend on baseline symptom severity. Therefore, future studies can systematically verify the targeting and effectiveness of probiotic interventions in patients with higher baseline anxiety or specific subclinical populations.

Subgroup analysis of probiotic intervention duration on anxiety and depression

In the subgroup analysis of anxiety, short-term (≤4 weeks), medium-term (6–8 weeks, inclusive), and long-term (>8 weeks) probiotic interventions all showed positive effects in reducing anxiety scores. However, due to clustered intervention durations in primary studies and limited evidence, consistent conclusions on probiotics' anxiety-relieving effects across different time periods require more data from well-powered trials.

For depression, short-term to medium-term probiotic interventions (≤ 12 weeks) significantly reduced depressive scores, whereas interventions lasting ≥ 12 weeks showed no significant improvement. A meta-analysis by Zhang et al. similarly reported that short-term probiotic use (< 8 weeks) significantly improved depressive symptoms [24]. One possible explanation is that shorter interventions may be associated with better adherence, which is often challenging among individuals with depression [126]. In contrast, probiotic interventions lasting ≥ 12 weeks showed no significant difference in depressive symptoms compared with controls. This may be attributed to gradual adaptation of the gut environment to long-term supplementation with the same probiotic strain, leading to reduced colonization and diminished functional benefits over time [127]. However, this subgroup included only two studies with relatively small sample sizes, and the removal of either study could reverse the direction of the effect, indicating limited result stability. Therefore, the observed differences may be attributable to random variation and should be interpreted with caution. In detail, there is an urgent need to conduct more long-term, large-scale RCTs to systematically explore the optimal intervention duration, especially for the stability and determinants of long-term effects, which is crucial to clarify its clinical application value in the management of anxiety and depression.

Subgroup analysis of different probiotic types on anxiety and depression

We found that interventions using Bifidobacterium alone, a combination of Lactobacillus and Bifidobacterium, or mixed formulations containing three or more strains all effectively improved symptoms of anxiety and depression, consistent with previous findings [14, 25, 128]. However, Lactobacillus alone significantly alleviated depressive symptoms but did not produce a significant effect on anxiety. This difference may be explained by variations in participant characteristics. Most participants in the depression subgroup were patients with major depressive disorder or chronic diseases, while those in the anxiety subgroup were mainly healthy individuals with relatively low baseline anxiety levels. As a result, the effect of Lactobacillus alone on anxiety may have been limited. At present, the number of high-quality trials directly comparing the effectiveness of single-strain and multi-strain preparations is limited, and the research methods and strain composition are heterogeneous, so it is difficult to form definite conclusions [129]. In the future, systematic studies on dose-response and formulation optimization should be prioritized to provide solid evidence for clinical development of accurate and evidence-based intervention strategies.

Limitations and advantages

Our study has several limitations. First, despite a comprehensive search strategy that spanned multiple databases, only four studies had sample sizes of more than 100 in both intervention and control groups, and most lacked follow-up assessments to verify large intervention effects over time. Second, substantial heterogeneity was observed among the included studies, which may be attributed to differences in study design, probiotic type and dosage, population characteristics, and environmental factors. To minimize heterogeneity, we excluded studies involving combined treatments other than psychotropic drugs and conducted subgroup analyses to explore potential moderators. However, because probiotics, prebiotics, and synbiotics are often used as adjunctive therapies, some participants may have received psychotropic medications concurrently. This could introduce additional variability. Moreover, prior research has shown that certain antidepressants have antibacterial properties and may interact with probiotics [130], potentially confounding results related to mental health outcomes. In addition, variations in the assessment tools used to measure anxiety and depression could influence the combined effect sizes, even after standardization, as different instruments emphasize distinct symptom dimensions. Individual differences in lifestyle and environmental factors may further contribute to inconsistencies in intervention effects. Moreover, our study focused solely on

research published in English. This language restriction may have excluded relevant research published in other languages, potentially introducing publication bias. Positive findings are more likely to be published than null or negative results, which may have led to an overestimation of the true effects of probiotics, prebiotics, and synbiotics. Finally, since the analysis of sleep index was an additional analysis content of the included studies, no special systematic retrieval was conducted for this index, and the reliability of the results needs to be carefully evaluated.

Despite these limitations, our study also has several strengths. In detail, our meta-analysis includes a large number of studies, ensuring comprehensiveness, representativeness, and enhancing the credibility and generalizability of the results. Additionally, we conducted a thorough analysis of probiotics, prebiotics, and synbiotics in alleviating anxiety and depression, as well as subgroup analyses of probiotics from different perspectives to explore factors influencing their effectiveness. Finally, we found a positive effect of probiotics on improving sleep, providing additional evidence of their beneficial effects.

Implication

Future studies can employ large and highly homogeneous sample recruitment strategies, develop long-term follow-up study protocols, and conduct multi-arm trials if necessary to evaluate the specific benefits of long-term interventions, as well as specific drug-microbiome interactions or complementary effects. At the same time, we also call for future systematic reviews to comprehensively search multilingual literature to assess the potential impact of language bias, and to develop targeted search strategies to explore the specific mechanisms of probiotics on sleep to address the limitations of this study.

