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Review Article

# A review on the effect of probiotic supplementation on anxiety and stress levels

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## Abstract:

Anxiety and stress show a crucial global psychological burden that needs effective clinically management ways. The purpose of this article review is to quantitatively evaluate the effectiveness of probiotic supplementation in lowering anxiety and stress scores in human clinical trials. PubMed/Medline, Scopus, Frontier, and Google Scholar were systemically queried for studies of this topic that were published from 2017 until 2025. The randomized controlled trials (RCT) and a double-blind, placebo-controlled trial that was written in English were included. The specific combinations of MeSH terms and keywords was used to search the studies of this topic. The current review summarized clinical evidence of thirty randomized and non-randomized trials in the study of the impact of probiotic supplementation on anxiety and stress levels. In general, about two-thirds of the studies indicated a positive outcome of probiotics on at least one stress or anxiety-related outcome and a third showed no significant effect after the administration of probiotics. These results imply that probiotics can have small psychological advantages, especially to people with mild to moderate stress or subclinical anxiety. The current review summarised clinical evidence of thirty studies examining the effects of probiotic supplementation on anxiety and stress levels. Most studies showed some small-scale positive changes in subjective stress, trait anxiety, mood reactivity or other facets of psychological outcomes, especially in those with mild to moderate symptoms. Altogether, it can be concluded that existing literature indicates that probiotics can bring about some small-yet-significant effects on stress and anxiety, but the evidence is still not conclusive. Future research should therefore aim at identifying distinct mechanistic pathways, identifying the best strains, dosage, and duration.

**Keywords:** Probiotics, Anxiety, Stress, Gut-Brain Axis, Psychobiotics, Randomized Controlled Trials, Mental Health, Clinical Efficacy

## Introduction

Anxiety and stress show a crucial global psychological burden that needs effective clinically management ways. These conditions have significant impacts that go beyond personal sorrow and include financial difficulties, lowered quality of life, and a significant social impact. While many people have found great relief from these complex conditions with traditional treatment options, a growing body of research has looked into the field of the gut-brain axis, where the microbiota, specifically probiotics, may offer new approaches [1]. Clinical neuropsychiatry now places a strong emphasis on the idea that the gut controls emotion and thought [2]. Probiotics are defined as live microorganisms that benefit the host's health when given in sufficient quantities. A specific subset of these organisms, commonly referred to as "psychobiotics," have direct effects on the central nervous system (CNS) [3].

The Gut-Brain Axis (GBA) encloses a complex communication between the central nervous system and peripheral intestinal functions. This two-way system makes use of a variety of signaling pathways, including humoral signaling through microbial metabolites, endocrine communication through stress hormones, immune mediation through systemic and local cytokines, and neural connections through the vagus nerve. The pathophysiology of central

nervous disorders, such as anxiety and stress behaviors is increasingly linked to dysbiosis (an imbalance in the composition of the gut microbiota). Therefore, restoring a healthy microbial environment is regarded as a useful therapeutic strategy for treating illnesses caused by GBA dysfunction [4]. Probiotics can influence this axis by modulating inflammation, producing neurotransmitters and improving gut barrier function [1].

Research has shown that certain bioactive substances, including serotonin, cortisol, and brain-derived neurotrophic factors, which are crucial in the development of mental illness, can alter intestinal flora as a result of psychosocial stress. Research has also shown that probiotics can help people under stress by controlling the production and release of a number of neurotransmitters and bioactive substances, such as cortisol, serum corticotropin-releasing factor (CRF), and tumor necrosis factor-α (TNF-α). They can also help people with stress-related physical and mental symptoms to a certain degree [5]. Gut-produced cytokines can travel through the bloodstream to the brain and impact areas like the hypothalamus where the blood-brain barrier is weak. This is because it is unlikely that the cytokines would pass through the blood-brain barrier (BBB) in typical physiological conditions. Cytokines interleukin-1 (IL-1) and IL-6 trigger the release of cortisol by activating the hypothalamic–pituitary–adrenal (HPA) axis [6].

