



# The Use of Probiotics for Pain Reduction in Patients With Fibromyalgia: A Systematic Review

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## Abstract

**Background:** Probiotics represent a potential therapeutic option for patients with fibromyalgia. Emerging evidence suggests that the gut-brain axis can modulate neuronal-mediated pain symptoms. This systematic review evaluates the efficacy of probiotic supplementation for pain reduction in patients with fibromyalgia.

**Methods:** Following the PRISMA 2020 guidelines, the databases search included MEDLINE (PubMed), Embase, Scopus, Web of Science, Cochrane CENTRAL, and ClinicalTrials.gov up to April 2025. Eligible studies included randomized controlled trials evaluating the use of probiotics for pain management in adults (age  $\geq 18$  years) with fibromyalgia. Interventions were multistrain probiotics for 8–12 weeks; outcomes included VAS pain, FIQ/FIQR, and SF-36. Studies involving pediatric populations, other chronic pain conditions, or lacking pain outcomes were excluded. Risk of bias was assessed using the Cochrane Risk-of-Bias 2 tool. (OSF Registries: <https://doi.org/10.17605/OSF.IO/KHVR7>)

**Results:** Of 923 records, 3 double-blind, placebo-controlled RCTs (2018–2024;  $n=213$ ; 198 women; ages  $\sim 46$ –55; Spain/Turkey) met eligibility criteria and were included. Pain was assessed as a primary and secondary outcome. One trial showed a greater VAS pain reduction with probiotics at 8 weeks (per-protocol;  $p=0.032$ ; moderate effect), while the other two reported no between-group differences in pain; SF-36 improvements favoring probiotics/prebiotics appeared in one study only. Heterogeneity in strains, dosing, and outcome reporting precluded meta-analysis. Overall risk of bias assessment showed some concerns or high, driven mainly by selective reporting.

**Conclusions:** Overall, partly due to the limited number of studies for this topic, the evidence for pain improvement using VAS, FIQ (FIQR), or SF-36 remains weak and inconclusive. Furthermore, the risk of bias assessment indicates the need for cautious interpretation of the current findings. It underscores the need for larger, high-quality randomized controlled trials to generate more reliable evidence regarding the efficacy of probiotics in managing pain among patients with fibromyalgia.

## Introduction

Fibromyalgia (FM) is a complex chronic illness characterized mainly by musculoskeletal pain and often accompanied by fatigue, sleep disturbances, cognitive symptoms, and mood disorders (Bhargava & Goldin, 2025; Siracusa et al., 2021). It affects approximately 2.7% of the global population, with a higher prevalence in women (female-to-male ratio of 3:1) (Soroosh, 2024). Current treatment options, includ-

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ing pharmacological agents such as antidepressants, anticonvulsants, and analgesics, provide only partial relief for many patients, while adverse effects and variable responses often limit long-term adherence (Furlan, A. D., 2024). The ongoing global opioid epidemic adds further complexity to pain management in FM, highlighting the need to explore safe and effective therapeutic alternatives (Bhargava & Goldin, 2025; Fernandez-Feijoo et al., 2022; Ramírez-Gil et al., 2025).

Among the emerging strategies, probiotics have attracted increasing attention. These are non-pathogenic microbes that are commonly consumed by food, drinks, or even dairy products, exerting health benefits to the host when administered in adequate quantities. Traditionally used to support gastrointestinal health, probiotics are now being investigated for their potential role in modulating pain, particularly through mechanisms involving the gut-brain axis, anti-inflammatory pathways, and immunomodulation (Latif, 2023). Dysbiosis, an imbalance in gut microbial composition, has been implicated in pain sensitization, systemic inflammation, and altered neuroimmune communication, all of which are relevant to FM pathophysiology (Zhao, M., Zhang, L., & Liu, Z., 2025).