Conclusion

The findings of this meta-analysis indicate that probiotics, prebiotics, and synbiotics have beneficial effects on anxiety and depression symptoms. However, the efficacy of probiotics appears to vary depending on the target population, intervention duration, and specific strains administered. Probiotics also contribute to improving sleep quality. Although these findings suggest potential strategies for adjunctive treatment of mental health and sleep disorders, the presence of publication bias in depression-related outcomes suggests that the true effects may be overestimated. Therefore, these results need to be interpreted with caution. Future studies should conduct more high-quality RCTs with large sample size and long-term follow-up to further verify the findings of this study and provide more precise recommendations for clinical practice.

Abbreviations

CBT	Cognitive behavioral therapy
PROSPERO	International Prospective Register of Systematic Reviews
SMD	Standardized mean difference
CIs	Confidence intervals
RCTs	Randomized controlled trials
5-HT	Serotonin
BDNF	Brain-derived neurotrophic factor
GABA	γ-aminobutyric acid

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-07644-z.

Supplementary Material 1

Acknowledgements

We would like to express our gratitude to all of the authors of the studies included in our systematic review and meta-analysis.

Author contributions

Conceptualization, Z.X.W, H.R.Z; data curation, J.L.Z, L.Q.Z, and Q.M; formal analysis, L.Q.Z; funding acquisition, H.R.Z; investigation, J.L.Z, L.Q.Z, and Q.M; methodology, Z.X.W, H.R.Z; project administration, J.L.Z, L.Q.Z; software, J.L.Z, L.Q.Z; Visualization: J.L.Z, L.Q.Z, and Q.M; writing-original draft, J.L.Z; writing-review and editing, Z.X.W, H.R.Z. All authors have read and agreed to the published version of the manuscript.

Funding

This study was financially supported by the National Natural Science Foundation of China (Grant No. 82171513); Clinical Research Innovation Project from West China Hospital, Sichuan University (Grant No. 2019HXCX03).

Data availability

All data generated or analyzed during this study are available from the corresponding author with a reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Mental Health Center, National Center for Mental Disorders, West China Hospital/West China School of Medicine, Sichuan University, Chengdu 610041, China
[2]Sichuan Provincial Center for Mental Health, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu 610072, China

Received: 17 May 2025 / Accepted: 17 November 2025
Published online: 27 November 2025

References

1. World Health Organization. Anxiety disorders. 2025. https://www.who.int/news-room/fact-sheets/detail/anxiety-disorders. Accessed 25 Oct 2025.
2. World Health Organization. Depression. 2025. https://www.who.int/news-room/fact-sheets/detail/depression. Accessed 25 Oct 2025.
3. Doran CM, Kinchin I. A review of the economic impact of mental illness. Aust Health Rev. 2019;43(1):43–8.