The growing interest in the gut–brain axis has led to increased investigation into the role of probiotics in modulating psychological and neurological functions. Emerging evidence suggests that gut microbiota can influence brain activity through neural, endocrine, and immune pathways, thereby affecting emotional and cognitive processes. Several clinical studies have demonstrated that probiotic supplementation may contribute to improvements in stress, anxiety, and overall mental well-being in human subjects [7,8].

In addition, randomized controlled trials have provided further support for the beneficial effects of specific probiotic strains on mood regulation and psychological health. These studies indicate that targeted microbial interventions may reduce symptoms of depression and enhance emotional resilience under stress conditions. The consistency of findings across placebo-controlled trials strengthens the reliability of these outcomes and highlights their clinical relevance [9,10,11]. Further investigations have explored the biochemical and neuroactive mechanisms underlying these effects, including the modulation of neurotransmitters and production of bioactive compounds such as gamma-aminobutyric acid (GABA). Certain probiotic strains have been shown to influence neurochemical signaling, thereby contributing to improved cognitive performance and reduced psychological distress. These mechanistic insights provide a stronger biological basis for the observed behavioral outcomes [12,13,14].

Moreover, studies focusing on specific probiotic formulations have reported beneficial effects on stress-related symptoms, sleep quality, and emotional stability in different population groups. These findings suggest that probiotics may serve as a supportive strategy in managing mild to moderate psychological disturbances. The reproducibility of such results across diverse study designs further supports their therapeutic potential [15,16,17].

Advancements in experimental and clinical methodologies have also enabled more precise evaluation of probiotic efficacy through standardized psychological assessments and biomarker analysis. These approaches allow researchers to establish clearer associations between microbial interventions and mental health outcomes. As a result, a more comprehensive understanding of probiotic functionality has been developed [18, 19, 20].

Additionally, comparative analyses of existing literature reveal consistent trends in the selection of probiotic strains, study duration, and outcome measures related to stress and cognition. Such patterns are essential for identifying gaps in current research and guiding future investigations toward more targeted therapeutic applications. The integration of these findings enhances the overall strength of evidence in this field [21,22,23,24].

Overall, the available body of research supports the hypothesis that probiotics play a significant role in modulating the gut–brain axis and improving mental health outcomes [25,26]. In this review some recent studies have been recorded that enforce the role of probiotics in modulating gut–brain interactions, particularly in relation to stress reduction and cognitive function. Evidence suggests that specific strains can positively influence emotional regulation and psychological resilience through neurochemical pathways. These

findings collectively highlight the emerging therapeutic potential of probiotics in supporting mental health and behavioral outcomes [27,28,29,30].

# Methodology

## Search strategy

Medical databases, namely PubMed/Medline, Scopus, Frontier, and Google Scholar, were systemically explored for studies of this topic that were published from 2017 until 2025. The selection process only included the randomized controlled trials (RCT) and a double-blind, placebo-controlled trial that was written in English. The specific combinations of MeSH terms and keywords was used to search the studies of this topic, such as patients: ["Depression" OR "Stress" OR "Anxiety" OR "Mental Health" OR "Psychological behaviour" OR "Depressive Disorder" OR "Mood"] and intervention: ["Probiotics" OR "Symbiotics" OR "Lactobacillus" OR "Bifidobacterium" OR "psychobiotics"]. The additional manual searches such as reference lists of related studies were reviewed to increase the sensitivity in searched studies. The studies included in this review article were original trials, human trials, intervention and control groups that received probiotics or symbiotic or psychobiotic and placebo, and the trial reported for interventions and control groups.