Several potential mechanisms of action have been described, including: 1) modulation of the gut-brain axis, 2) anti-inflammatory effects, and 3) strengthening of the gut barrier and immunomodulation (Fytanidou et al., 2023; Matzaras et al., 2023). Experimental studies in animal models have shown that probiotics can alter pain thresholds, attenuate central sensitization, and even influence emotional behaviors related to chronic pain (Wang, H., et al., 2016). However, while preclinical findings are compelling, translation into human populations has been limited, especially in fibromyalgia. Only a few randomized controlled trials (RCTs) have assessed probiotics in FM specifically, and results remain inconsistent.

Given this context, the present systematic review aims to assess the effects of probiotic supplementation on pain in patients with fibromyalgia. This topic is particularly important because probiotics are widely accessible, have a favorable safety profile, and could represent a cost-effective adjunctive strategy to current multimodal management approaches in FM.

## Materials and Methods

### Search strategy

In April 2025, this systematic review was conducted following the PRISMA 2020 guidelines. Six electronic databases were searched: MEDLINE (PubMed), Embase, Scopus, Web of Science,

Cochrane CENTRAL, and ClinicalTrials.gov. The searches were performed and completed by April 26th, 2025, without restrictions on publication date, but were limited to studies published in English. The search query was as follows: ((Fibromyalgia[Mesh] OR fibromyalgia[tw] OR fibromyalgic[tw] OR "chronic pain"[tw] OR "central sensitization"[tw])) AND ((Probiotics[Mesh] OR probiotics[tw] OR probiotic[tw] OR microbiome[tw] OR "Lactobacillus"[tw] OR "Bifidobacterium"[tw] OR "Lactobacillus rhamnosus"[tw] OR "Bifidobacterium longum"[tw] OR "Lactobacillus acidophilus"[tw] OR "VSL#3"[tw])) AND ((Pain[Mesh] OR pain[tw] OR "pain reduction"[tw] OR "pain management"[tw] OR "pain intensity"[tw] OR "pain scale"[tw] OR "pain relief"[tw] OR "pain score"[tw] OR "analgesic effect"[tw])). The search strategy was developed based on PubMed syntax as shown in the query, and then adapted for use in the other databases using their specific syntax.

### Inclusion and exclusion

We identified randomized controlled trials that compared probiotics with placebo, no treatment, or other interventions for pain reduction in fibromyalgia. Our review was restricted to adult populations ( $\geq 18$  years) to minimize heterogeneity resulting from developmental differences in gut microbiota and disease presentation. Studies were eligible for inclusion if they assessed pain reduction using validated and standardized outcome measures. Accepted measures as primary or secondary outcomes included the Visual Analogue Scale (VAS), Fibromyalgia Impact Questionnaire (FIQ or the revised version FIQR), Short Form Health Survey (SF-36), Numeric Rating Scale (NRS), Brief Pain Inventory (BPI), and McGill Pain Questionnaire (MPQ). Studies utilizing other pain assessment tools were considered only if the instrument's validity and standardization had been previously established in fibromyalgia research. We broadly defined the experimental intervention to include any probiotic strain administered at any dose. We excluded observational study designs, restricting eligibility to randomized controlled trials to ensure a clear assessment of causality.

### Selection of studies and data extraction

Duplicate records were detected using the Covidence automation tool. All titles and abstracts identified through the initial primary search were screened. Ten review authors independently screened the record title and abstract, based on predefined inclusion and exclusion criteria. Each record was

screened by two independent reviewers. The screening process was blinded, and any record that received two approvals proceeded to full-text review. Subsequently, three authors independently conducted a full-text review to finalize the inclusion of studies. Any disagreements between screeners during this phase were resolved by consultation with a third reviewer. Studies were excluded if they did not meet the eligibility criteria or were deemed off topic according to the predefined section framework.