4. Ashton AK, Jamerson BD, Wagoner LWW. Antidepressant-related adverse effects impacting treatment compliance: results of a patient survey. Curr Ther Res Clin E. 2005;66(2):96–106.
5. Shin E, Renzi D, Canales C, Ravichandran C, McDougle CJ, Thom RP. Buspirone for the treatment of anxiety in Williams syndrome: a retrospective chart review study. Expert Opin Pharmaco. 2024;25(1):113–20.
6. Yarwood B, Taylor R, Angelakis I. User experiences of CBT for anxiety and depression: a qualitative systematic review and meta-synthesis. Community Ment Hlt J. 2024;60(4):662–71.
7. Loughman A, Ponsonby AL, O'Hely M, Symeonides C, Collier F, Tang M, Carlin J, Ranganathan S, Allen K, Pezic A, et al. Gut microbiota composition during infancy and subsequent behavioural outcomes. Ebiomedicine. 2020;52:102640.
8. Liu RT. The Microbiome as a novel paradigm in studying stress and mental health. Am Psychol. 2017;72(7):655–67.
9. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S, et al. Expert consensus document. The international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastro Hepat. 2014;11(8):506–14.
10. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, Scott K, Stanton C, Swanson KS, Cani PD, et al. Expert consensus document: the international scientific association for probiotics and prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nat Rev Gastro Hepat. 2017;14(8):491–502.
11. Swanson KS, Gibson GR, Hutkins R, Reimer RA, Reid G, Verbeke K, Scott KP, Holscher HD, Azad MB, Delzenne NM, et al. The international scientific association for probiotics and prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics. Nat Rev Gastro Hepat. 2020;17(11):687–701.
12. Ng QX, Peters C, Ho C, Lim DY, Yeo WS. A meta-analysis of the use of probiotics to alleviate depressive symptoms. J Affect Disorders. 2018;228:13–9.
13. Liu RT, Walsh R, Sheehan AE. Prebiotics and probiotics for depression and anxiety: a systematic review and meta-analysis of controlled clinical trials. Neurosci Biobehav R. 2019;102:13–23.
14. Goh KK, Liu YW, Kuo PH, Chung YE, Lu ML, Chen CH. Effect of probiotics on depressive symptoms: a meta-analysis of human studies. Psychiat Res. 2019;282:112568.
15. Zhao Z, Xiao G, Xia J, Guo H, Yang X, Jiang Q, Wang H, Hu J, Zhang C. Effectiveness of probiotic/prebiotic/synbiotic treatments on anxiety: A systematic review and meta-analysis of randomized controlled trials. J Affect Disorders. 2023;343:9–21.
16. Allen AP, Hutch W, Borre YE, Kennedy PJ, Temko A, Boylan G, Murphy E, Cryan JF, Dinan TG, Clarke G. Bifidobacterium longum 1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. Transl Psychiat. 2016;6(11):e939.
17. Zandifar A, Badrfam R, Mohammaditabar M, Kargar B, Goodarzi S, Hajialigol A, Ketabforoush S, Heidari A, Fathi H, Shafiee A, et al. The effect of prebiotics and probiotics on levels of depression, anxiety, and cognitive function: a meta-analysis of randomized clinical trials. Brain Behav. 2025;15(3):e70401.
18. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. BMJ-Brit Med J. 2011;343:d5928.
19. Da CB, Juni P. Systematic reviews and meta-analyses of randomized trials: principles and pitfalls. Eur Heart J. 2014;35(47):3336–45.
20. Rücker G, Cates CJ, Schwarzer G. Methods for including information from multi-arm trials in pairwise meta-analysis. Res Synth Methods. 2017;8(4):392–403.
21. Egger M, Davey SG, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ-Brit Med J. 1997;315(7109):629–34.
22. Colditz GA, Burdick E, Mosteller F. Heterogeneity in meta-analysis of data from epidemiologic studies: a commentary. Am J Epidemiol. 1995;142(4):371–82.
23. Liu B, He Y, Wang M, Liu J, Ju Y, Zhang Y, Liu T, Li L, Li Q. Efficacy of probiotics on anxiety-A meta-analysis of randomized controlled trials. Depress Anxiety. 2018;35(10):935–45.
24. Zhang Q, Chen B, Zhang J, Dong J, Ma J, Zhang Y, Jin K, Lu J. Effect of prebiotics, probiotics, synbiotics on depression: results from a meta-analysis. BMC Psychiatry. 2023;23(1):477.
25. Yang Y, Yang L, Wan M, Pan D, Sun G, Yang C. Assessment of optimal combinations of therapeutic probiotics for depression, anxiety, and stress. Psychol Med. 2024;54(10):2547–61.
26. Akkasheh G, Kashani-Poor Z, Tajabadi-Ebrahimi M, Jafari P, Akbari H, Taghizadeh M, Memarzadeh MR, Asemi Z, Esmaillzadeh A. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: a randomized, double-blind, placebo-controlled trial. Nutrition. 2016;32(3):315–20.
27. Ayubi E, Abdoli S, Mehrpooya M, Karami Z, Jenabi E, Ghaleiha A, Soltani F, Salehi AM. The effect of probiotic administration on the severity of menopausal symptoms and mental health of postmenopausal women: a triple-blind randomized controlled trial in the West of Iran. Menopause. 2025;32(2):166–73.
28. Baião R, Capitão LP, Higgins C, Browning M, Harmer CJ, Burnet P. Multispecies probiotic administration reduces emotional salience and improves mood in subjects with moderate depression: a randomised, double-blind, placebo-controlled study. Psychol Med. 2023;53(8):3437–47.
29. Boehme M, Rémond-Derbez N, Lerond C, Lavalle L, Keddani S, Steinmann M, Rytz A, Dalile B, Verbeke K, Van Oudenhove L, et al. Bifidobacterium longum subsp. longum reduces perceived psychological stress in healthy adults: an exploratory clinical trial. Nutrients. 2023;15(14).
30. Calandre EP, Hidalgo-Tallon J, Molina-Barea R, Rico-Villademoros F, Molina-Hidalgo C, Garcia-Leiva JM, Carrillo-Izquierdo MD, Slim M. The Probiotic VSL#3(®) Does not seem to be efficacious for the treatment of gastrointestinal symptomatology of patients with fibromyalgia: a randomized, double-blind, placebo-controlled clinical trial. Pharmaceut-Base. 2021;14(10).
31. Cannavale CN, Mysonhimer AR, Bailey MA, Cohen NJ, Holscher HD, Khan NA. Consumption of a fermented dairy beverage improves hippocampal-dependent relational memory in a randomized, controlled cross-over trial. Nutr Neurosci. 2023;26(3):265–74.
32. Chahwan B, Kwan S, Isik A, van Hemert S, Burke C, Roberts L. Gut feelings: A randomised, triple-blind, placebo-controlled trial of probiotics for depressive symptoms. J Affect Disorders. 2019;253:317–26.
33. Davoodabadi A, Rohani SH, Hajian A. Effects of the oral probiotics to control pain and stress disorders of cyclical mastalgia associated with fibrocystic breast changes; a randomised controlled trial. Int J Surg Open. 2021;33.
34. Dawe JP, McCowan L, Wilson J, Okesene-Gafa K, Serlachius AS. Probiotics and maternal mental health: a randomised controlled trial among pregnant women with obesity. Sci REP-UK. 2020;10(1):1291.
35. Eskandarzadeh S, Effatpanah M, Khosravi-Darani K, Askari R, Hosseini AF, Reisian M, Jazayeri S. Efficacy of a multispecies probiotic as adjunctive therapy in generalized anxiety disorder: a double blind, randomized, placebo-controlled trial. Nutr Neurosci. 2021;24(2):102–8.
36. Gawlik-Kotelnicka O, Margulska A, Płeska K, Skowrońska A, Strzelecki D. Metabolic status influences probiotic efficacy for depression-PRO-DEMET randomized clinical trial results. Nutrients. 2024;16(9).
37. Hashemi-Mohammadabad N, Taghavi SA, Lambert N, Moshtaghi R, Bazargan-ipour F, Sharifi M. Adjuvant administration of probiotic effects on sexual function in depressant women undergoing SSRIs treatment: a double-blinded randomized controlled trial. BMC Psychiatry. 2024;24(1):44.
38. Kelly JR, Allen AP, Temko A, Hutch W, Kennedy PJ, Farid N, Murphy E, Boylan G, Bienenstock J, Cryan JF, et al. Lost in translation? The potential psychobiotic Lactobacillus rhamnosus (JB-1) fails to modulate stress or cognitive performance in healthy male subjects. Brain Behav Immun. 2017;61:50–9.
39. Kitaoka K, Uchida K, Okamoto N, Chikahisa S, Miyazaki T, Takeda E, Séi H. Fermented ginseng improves the first-night effect in humans. Sleep. 2009;32(3):413–21.
40. Kouchaki E, Tamtaji OR, Salami M, Bahmani F, Daneshvar KR, Akbari E, Tajabadi-Ebrahimi M, Jafari P, Asemi Z. Clinical and metabolic response to probiotic supplementation in patients with multiple sclerosis: a randomized, double-blind, placebo-controlled trial. Clin Nutr. 2017;36(5):1245–9.
41. Lee DS, Kim M, Nam SH, Kang MS, Lee SA. Effects of oral probiotics on subjective Halitosis, oral health, and psychosocial health of college students: a randomized, double-blind, placebo-controlled study. Int J Env Res Pub He. 2021;18(3).
42. Lee HJ, Hong JK, Kim JK, Kim DH, Jang SW, Han SW, Yoon IY. Effects of probiotic NVP-1704 on mental health and sleep in healthy adults: an 8-week randomized, double-blind, placebo-controlled trial. Nutrients. 2021;13(8).
43. Li J, Li Y, Zhao J, Li L, Wang Y, Chen F, Li Y, Cheng R, He F, Ze X, et al. Effects of bifidobacterium Breve 207-1 on regulating lifestyle behaviors and mental wellness in healthy adults based on the microbiome-gut-brain axis: a randomized, double-blind, placebo-controlled trial. Eur J Nutr. 2024;63(7):2567–85.
44. Lyra A, Hillilä M, Huttunen T, Männikkö S, Taalikka M, Tennilä J, Tarpila A, Lahtinen S, Ouwehand AC, Veijola L. Irritable bowel syndrome symptom severity improves equally with probiotic and placebo. World J Gastroentero. 2016;22(48):10631–42.