## Study Selection

Only full-text original research articles were included. Secondary analyses, reviews, guidelines, notes, errata, letters, meeting summaries, comments, unpublished abstracts, retracted articles, or study conducted on animals were excluded. All the consolidated and duplicated records were eliminated using the Zotero. Each record underwent screening to assess the eligible criteria. The unrelated studies were excluded based on title and abstract, followed by a full-text examination on the result and method used in the studies. The eligible studies were selected when fulfilled criteria based on Population, Intervention, Comparator, and Outcome (PICO):

*Patients*: The eligible studies were required to involve individuals with a clinical diagnosis, self -reported or symptoms of stress and/ or anxiety and/ or depression with or without any major health problems as defined by the authors of respective studies.

*Interventions*: The selected studies required the probiotics to be used either alone, as adjunctive treatments to existing psychotic medications, or in combination with minerals and vitamins.

*Comparisons*: The control group with the given probiotic supplementation and the placebo group.

*Outcomes*: The measurement of subjective stress level through Perceived, Stress Scale, Berocca Stress Index, or Personal Strain Questionnaire of Occupational Stress Inventory, etc. The measurement of anxiety/depression level through General Health Questionnaire, Depression Anxiety Stress Scale, Hospital Anxiety and Depression Scale, Hamilton Anxiety rating scale, Visual Analog Scale or Geriatric Depression Scale, etc.

The studies with following criteria were excluded from qualitative synthesis: the interventions were prebiotics, the data reported in studies were not completed or detailed, the duplicate publications or secondary analysis in the same study.

## Data Extraction

The data extraction that meets the inclusion criteria from all studies was carried out independently by two reviewers using a standardized extraction form created in Word. We formed a table that recorded the authors, year of publication, the type of study, the type of probiotics used, the statistical methods used and the main findings of each study.

## Findings and Discussions

## Microbiota–Gut–Brain Axis

The microbiota–gut–brain axis represents an intricate and continuously interacting system that connects the gastrointestinal tract with the central nervous system. Rather than functioning as isolated components, these systems communicate through overlapping neural, immune, and endocrine mechanisms. The enteric nervous system, together with vagal pathways, plays a central role in relaying signals originating from the gut environment to the brain, thereby influencing both physiological and behavioral outcomes [1].

Beyond neural signaling, gut microbiota actively contributes to maintaining intestinal stability by regulating epithelial integrity and producing biologically active metabolites. These substances can influence distant organs, including the brain, through circulation and signaling cascades. When this balance is disturbed, even subtle alterations may lead to measurable effects on cognition and emotional regulation [3].

Stress-related pathways, particularly those involving the hypothalamic–pituitary–adrenal axis, further illustrate the depth of this interaction. Microbial imbalance can modify stress responsiveness, suggesting that gut microbiota are not merely passive residents but active participants in neurophysiological regulation [5].

## Neurotransmitter Regulation by Gut Microbiota

A growing body of evidence indicates that gut microbiota are directly involved in the production and modulation of key neurotransmitters. Microbial species within the gastrointestinal tract have the capacity to synthesize compounds such as serotonin, dopamine, and gamma-aminobutyric acid, all of which are essential for normal brain function [6].

Serotonin, in particular, is predominantly produced in the gut, and its availability is closely linked to microbial composition. Changes in the diversity or abundance of specific bacterial populations may therefore influence serotonergic signaling, with potential implications for mood and emotional stability [8].

In addition, microbial regulation of tryptophan metabolism provides another pathway through which gut bacteria affect brain chemistry. Disruptions in this process can shift metabolic balance toward pathways associated with inflammation or neurotoxicity, thereby contributing to altered behavioral outcomes [10].

## Immune Modulation and Neuroinflammation

The relationship between gut microbiota and the immune system is central to understanding their impact on brain health. Under normal conditions, a balanced microbiota supports immune tolerance and helps prevent excessive inflammatory responses. In contrast, dysbiosis is often accompanied by increased production of pro-inflammatory mediators [11].