Six reviewers independently extracted data from eligible studies using a standardized data extraction template, along with detailed instructions outlining the requirements for each data element. The data extraction form included study identification, including the country of origin, authors, affiliated institutions, and year of publication. Methodological details were also recorded, including the study design, randomization methods, blinding procedures, allocation strategies, and the primary outcome assessed. Population characteristics were documented, including inclusion and exclusion criteria as well as sample size. Intervention-related information included dosage, frequency, adherence, treatment details, and route of administration. Finally, outcome measures and results related to pain were extracted using validated instruments, such as the VAS, FIQ, FIQR, and SF-36. Extracted data were compared among reviewers, and study authors were contacted if additional information was necessary.

### *Data synthesis*

This systematic review followed the PRISMA 2020 framework and aimed to assess the effects of probiotic supplementation on pain in patients with fibromyalgia. Characteristics of the studies, such as sample size, type of intervention, dosage, duration, and outcome measures, were extracted and classified to enable structured comparison. The primary outcome was pain intensity, with secondary outcomes being fibromyalgia symptom burden (assessed by FIQ) and quality of life (SF-36). Quantitative data were narratively synthesised within-group variations over time and between-group comparisons at the study endpoint.

Treatment effects were reported as available means, standard deviations, and p-values, and when available, 95% confidence intervals (CIs). Comparisons of intervention (probiotic, prebiotic, placebo) and treatment duration, rather than follow-up duration, were made when appropriate, but no specific subgroup analyses were performed. However, no meta-analysis was conducted because of the limited number of eligible randomized

controlled trials and differences in the type of probiotic, intervention format, and major outcome measures. No imputation was made for missing data. We therefore conducted a qualitative synthesis to evaluate the expected efficacy and acceptability of probiotics on fibromyalgia. Lastly, the synthesis examined patterns of outcome direction, placebo responses, and mechanisms suggested by individual studies.

The Visual Analog Scale (VAS) is a tool used to assess the intensity of pain. The VAS consists of 11 points in total, ranging from 0 to 10, where 0 represents no pain, and 10 represents the worst pain imaginable. The Fibromyalgia Impact Questionnaire (FIQ) was used in all studies, with a variation of the revised version (FIQR) in the study conducted by Calandre et al. (2021). The questionnaires consist of self-reported symptoms, including perceived pain intensity. There is a variation between FIQ and FIQR. The FIQ consists of one functional domain with 10 questions, including 7 different symptoms. On the other hand, the FIQR has 21 functions with 21 items, including 10 symptoms other than pain. Scores are ranked between 0 and 100. The Short-Form Health Survey SF-36 is a multi-item generic health survey that assesses health-related quality of life. It consists of 36 items grouped into eight domains: physical functioning, role limitations due to physical or emotional problems, social functioning, mental health, vitality, general health perceptions, bodily pain, and perceived health changes over time, with a score ranking from 0 to 100.

### *Risk of bias assessment*

Risk of bias was assessed for all included randomized controlled trials (RCTs) using the Cochrane Risk of Bias (RoB) 2.0 tool (Higgins, 2019). The assessment covered five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported results. Two reviewers independently assessed each study, and disagreements were first discussed to reach consensus. If consensus could not be reached, a third reviewer adjudicated the decision. When information was unclear, study authors were contacted for clarification; if no response was obtained, judgments were based on available data and conservatively rated as “some concerns”. For each domain and study, the RoB for RCTs was classified as low, some concerns, or high.

## Results

### Study selection

A total of 923 articles were identified through database searches. After removing 439 duplicates, 484 unique records were screened for titles and abstracts. Of these, 476 were excluded for not meeting the inclusion criteria. Therefore, eight full-text articles were assessed for eligibility, with five being excluded: two for being a protocol, two for having the wrong study design, and one for having the wrong patient population. Ultimately, three studies ( $n = 3$ ) were included in the final review for qualitative analysis. A PRISMA flow diagram (Figure 1) provides detailed selection steps.