45. Marcos A, Wärnberg J, Nova E, Gómez S, Alvarez A, Alvarez R, Mateos JA, Cobo JM. The effect of milk fermented by yogurt cultures plus Lactobacillus casei DN-114001 on the immune response of subjects under academic examination stress. Eur J Nutr. 2004;43(6):381–9.
46. Marques CG, Dos SQM, França FC, Alves CF, Nakamoto FP, Lucin GA, Oumatu MA, Mendes GL, Alvares LA, Thomatieli-Santos RV. Effect of caloric restriction with probiotic supplementation on body composition, quality of life, and Psychobiological factors of obese men: a randomized, double-blinded placebo-controlled clinical trial. Clin Nutr. 2025;45:234–49.
47. Messaoudi M, Lalonde R, Violle N, Javelot H, Desor D, Nejdi A, Bisson JF, Rougeot C, Pichelin M, Cazaubiel M, et al. Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and bifidobacterium longum R0175) in rats and human subjects. Brit J Nutr. 2011;105(5):755–64.
48. Moludi J, Alizadeh M, Mohammadzad M, Davari M. 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. Psychosom Med. 2019;81(9):770–7.
49. Moschonis G, Sarapis K, Resciniti S, Hall R, Yim K, Tonkovic M, Fitzgerald C, Anixiadis F, Vinh A, Dinh Q, et al. Evaluation of a probiotic blend on psychosocial health and biomarkers of inflammatory, immune and stress response in adults with subthreshold depression: a double-blind, randomised, placebo-controlled trial. Brit J Nutr. 2024;1:1–15.
50. Mullish BH, Michael DR, Dabcheva M, Webberley TS, Coates N, John DA, Wang D, Luo Y, Plummer SF, Marchesi JR. A double-blind, randomized, placebo-controlled study assessing the impact of probiotic supplementation on the symptoms of irritable bowel syndrome in females. Neurogastroent Motil. 2024;36(4):e14751.
51. Mutoh N, Kakiuchi I, Hiraku A, Iwabuchi N, Kiyosawa K, Igarashi K, Tanaka M, Nakamura M, Miyasaka M. Heat-killed Lactobacillus helveticus improves mood states: a randomised, double-blind, placebo-controlled study. Benef Microbes. 2023;14(2):109–18.
52. Nikolova VL, Cleare AJ, Young AH, Stone JM. Acceptability, Tolerability, and estimates of putative treatment effects of probiotics as adjunctive treatment in patients with depression: a randomized clinical trial. Jama Psychiat. 2023;80(8):842–7.
53. Nisaa AA, Mageswary U, Pei X, Kadir MN, Oon CE, Rajendran D, Tan JJ, Roslan FF, Balasubramaniam SD, Sany S, et al. Probiotic enhanced immunity and mental wellbeing of generally healthy women: a randomised, placebo-controlled and double-blind study. Benef Microbes. 2025:1–18.
54. Noori M, Shateri Z, Babajafari S, Eskandari MH, Parastouei K, Ghasemi M, Afshari H, Samadi M. The effect of probiotic-fortified kefir on depression, appetite, oxidative stress, and inflammatory parameters in Iranian overweight and obese elderly: a randomized, double-blind, placebo-controlled clinical trial. J Health Popul Nutr. 2025;44(1):30.
55. Östlund-Lagerström L, Kihlgren A, Repsilber D, Björkstén B, Brummer RJ, Schoultz I. Probiotic administration among free-living older adults: a double blinded, randomized, placebo-controlled clinical trial. Nutr J. 2016;15(1):80.
56. Patterson E, Tan H, Groeger D, Andrews M, Buckley M, Murphy EF, Groeger JA. Bifidobacterium longum 1714 improves sleep quality and aspects of well-being in healthy adults: a randomized, double-blind, placebo-controlled clinical trial. Sci REP-UK. 2024;14(1):3725.
57. Pinto-Sanchez MI, Hall GB, Ghajar K, Nardelli A, Bolino C, Lau JT, Martin FP, Cominetti O, Welsh C, Rieder A, et al. Probiotic bifidobacterium longum NCC3001 reduces depression scores and alters brain activity: a pilot study in patients with irritable bowel syndrome. Gastroenterology. 2017;153(2):448–59.
58. Rahimlou M, Hosseini SA, Majdinasab N, Haghighizadeh MH, Husain D. Effects of long-term administration of multi-strain probiotic on circulating levels of BDNF, NGF, IL-6 and mental health in patients with multiple sclerosis: a randomized, double-blind, placebo-controlled trial. Nutr Neurosci. 2022;25(2):411–22.
59. Reale M, Boscolo P, Bellante V, Tarantelli C, Di Nicola M, Forcella L, Li Q, Morimoto K, Muraro R. Daily intake of Lactobacillus casei Shirota increases natural killer cell activity in smokers. Brit J Nutr. 2012;108(2):308–14.
60. Roman P, Estévez AF, Miras A, Sánchez-Labraca N, Cañadas F, Vivas AB, Cardona D. A pilot randomized controlled trial to explore cognitive and emotional effects of probiotics in fibromyalgia. Sci REP-UK. 2018;8(1):10965.
61. Romijn AR, Rucklidge JJ, Kuijer RG, Frampton C. A double-blind, randomized, placebo-controlled trial of Lactobacillus helveticus and bifidobacterium longum for the symptoms of depression. Aust Nz J Psychiat. 2017;51(8):810–21.