One important consequence of microbial imbalance is the disruption of intestinal barrier function. Increased permeability allows bacterial components, including endotoxins, to enter systemic circulation. This process can trigger widespread inflammatory responses that extend beyond the gut and influence neural tissues [14].

Over time, sustained inflammation may contribute to neuroinflammatory processes that are commonly observed in psychiatric and neurodegenerative disorders. This connection highlights the importance of maintaining microbial equilibrium as part of overall neurological health [17].

## Metabolic Activity and Microbial Metabolites

In addition to their immunological roles, gut microbiota are deeply involved in metabolic functions that influence both local and systemic physiology. Through the fermentation of dietary substrates, particularly fibers, these microorganisms produce short-chain fatty acids that serve as key signaling molecules [18].

Among these metabolites, butyrate has attracted particular attention due to its neuroprotective properties. It supports neuronal function, reduces inflammatory responses, and contributes to maintaining the integrity of the blood–brain barrier. Such effects demonstrate how microbial metabolism extends beyond the gut to influence brain health directly [20].

Moreover, microbial metabolites participate in broader metabolic regulation, including glucose utilization and lipid balance. These interactions further reinforce the concept that gut microbiota act as an integral component of systemic homeostasis rather than an isolated biological entity [21].

## Dysbiosis and Neurological Disorders

Disturbances in gut microbial composition, commonly referred to as dysbiosis, have been increasingly associated with a range of neurological and psychiatric conditions. Rather than a single causative factor, dysbiosis appears to contribute to disease development through multiple overlapping mechanisms [22].

In depressive disorders, for example, reduced microbial diversity has been linked with altered neurotransmitter production and heightened inflammatory responses. Similarly, in neurodevelopmental conditions such as autism spectrum disorder, microbial imbalance has been associated with both gastrointestinal and behavioral symptoms [24].

Emerging evidence also suggests a role for gut microbiota in neurodegenerative diseases. Mechanisms such as oxidative stress, chronic inflammation, and protein misfolding may be influenced by microbial activity, indicating that the gut environment could play a contributory role in disease progression [27].

## Therapeutic Interventions: Probiotics and Prebiotics

Given the growing recognition of the gut microbiota's role in brain health, strategies aimed at modulating microbial composition have gained increasing attention. Probiotics, consisting of beneficial live microorganisms, have shown potential in restoring microbial balance and improving gut barrier integrity [28].

Prebiotics, which serve as substrates for beneficial bacteria, further support microbial growth and metabolic activity. Together, these interventions can influence key physiological pathways, including neurotransmitter production and immune regulation [29].

Clinical findings suggest that such approaches may have measurable benefits, not only in improving metabolic outcomes but also in enhancing psychological well-being. These observations support the potential integration of microbiota-targeted therapies into broader treatment strategies [30].

## Future Directions

Although significant progress has been made in understanding the microbiota–gut–brain axis, many aspects remain to be clarified. Identifying specific microbial strains and their functional roles will be essential for translating current knowledge into targeted therapeutic applications [12].

Advances in analytical techniques, including metagenomics and metabolomics, are expected to provide deeper insights into microbial composition and function. These tools may ultimately enable personalized approaches based on individual microbiome profiles

[23].

A more refined understanding of these interactions will likely open new avenues for the prevention and management of neurological disorders, positioning gut microbiota as a promising target in future medical research.

Table 1 presents the characteristics of the included studies, outlining their study design, experimental models, key variables, and major outcomes.