### Description of studies and population

Three studies published between 2018 and 2024 met the inclusion criteria; all were double-blind and placebo-controlled RCTs with a parallel design (Aslan Çin et al., 2023; Calandre et al., 2021; Roman et al., 2018). The studies enrolled 213 total participants: 198 females, 6 males, and 9 with unreported gender (Roman et al.). The mean participant age ranged from 46 to 55 years. All participants had fibromyalgia diagnoses based on American College of Rheumatology criteria. The included studies used different versions of the criteria, as shown in Table 1. Two studies were conducted in Spain (Calandre et al., 2021; Roman et al., 2018) and one in Turkey (Aslan Çin et al., 2023). Characteristics of the included studies are presented in Table 1.

### Interventions

Table 2 describes in detail the interventions of the three RCTs, including the type of intervention, dosage, duration, and route of administration. Despite variations in specific formulations and durations, all interventions consisted of orally administered multistrain probiotics for 8–12 weeks. None of the studies combined the interventions with pharmacological treatments, and each employed a placebo group receiving capsules or sachets identical in appearance and dosing schedule to the active intervention. Treatment duration ranged from 8 to 12 weeks, with daily administration of either probiotics or placebo. Each study provided comprehensive details on the composition and dosage of the multistrain probiotics.

Roman et al. (2018) investigated the efficacy of a multistrain probiotic administered in pill form over eight weeks. Participants in the control group received visually identical placebo capsules

containing no live bacteria.

Aslan Çin et al. (2024) evaluated the effects of probiotic, prebiotic, and placebo over eight weeks. The probiotic formulation included commonly utilized strains such as *Lactobacillus acidophilus* and *Bifidobacterium bifidum* (Table 2). Interventions were delivered once daily in capsule form, with the placebo group receiving identically matched inert capsules.

Calandre et al. (2021) employed VSL#3, a high-potency probiotic comprising eight bacterial strains, delivered in sachets containing 450 billion CFUs per day over a twelve-week period. The placebo consisted of identically flavored sachets without live organisms.

### Outcomes

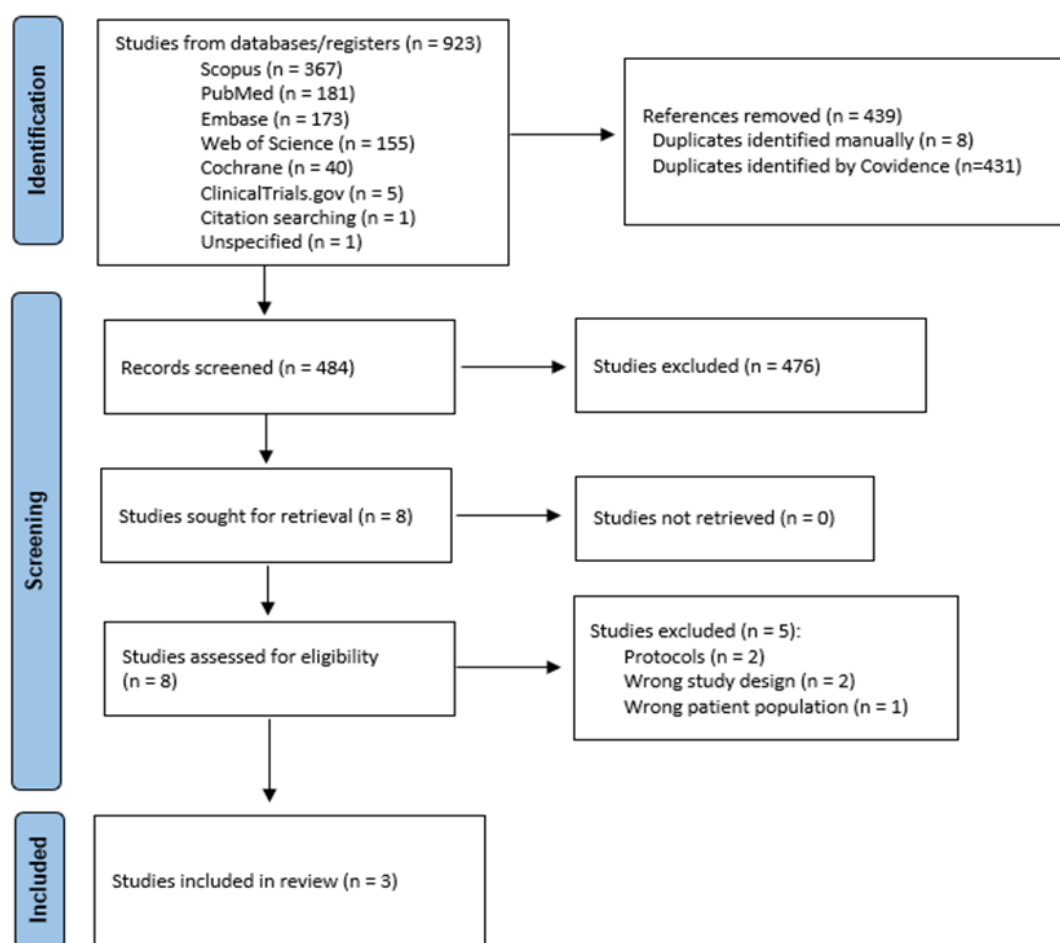
The VAS results varied across the studies. Aslan et al. (2023) used this tool in a customized form to assess abdominal pain and gastrointestinal symptoms rather than generalized pain, representing a non-validated variant. The FIQ and FIQR were completed at baseline and collected periodically, with results reported from baseline to the end of the study (8–12 weeks). For the SF-36, all studies included baseline assessments and follow-up measurements during and after the intervention. One study did not report an overall SF-36 score, instead dividing results into physical and mental component scores.