62. Rudzki L, Ostrowska L, Pawlak D, Małus A, Pawlak K, Waszkiewicz N, Szulc A. Probiotic Lactobacillus plantarum 299v decreases kynurenine concentration and improves cognitive functions in patients with major depression: a double-blind, randomized, placebo controlled study. Psychoneuroendocrino. 2019;100:213–22.
63. Ruiz-Gonzalez C, Cardona D, Rueda-Ruzafa L, Rodriguez-Arrastia M, Ropero-Padilla C, Roman P. Cognitive and emotional effect of a multi-species probiotic containing *Lactobacillus rhamnosus* and *Bifidobacterium lactis* in healthy older adults: a double-blind randomized placebo-controlled crossover trial. Probiotics Antimicro. 2024.
64. Sarkawi M, Raja AR, Abdul WN, Abdul RN, Mokhtar NM. A randomized, double-blinded, placebo-controlled clinical trial on Lactobacillus-containing cultured milk drink as adjuvant therapy for depression in irritable bowel syndrome. Sci REP-UK. 2024;14(1):9478.
65. Sashihara T, Nagata M, Mori T, Ikegami S, Gotoh M, Okubo K, Uchida M, Itoh H. Effects of Lactobacillus gasseri OLL2809 and α-lactalbumin on university-student athletes: a randomized, double-blind, placebo-controlled clinical trial. Appl Physiol Nutr Me. 2013;38(12):1228–35.
66. Srivastava S, Basak U, Naghibi M, Vijayakumar V, Parihar R, Patel J, Jadon PS, Pandit A, Dargad RR, Khanna S, et al. A randomized double-blind, placebo-controlled trial to evaluate the safety and efficacy of live bifidobacterium longum CECT 7347 (ES1) and heat-treated bifidobacterium longum CECT 7347 (HT-ES1) in participants with diarrhea-predominant irritable bowel syndrome. Gut Microbes. 2024;16(1):2338322.
67. Steenbergen L, Sellaro R, van Hemert S, Bosch JA, Colzato LS. A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. Brain Behav Immun. 2015;48:258–64.
68. Tanihiro R, Yuki M, Sakano K, Sasai M, Sawada D, Ebihara S, Hirota T. Effects of heat-treated *Lactobacillus helveticus* CP790-fermented milk on gastrointestinal health in healthy adults: a randomized double-blind placebo-controlled trial. Nutrients. 2024;16(14).
69. Tian P, Chen Y, Zhu H, Wang L, Qian X, Zou R, Zhao J, Zhang H, Qian L, Wang Q, et al. Bifidobacterium Breve CCFM1025 attenuates major depression disorder via regulating gut Microbiome and Tryptophan metabolism: a randomized clinical trial. Brain Behav Immun. 2022;100:233–41.
70. Walden KE, Moon JM, Hagele AM, Allen LE, Gaige CJ, Krieger JM, Jäger R, Mumford PW, Pane M, Kerksick CM. A randomized controlled trial to examine the impact of a multi-strain probiotic on self-reported indicators of depression, anxiety, mood, and associated biomarkers. Front Nutr. 2023;10:1219313.
71. Wang Y, Wang Y, Ding K, Liu Y, Liu D, Chen W, Zhang X, Luo C, Zhang H, Xu T, et al. Effectiveness of Psychobiotic Bifidobacterium breve BB05 in managing Psychosomatic Diarrhea in college students by regulating Gut Microbiota: a randomized, double-blind, placebo-controlled trial. Nutrients. 2024;16(13).
72. Wang Y, Zhang X, Wang Y, Lu L, Wei R, Xu B, Hu X, Jiang X, Du L. Effects of combined live Bifidobacterium, Lactobacillus, Enterococcus and Bacillus cereus tablets on post-stroke depression and serum inflammatory factorse. Discov Med. 2023;35(176):312–20.
73. Wu SI, Wu CC, Cheng LH, Noble SW, Liu CJ, Lee YH, Lin CJ, Hsu CC, Chen WL, Tsai PJ, et al. Psychobiotic supplementation of HK-PS23 improves anxiety in highly stressed clinical nurses: a double-blind randomized placebo-controlled study. Food Funct. 2022;13(17):8907–19.
74. Zhang X, Chen S, Zhang M, Ren F, Ren Y, Li Y, Liu N, Zhang Y, Zhang Q, Wang R. Effects of fermented milk containing *Lacticaseibacillus paracasei* strain Shirota on constipation in patients with depression: a randomized, double-blind, placebo-controlled trial. Nutrients. 2021;13(7).
75. Zhu R, Fang Y, Li H, Liu Y, Wei J, Zhang S, Wang L, Fan R, Wang L, Li S, et al. Psychobiotic Lactobacillus plantarum JYLP-326 relieves anxiety, depression, and insomnia symptoms in test anxious college via modulating the gut microbiota and its metabolism. Front Immunol. 2023;14:1158137.
76. Abe A, Kapoor MP, Morishima S, Ozeki M, Sato N, Takara T, Naito Y. Effectiveness of partially hydrolyzed guar gum on cognitive function and sleep efficiency in healthy elderly subjects in a randomized, double-blind, placebo-controlled, and parallel-group study. Nutrients. 2024;16(8).
77. Hall CV, Hepsomali P, Dalile B, Scapozza L, Gurry T. Effects of a diverse prebiotic fibre blend on inflammation, the gut microbiota and affective symptoms in metabolic syndrome: a pilot open-label randomised controlled trial. Brit J Nutr. 2024;132(8):1002–13.
78. Jackson PP, Wijeyesekera A, Williams CM, Theis S, van Harsselaar J, Rastall RA. Inulin-type Fructans and 2'fucosyllactose alter both microbial composition and appear to alleviate stress-induced mood state in a working population compared to placebo (maltodextrin): the EFFICAD Trial, a randomized, controlled trial. Am J Clin Nutr. 2023;118(5):938–55.