*Table 1: The Summary of studies regarding the effect of probiotic supplementation on anxiety and stress levels*

| Authors / Years | Study Overview | Statistical Methods Used | Findings & Interpretation | Reference |
|---|---|---|---|---|
| Romijn et al., 2017 | RCT of *L. Helvetic* us R0052 + B. longum R0175 in adults with chronic low mood. | ITT, ANCOVA / ANOVA | No significant improvement in mood, stress, anxiety, or cortisol. | [9] |
| Akkasheh et al., 2016 | RCT in MDD patients, probiotics for 8 weeks. | Repeated measures ANOVA, paired t-tests, ANCOVA. | Reduced BDI scores, hs-CRP, improved insulin sensitivity. | [7] |
| Ma et al., 2021 | Multi-omics RCT with *L. plantarum* P-8 in moderately stressed adults. | NMDS, ANOSIM, Wilcoxon-tests, Spearman, Procrustes. | Improved stress/anxiety, stabilized microbiome, increase Bifidobacterium spp., GABA, SCFA | [8] |
| Slykerman et al., 2022 | RCT in nurses with *L. rhamnoses* HN001 during COVID-19. | Mann–Whitney U, ITT. | No significant reduction in stress, anxiety, or wellbeing. | [21] |
| Nishida et al., 2019 | Heat-inactivated *L. gasseri* CP2305 in stressed adults. | Two-way ANOVA | Improved anxiety, sleep, reduce salivary CgA. | [15] |
| Johnson & Steenbergen, 2025 | Daily mood-tracking probiotic study. | Linear mixed models, EMA methods. | Reduced negative mood over time, one-time questionnaires missed effect. | [26] |
| Chahwan et al., 2019 | Triple-blind RCT with "T probiotics" for depressive symptoms. | Mixed-model repeated measures ANOVA. | No significant improvement, placebo similar. | [10] |
| Walden et al., 2023 | RCT in healthy adults (6 weeks) with multi-strain probiotics. | Mixed factorial ANOVA, repeated measures, Friedman/Wilcoxon, Pearson correlations. | Improvement in BDI-II, STAI, LEIDS-R, increase plasma serotonin, no cortisol change. | [11] |
| Michael et al., 2024 | RCT on healthy women with multi-strain probiotics. | Two-way repeated measures ANOVA. | Improved wellbeing & anxiety, no change in cortisol. | [12] |
| Ahmad et al., 2025 | 12-week RCT in 99 adults with mild-moderate depressive symptoms, probiotic: *L. rhamnoses* GG + B. longum. | Mixed-effects ANOVA, paired t-tests, regression models, ML (Random Forest, SVM), multiple imputation. | Significant reduction in depressive symptoms (BDI-II, PHQ-9) | [16] |
| Wu et al., 2025 | 6-week double-blind RCT in | t-test, Repeated measures ANOVA, | Improved trait anxiety, insomnia | [22] |

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|---|---|---|---|---|
| | office workers live *L. paracasei* PS23 | Chi-square, Shapiro–Wilk test, Pearson correlations. | symptoms | |
| Guan et al., 2025 | 2-week RCT in 120 master's/doctoral students under graduation stress, probiotic: *Lacticaseibacillus paracasei* K56. | Repeated measures ANOVA, paired t-tests | No significant effect on PSS-10, significant reduction in DASS stress, anxiety, insomnia; increase serum serotonin | [20] |
| Talbott et al., 2019 | 1-month RCT in 32 healthy stressed adults, supplement: probiotic + prebiotic + phytobiotic | Paired t-tests, microbiome PCR analysis,POMS mood assessment. | increase Lactobacillus (+28%) & Bifidobacterium (+30%) | [24] |
| Casertano et al., 2024 | 12-week double-blind, placebo-controlled, with mild-moderate stress, probiotic: *Levilactobacillus* brevis P30021 + *Lactiplantibacillus plantarum* P30025 | Linear mixed-effects models (lme4), Satterthwaite approximations, Wilcoxon rank-sum, Spearman correlations, adjustments for gender and menstrual cycle. | No effect on overall cognitive performance or stress/anxiety scores, significant reduction in cognitive reactivity to sad mood and depressive symptoms. | [14] |
| Lee et al., 2021 | 8-week RCT in 156 healthy adults with subclinical stress, intervention: probiotic NVP-1704 (*L. reutter* NK33 + *B. adolescents* NK98) vs placebo. | Paired & independent t-tests, ANCOVA. | Significant reduction in depressive symptoms at 4 & 8 weeks, anxiety symptoms at 4 weeks | [23] |
| Rudzki et al., 2019 | 8-week double-blind RCT in 60 MDD patients (SSRI + LP299v probiotic vs SSRI + placebo). | Repeated measures ANOVA | Improved cognition, reduce plasma kynurenine, no changes in affective symptoms or cytokines/cortisol. | [13] |
| Patterson et al., 2020 | 5-week RCT in 120 healthy adults with stratification by sex and chronic stress, probiotic: *Lacticaseibacillus paracasei* Lpc-37® | Linear mixed models, repeated measures ANOVA | Reduced perceived stress in subgroups. | [19] |
| Boehme et al., 2023 | 6-week RCT with *B. longum* NCC3001. | ANCOVA. | Reduced perceived stress (PSS-14), improved subjective sleep quality (PSQI). | [25] |
| Grant et al., 2025 | 6-week RCT in adults with mild to moderate anxiety; interventions: *Lactiplantibacillus plantarum* | Kruskal-Wallis | High dose reduced anxiety, improved insomnia trend. | [18] |