### Results according to the pain scale

In the study by Aslan Çin et al. (2023), analyses were conducted exclusively within the per-protocol population. Although overall group and time-by-group interaction effects were not statistically significant, a significant reduction in pain was observed in the probiotic group compared to the placebo group at week 8 ( $p = 0.032$ ), with a moderate effect size (Cohen's  $d = -0.76$ ). No significant differences were observed for the prebiotic group.

In Roman et al. (2018), VAS was assessed as a secondary outcome. The probiotic group showed a reduction in mean VAS pain scores from 6.69 (SD 0.41) at baseline to 5.49 (SD 0.38) post-intervention, while the placebo group decreased from 7.50 (SD 0.50) to 6.05 (SD 0.62). However, the between-group difference was not statistically significant ( $p = 0.72$ ). In Calandre et al. (2021), VAS was a planned outcome, but interpretation was limited due to insufficient reporting.

All three studies used the Fibromyalgia Impact Questionnaire (FIQ), with Calandre et al. (2021) employing the revised FIQR. Roman et al. (2018)



**Figure 1:** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart, n= number.

Study (Author, Year)	Intervention Description	Duration	Mode of Delivery	Control Description	Dosage
Roman et al., 2018	Multistrain probiotic (ERGYPHILUS Plus containing <i>L. Rhamnosus</i> GG, <i>L. Casei</i> , <i>L. Acidophilus</i> , and <i>Bifidobacterium Bifidus</i> )	8 weeks	Oral capsules	Matched placebo capsule without live bacteria (cellulose)	2 pills two times a day
AslanÇin et al., 2024	Probiotic and/or prebiotic ( <i>L. acidophilus</i> , <i>L. rhamnosus</i> liobif, <i>B. longum</i> , and <i>Saccharomyces</i> )	8 weeks	Oral capsules	Matched placebo capsules with inert contents (fructo-oligosaccharide and magnesium stearate)	1 capsule/day
Calandre et al., 2021	VSL#3 ( <i>S. thermophilus</i> BT01, <i>B. breve</i> BB02, <i>B. animalis</i> subsp. <i>lactis</i> BL03, <i>B. animalis</i> subsp. <i>lactis</i> BI04, <i>L. acidophilus</i> BA05, <i>L. plantarum</i> BP06, <i>L. paracasei</i> BP07, and <i>L. helveticus</i> BD08)	12 weeks	Oral sachets (powder)	Matched placebo sachets without active probiotic strains (maltose, cornstarch and silicon dioxide)	2 sachets two times a day