79. Khademi F, Tutunchi H, Vaghef-Mehrabani E, Ebrahimi-Mameghani M. The effect of prebiotic supplementation on serum levels of Tryptophan and kynurenine in obese women with major depressive disorder: a double-blinded placebo-controlled randomized clinical trial. BMC Res Notes. 2024;17(1):316.
80. Mysonhimer AR, Cannavale CN, Bailey MA, Khan NA, Holscher HD. Prebiotic consumption alters microbiota but not biological markers of stress and inflammation or mental health symptoms in healthy adults: a randomized, controlled, crossover trial. J Nutr. 2023;153(4):1283–96.
81. Schmidt K, Cowen PJ, Harmer CJ, Tzortzis G, Errington S, Burnet PW. Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers. Psychopharmacol. 2015;232(10):1793–801.
82. Silk DB, Davis A, Vulevic J, Tzortzis G, Gibson GR. Clinical trial: the effects of a trans-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. Aliment Pharm Ther. 2009;29(5):508–18.
83. Smith AP. The concept of well-being: relevance to nutrition research. Brit J Nutr. 2005;93(Suppl 1):S1–5.
84. Smith AP, Sutherland D, Hewlett P. An investigation of the acute effects of oligofructose-enriched inulin on subjective wellbeing, mood and cognitive performance. Nutrients. 2015;7(11):8887–8896.
85. Vajdi M, Khorvash F, Askari G. A randomized, double-blind, placebo-controlled parallel trial to test the effect of inulin supplementation on migraine headache characteristics, quality of life and mental health symptoms in women with migraine. Food Funct. 2024;15(19):10088–98.
86. Vulevic J, Tzortzis G, Juric A, Gibson GR. Effect of a prebiotic galactooligosaccharide mixture (B-GOS®) on gastrointestinal symptoms in adults selected from a general population who suffer with bloating, abdominal pain, or flatulence. Neurogastroent Motil. 2018;30(11):e13440.
87. Bozdogan FBK, Kabaran S, Tazeoglu A. Effect of probiotic supplementation on maternal depression, anxiety and attachment in gestational diabetes by improving mediterranean diet quality: a randomized controlled trial. Clin Exp Obstet Gyn. 2024;51(11).
88. Ghorbani Z, Nazari S, Etesam F, Nourimajd S, Ahmadpanah M, Jahromi SR. The effect of synbiotic as an adjuvant therapy to Fluoxetine in moderate depression: a randomized multicenter trial. Arch Neurosci. 2018;5(2):e60507.
89. Hadi A, Sepandi M, Marx W, Moradi S, Parastouei K. Clinical and psychological responses to synbiotic supplementation in obese or overweight adults: a randomized clinical trial. Complement Ther Med. 2019;47:102216.
90. Louzada ER, Ribeiro S. Synbiotic supplementation, systemic inflammation, and symptoms of brain disorders in elders: a secondary study from a randomized clinical trial. Nutr Neurosci. 2020;23(2):93–100.
91. Ramezani M, Reisian M, Sajadi HZ. The effect of synbiotic supplementation on hypothyroidism: a randomized double-blind placebo controlled clinical trial. PLoS One. 2023;18(2):e277213.
92. Aslan ÇN, Açik M, Tertemİz OF, Aktan Ç, Akçali DT, Çakiroğlu FP, Özçelİk AÖ. Effect of prebiotic and probiotic supplementation on reduced pain in patients with fibromyalgia syndrome: a double-blind, placebo-controlled randomized clinical trial. Psychol Health Med. 2024;29(3):528–41.
93. Heidarzadeh-Rad N, Gökmen-Özel H, Kazemi A, Almasi N, Djafarian K. Effects of a psychobiotic supplement on serum Brain-derived neurotrophic factor levels in depressive patients: a post hoc analysis of a randomized clinical trial. J Neurogastroenterol. 2020;26(4):486–95.
94. Kazemi A, Noorbala AA, Azam K, Eskandari MH, Djafarian K. Effect of probiotic and prebiotic vs placebo on psychological outcomes in patients with major depressive disorder: a randomized clinical trial. Clin Nutr. 2019;38(2):522–8.
95. Haghighat N, Mohammadshahi M, Shayanpour S, Haghighizadeh MH, Rahmdel S, Rajaei M. The effect of synbiotic and probiotic supplementation on mental health parameters in patients undergoing hemodialysis: a double-blind, randomized, placebo-controlled trial. Indian J Nephrol. 2021;31(2):149–56.
96. Freijy TM, Cribb L, Oliver G, Metri NJ, Opie RS, Jacka FN, Hawrelak JA, Ruckliddge JJ, Ng CH, Sarris J. Effects of a high-prebiotic diet versus probiotic supplements versus synbiotics on adult mental health: the gut feelings randomised controlled trial. Front Neurosci-Switz. 2022;16:1097278.
97. Moludi J, Khedmatgozar H, Nachvak SM, Abdollahzad H, Moradinazar M, Sadeghpour TA. The effects of co-administration of probiotics and prebiotics on chronic inflammation, and depression symptoms in patients with coronary artery diseases: a randomized clinical trial. Nutr Neurosci. 2022;25(8):1659–68.
98. Collins SM, Surette M, Bercik P. The interplay between the intestinal microbiota and the brain. Nat Rev Microbiol. 2012;10(11):735–42.