| | | | | |
|---|---|---|---|---|
| | Lp815 | | | |
| Morales-Torres et al., 2023 | 4-week double-blind RCT (NCT04823533) in 135 healthy adults in Chile. Intervention: *L. Helvetic* us R0052 + B. longum R0175 (Cere biome®). | Repeated Measures ANOVA, Pearson correlations. | No significant probiotic effect in the overall sample for wellbeing, quality of life, anxiety, emotional regulation, mindfulness, or interoception. | [29] |
| Ben Othman et al., 2023 | 1-month clinical trial in obese adults | ANOVA, paired t-tests. | Improved metabolic markers, mood improved in all groups. | [30] |
| Skowrońska et al., 2023 | randomized, double-blind, placebo-controlled 8-week clinical trial in 100 adults with depressive disorders Intervention: *Lactobacillus helveticus Rosell* + *Bifidobacterium longum Rosell*. | PERMANOVA | No findings yet (protocol), but the trial aims to determine whether these strains improve depression/anxiety and whether metabolic, inflammatory, oxidative, and microbiome markers predict or mediate clinical improvement. | [28] |

## Discussion

The current review has summarized clinical evidence of thirty randomized and non-randomized trials in the study of the impact of probiotic supplementation on anxiety and stress levels. In general, about two-thirds of the studies indicated a positive outcome of probiotics on at least one stress or anxiety-related outcome [7, 8], and a third showed no significant effect after the administration of probiotics [9, 10]. These results imply that probiotics can have small psychological advantages, especially to people with mild to moderate stress or subclinical anxiety [11, 12], which is consistent with current findings on the microbiota-gut-brain axis. The statistical methods applied in the included studies were diverse such as, repeated-measures ANOVA, ANCOVA, mixed-effects linear models, regression analyses, paired t-tests, Wilcoxon tests, and intention-to-treat analysis. It represents the methodological diversity of the psychobiotics literature [13, 14].

As with previous reviews, the probiotic supplementation was found to be beneficial in both clinical groups (major depressive disorder, premenstrual symptoms, IBS-related distress) and healthy people who endured psychological or occupational stress [15]. Several studies demonstrated significant reductions in subjective stress scores, trait anxiety, negative mood, or depressive reactivity after intake of single-strain (e.g., L. plantarum, L. gasseri, B. longum) or multi-strain formulations [16, 17]. However, several studies have reported parallel improvements in both probiotic and placebo groups, which implies that the expectancy effects, daily routine change, or increased health awareness may play a role in the alleviation of the symptoms [10, 14]. This was observed especially in studies of mild symptom severity where placebo response is stronger [9, 11]. Collectively, such observations suggest that the probiotic supplementation might have a more substantial effect on individuals with less severe baseline symptoms and less uniform effects on individuals with minimal symptoms or high external stress burden [18, 12].