**Table 1:** Intervention characteristics, exposure, and control of included studies.

Study	Year	Country	Study design	Registered	Population	Arms	N*	Age (Mean ± SD)	F	M	Treatment Group	Control Group	Outcomes
Aslan Çın et al.	2024	Turkey	Double-blind, Placebo-controlled, Single-center, Parallel RCT	NCT04607278	Female patients with fibromyalgia syndrome according to ACR 2010 criteria	3	63	T: 45.4 ± 10.7 C: 46.1 ± 10.0	63	0	Probiotics: 21 Prebiotics: 21	Placebo 21	VAS FIQ Pain-Score SF-36
Calandre et al.	2021	Spain	Double-blind, Placebo-controlled, Parallel RCT	NCT04256785	Patients with a diagnosis of fibromyalgia using ACR 2016 criteria	2	110	T: 56 ± 7.5 C: 55.5 ± 8.6	107	3	Probiotics 54	Placebo 56	VAS-GI FIQ-R Pain score-FIQ-R SF-36
Roman et al.	2018	Spain	Double-blind, Placebo-controlled, Single-center, Parallel RCT	NCT02642289	Patients diagnosed with fibromyalgia syndrome according to ACR criteria from both 1990 and 2010	2	40	T: 55 ± 2.09 C: 50.27 ± 7.86	28*	3*	Probiotics 16	Placebo 15	VAS FIQ Pain-Score SF-36

ACR = American College of Rheumatology, C = Control group, FIQ = Fibromyalgia Impact Questionnaire, FIQ-R = Revised Fibromyalgia Impact Questionnaire RCT = Randomized controlled trial, SD = Standard deviation, SF-36 = Short Form-36 Quality of Life Questionnaire, T = Treatment group, VAS = Visual Analog Scale, VAS-GI = Visual Analog Scale modified to measure abdominal pain \*Randomized patients. +Data available only for per protocol population, excluding dropouts.

Table 2: Main characteristics of the included studies.

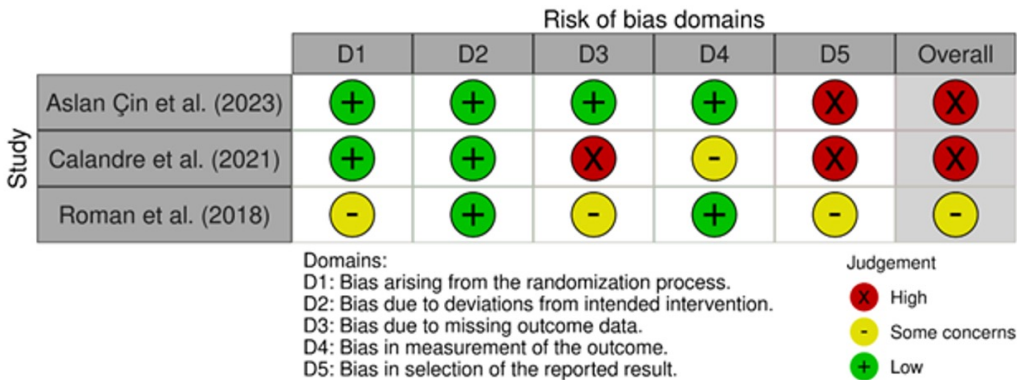


Figure 2: Traffic-light plot showing risk of bias judgments across five domains for each study.