99. Saccarello A, Montarsolo P, Massardo I, Picciotto R, Pedemonte A, Castagnaro R, Brasesco PC, Guida V, Picco P, Fioravanti P, et al. Oral administration of S-Adenosylmethionine (SAMe) and *Lactobacillus plantarum* HEAL9 improves the mild-to-moderate symptoms of depression: a randomized, double-blind, placebo-controlled study. Prim Care Companion CNS Disord. 2020;22(4).
100. Nyangale EP, Farmer S, Keller D, Chernoff D, Gibson GR. Effect of prebiotics on the fecal microbiota of elderly volunteers after dietary supplementation of Bacillus coagulans GBI-30, 6086. Anaerobe. 2014;30:75–81.
101. Ramnani P, Costabile A, Bustillo AG, Gibson GR. A randomised, double- blind, cross-over study investigating the prebiotic effect of agave fructans in healthy human subjects. J Nutr Sci. 2015;4:e10.
102. Vulevic J, Juric A, Walton GE, Claus SP, Tzortzis G, Toward RE, Gibson GR. Influence of galacto-oligosaccharide mixture (B-GOS) on gut microbiota, immune parameters and metabonomics in elderly persons. Brit J Nutr. 2015;114(4):586–95.
103. Jung S, Kim KM, Youn SM, Kim KN. A randomized, double-blind, placebo-controlled trial to evaluate the effects of multi-strain synbiotic in patients with functional diarrhea and high fecal calprotectin levels: a pilot study. Nutrients. 2022;14(23).
104. Saulnier DM, Gibson GR, Kolida S. In vitro effects of selected synbiotics on the human faecal microbiota composition. FEMS Microbiol Ecol. 2008;66(3):516–27.
105. van Zanten GC, Krych L, Röytiö H, Forssten S, Lahtinen SJ, Abu AW, Sørensen S, Svensson B, Jespersen L, Jakobsen M. Synbiotic Lactobacillus acidophilus NCFM and cellobiose does not affect human gut bacterial diversity but increases abundance of lactobacilli, bifidobacteria and branched-chain fatty acids: a randomized, double-blinded cross-over trial. FEMS Microbiol Ecol. 2014;90(1):225–36.
106. Pascale A, Marchesi N, Govoni S, Barbieri A. Targeting the microbiota in pharmacology of psychiatric disorders. Pharmacol Res. 2020;157:104856.
107. Beurel E, Toups M, Nemeroff CB. The bidirectional relationship of depression and inflammation: double trouble. Neuron. 2020;107(2):234–56.
108. Chu AL, Hickman M, Steel N, Jones PB, Davey SG, Khandaker GM. Inflammation and depression: a public health perspective. Brain Behav Immun. 2021;95:1–3.
109. McLoughlin RF, Berthon BS, Jensen ME, Baines KJ, Wood LG. Short-chain fatty acids, prebiotics, synbiotics, and systemic inflammation: a systematic review and meta-analysis. Am J Clin Nutr. 2017;106(3):930–45.
110. Desbonnet L, Garrett L, Clarke G, Kiely B, Cryan JF, Dinan TG. Effects of the probiotic bifidobacterium infantis in the maternal separation model of depression. Neuroscience. 2010;170(4):1179–88.
111. Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. Nat Rev Gastro Hepat. 2019;16(10):605–16.
112. Wall R, Ross RP, Shanahan F, O'Mahony L, Kiely B, Quigley E, Dinan TG, Fitzgerald G, Stanton C. Impact of administered bifidobacterium on murine host fatty acid composition. Lipids. 2010;45(5):429–36.
113. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, Cryan JF. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. P Natl Acad Sci USA. 2011;108(38):16050–5.
114. Haghighat N, Rajabi S, Mohammadshahi M. Effect of synbiotic and probiotic supplementation on serum brain-derived neurotrophic factor level, depression and anxiety symptoms in Hemodialysis patients: a randomized, double-blinded, clinical trial. Nutr Neurosci. 2021;24(6):490–9.
115. Matin S, Dadkhah M. BDNF/CREB signaling pathway contribution in depression pathogenesis: A survey on the non-pharmacological therapeutic opportunities for gut microbiota dysbiosis. Brain Res Bull. 2024;207:110882.
116. Pokusaeva K, Johnson C, Luk B, Uribe G, Fu Y, Oezguen N, Matsunami RK, Lugo M, Major A, Mori-Akiyama Y, et al. GABA-producing bifidobacterium dentium modulates visceral sensitivity in the intestine. Neurogastroent Motil. 2017;29(1).
117. Yano JM, Yu K, Donaldson GP, Shastri GG, Ann P, Ma L, Nagler CR, Ismagilov RF, Mazmanian SK, Hsiao EY. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell. 2015;161(2):264–76.
118. Haarhuis JE, Kardinaal A, Kortman G. Probiotics, prebiotics and postbiotics for better sleep quality: a narrative review. Benef Microbes. 2022;13(3):169–82.
119. Chen Y, Xu J, Chen Y. Regulation of neurotransmitters by the gut microbiota and effects on cognition in neurological disorders. Nutrients. 2021;13(6).
120. Foshati S, Akhlaghi M, Babajafari S. The effect of pro-/synbiotic supplementation on the brain-derived neurotrophic factor: a systematic review and meta-analysis of randomized controlled trials. Food Funct. 2022;13(17):8754–65.
121. Ribera C, Sánchez-Ortí JV, Clarke G, Marx W, Mörkl S, Balanzá-Martínez V. Probiotic, prebiotic, synbiotic and fermented food supplementation in