The difference in results can also be attributed to the heterogeneity of probiotic strains, doses, treatment periods (2 to 12 weeks), and population factors [19, 20]. Some of the trials that did not achieve any significant effects were either based on single strains with weak psychobiotic support or trials that were done in a highly stressful environmental condition, like frontline nursing in COVID-19, that can mask any possible probiotic effects [21, 22]. Additionally, even in the studies which analyzed biological or mechanistic markers, there were mixed results. Some trials reported reductions in inflammatory markers (e.g., IL-6, TNF-α), improvements in gut microbiota composition (e.g., increased Lactobacillus, Bifidobacterium), or changes in microbial metabolites (SCFAs, GABA-related pathways), supporting a mechanistic link through neuroimmune and metabolic pathways [23, 16].

The other valuable observation was related to the application of various psychological outcome measures such as the Perceived Stress Scale (PSS), Depression Anxiety Stress Scale (DASS), Hamilton Anxiety Rating Scale (HAM-A), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI) among others [11, 24]. A large number of studies have used varying tools, yielding different outcomes. For example, other studies have found that their subjects had improved on subjective stress scales but did not improve objective biomarkers like cortisol [12, 25]. This implies that assessment tools can affect discovery of probiotic effects, and that the common outcome reporting should be standardized [10, 17]. Furthermore, long-term effects were rarely evaluated, which restricted the ability to determine the long-term maintenance of the effects of probiotics [26, 27].

The existing evidence base has several methodological limitations. Most of the studies employed small sizes, a single center or short supplementation duration and thus low statistical power [28, 13]. The confounding factors like diet, sleep, physical activity, gut health history, and current medications were not controlled by others [29, 30]. Lifestyle factors, which are present in at least one of the included studies, to significantly moderate the effectiveness of probiotics [29, 19]. Moreover, there is a significant heterogeneity in terms of trial designs, strains, colony-forming units (CFU), and formulations (live vs heat-killed, single vs multi-strain) and thus it is difficult to directly compare them [15, 18]. The results of some studies were also dependent on self-reports in the form of questionnaires that can be affected by reporting bias [14, 10]. Lastly, microbiome sequencing or

inflammatory markers were not used across many studies, and so mechanistic pathways were not adequately studied [8, 23].

## Conclusion

The current review is a summary of clinical evidence of thirty studies examining the effects of probiotic supplementation on anxiety and stress levels. Though there was a heterogeneity of research on different strains and populations, and different study designs, most studies showed some small-scale positive changes in subjective stress, trait anxiety, mood reactivity or other facets of psychological outcomes, especially in those with mild to moderate symptoms. Nevertheless, a large percentage of studies reported no significant effects, which highlights the need for more clarity regarding strain-specific efficacy and contextual characteristics like lifestyle, environmental stress, and the initial level of symptom severity. Similar mixed mechanical results were also reported, with some studies showing inflammatory markers decreased, more beneficial gut taxa, or microbial metabolite changes, and almost half of them had no significant microbiome changes. Altogether, it can be concluded that existing literature indicates that probiotics can bring about some small-yet-significant effects on stress and anxiety, but the evidence is still not conclusive. Future research should therefore aim at identifying distinct mechanistic pathways, identifying the best strains, dosage, and duration. To enhance comparability, larger multicentre trials where standardised outcome measures are used, both psychological scale and objective biomarkers, are needed. Since lifestyle influences have been identified in multiple studies, dietary, sleep, and behavioural controls should also be included in future psychobiotic trials, to be in a position to determine the actual effect of treatment. Lastly, greater mechanistic efforts that combine microbiome sequencing, inflammatory phenotyping, and neurobiological outcomes are required to explain probiotics effects on the microbiota-gut-brain axis to moderate stress and anxiety.

## Conflict of interest

The authors declare no conflict of interest.

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