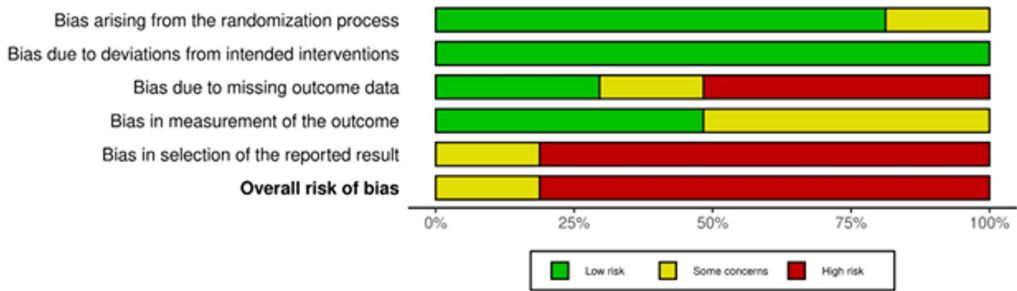


Figure 3: Summary plot displaying the proportion of studies rated at each level of risk of bias across domains.

reported improvements in FIQ scores in both probiotic and placebo groups, but no statistically significant between-group differences were observed ( $p = 0.17$ ). Calandre et al. (2021) found no significant differences between groups in total FIQR scores or FIQR pain subscores. Aslan Çin et al. (2023) reported statistically significant within-group improvements in FIQ scores across probiotic, prebiotic, and placebo groups, with no significant between-group differences.

The SF-36 pain subscale was assessed in all studies. Only Aslan Çin et al. (2023) demonstrated statistically significant between-group improvements favoring probiotic and prebiotic interventions. Roman et al. (2018) and Calandre et al. (2021) reported no significant differences between probiotic and placebo groups, with incomplete reporting of overall SF-36 pain scores in the latter study.

### Individual study results

Beyond pain-related outcomes, Roman et al. (2018) reported significant improvements in cognitive outcomes within the probiotic group, including impulsive choice and emotion-based decision-making, despite no differences in pain, mood, or anxiety measures. Calandre et al. (2021) primarily assessed gastrointestinal symptoms and found no significant differences in primary or secondary outcomes, although a modest trend favoring probiotics was observed in symptom maintenance post-treatment. Aslan Çin et al. (2024) reported significant reductions in pain, improved sleep quality, and decreased depression and anxiety scores in the probiotic group compared to placebo.

### Assessment of risk of bias in individual studies

Figures 1 and 2 present summary bar plots of the risk-of-bias judgments across all included studies. The most frequent high-risk domain was selective reporting (D5), affecting all three studies. Domains related to intervention adherence (D2) and outcome measurement (D4) were generally rated as low risk. These bias assessments were considered in the interpretation of the results.

## Discussion

This systematic review synthesized the findings of three double-blind, randomized, placebo-controlled trials on probiotics' effectiveness in fibromyalgia pain reduction. The use of probiotics is widely recommended and has an overall favorable and well-established safety profile. The number of randomized

clinical trials assessing efficacy in pain relief remains limited, as identified through our search strategy. Although our search strategy included only English publications, the included studies originated from Spain and Turkey, demonstrating that English dissemination did not restrict geographic diversity, and the risk of language bias was considered minimal. The Clinical Trials Registry (Clinicaltrials.gov) was used as the largest international registry for interventional trials to capture grey literature and ongoing trials, to increase the number of available studies.

A high concern for risk of bias was identified due to missing outcome and selective reporting, including a lack of adherence to or reporting of a pre-specified statistical analysis plan. The attrition was high in two studies, except in Aslan et al. (2024), but in this study, there were inconsistencies found in the results reported. Other serious concerns due to inconsistencies and substantial heterogeneity were found in the studies. When assessing results, only one study reported statistically significant pain improvement. Sample size was another limitation identified, making the study unable to detect a minimal clinically important difference for pain reduction due to reduced power.