psychiatric disorders: a systematic review of clinical trials. Neurosci Biobehav R. 2024;158:105561.
122. Li J, Li H, Deng W, Meng L, Gong W, Yao H. The effect of combination use of hemodialysis and hemoperfusion on microinflammation in elderly patients with maintenance hemodialysis. Blood Purificat. 2022;51(9):739–46.
123. Li Y, Xia S, Jiang X, Feng C, Gong S, Ma J, Fang Z, Yin J, Yin Y. Gut microbiota and diarrhea: an updated review. Front Cell Infect Mi. 2021;11:625210.
124. Major G, Spiller R. Irritable bowel syndrome, inflammatory bowel disease and the microbiome. Curr Opin Endocrinol. 2014;21(1):15–21.
125. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. Nature. 2006;444(7122):1022–3.
126. Rheker J, Winkler A, Doering BK, Rief W. Learning to experience side effects after antidepressant intake - Results from a randomized, controlled, double-blind study. Psychopharmacol. 2017;234(3):329–38.
127. Zmora N, Zilberman-Schapira G, Suez J, Mor U, Dori-Bachash M, Bashiardes S, Kotler E, Zur M, Regev-Lehavi D, Brik RB, et al. Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. Cell. 2018;174(6):1388–1405.
128. Cheng Q, Ran Y, Mo X, Xiao R, He D, Guo S, Wang H, Liu L, Xie P. The efficacy and acceptability of Lactobacillus reuteri for the treatment of depression: a systematic review and meta-analysis. Gen Hosp Psychiat. 2025;95:122–32.
129. Liu L, Wang H, Chen X, Zhang Y, Zhang H, Xie P. Gut microbiota and its metabolites in depression: from pathogenesis to treatment. Ebiomedicine. 2023;90:104527.
130. Ait CY, Mottawea W, Tompkins TA, Hammami R. Unravelling the antimicrobial action of antidepressants on gut commensal microbes. Sci REP-UK. 2020;10(1):17878.

Publisher's note