The studies were conducted at one or two sites in outpatient clinics, limiting access to a broader population. Female predominance incidence has been reported in chronic pain, and specifically in fibromyalgia. However, Ruschak (2023) reported that the predominance of the illness is similar for both sexes, with men being underdiagnosed. This factor can limit the generalizability of the study's results. One study exclusively recruited female patients (Aslan, 2024), and the other two were open to both female and male patients. Each study used a variation of probiotic combination that included *Lactobacillus acidophilus*, introducing variability that hinders direct comparison and complicates interpretation of the intervention's true effect. The three studies explored a range of fibromyalgia symptoms, including pain, gastrointestinal symptoms, general health status, psychiatric, sleep quality, and cognitive function. Multiple differences in the criteria to assess the diagnosis were identified across studies. Aslan Çin et al. used the American College of Rheumatology (ACR) criteria from 2010, Calandre et al. used the criteria from 2016, and Roman et al. used the criteria from both 1990 and 2010. The variations within the criteria versions have marked differences across versions, including variation in the number of symptoms or requirements to make a diagnosis, including missing or adding pain severity or pain index. The use of mixed criteria may lead to misclassification, as reported by Wolfe et al. (2016).



The three studies explored the impact of probiotics on pain in patients with fibromyalgia. However, heterogeneity in the survey tools and inconsistencies in the outcome measures used across trials, such as variations in VAS scoring, use of FIQ versus FIQR, and partial reporting of SF-36 domains, limit cross-study comparability. These differences among the studies limit the ability to conduct a subgroup analysis or meta-analysis as well as the generalizability of the results. The treatment effects were reported with inconsistent full disclosure of the statistical results, lacking a 95% CI that would help illustrate the precision of the effect estimates, relying only on p-values and descriptive statistics. Aslan et al. reported statistically significant improvement in pain intensity and fibromyalgia symptom severity (FIQ). The findings suggest that probiotics may have a mild effect in reducing pain in fibromyalgia patients. These effects are neither consistent nor robust across studies. In comparison, the other two studies (Roman et al., 2018; Calandre et al., 2021) failed to show improvement in pain relief. The use of validated pain scales is important to ensure reliable and replicable results. There was an instrumentation inconsistency observed among studies. The use of an ad hoc version of the VAS could contribute to Calandre et al.'s negative results, introducing information and measurement bias, as the tool was not designed to measure symptoms other than generalized pain. The use of fibromyalgia-related quality of life instruments to indirectly measure pain intensity and determine improvement was challenged by reporting bias. Studies used the FIQ, and one study used the revised version (FIQ-R). All reported quality of life, including the SF-36, differently, either by domain and/or overall score, introducing reporting bias. No meta-analysis was conducted due to the lack of consistency in outcome measures and reporting of results, which reduced the precision of any analysis. Although small improvements were often observed in both intervention and control groups, consistent responses in the placebo arm highlight the important placebo effect commonly described in fibromyalgia and make it more difficult to evaluate the effect of the treatment. These findings are generally consistent with a prior systematic review and meta-analysis conducted by Hui Lim (2022), who found no improvement in overall quality of life when using different dietary supplements for pain relief in fibromyalgia patients, including probiotics, compared to control groups. Roman et al.'s (2018) systematic review included a broader scope of fibromyalgia symptoms, including chronic fatigue and psychological symptoms, which is consistent with the studies in which pain was a secondary outcome.

This systematic review was limited by the small

number of included trials. Important methodological inconsistencies among studies introduced heterogeneity, reduced internal validity, and prevented generalizability of the results. These inconsistencies include the specific study populations (mostly females from Turkey and Spain), variation in diagnostic criteria, significant differences in outcome measures and their versions or non-validated adaptations, missing complete statistical reporting, and the use of different probiotic strains. Additionally, the lack of a robust pre-specified statistical analysis plan in the original studies hinders the ability to draw consistent and reliable conclusions.

Given the current evidence, probiotics cannot be recommended as a primary or standalone therapy for pain management in fibromyalgia. However, given their favorable safety profile and possible benefits in mood and gastrointestinal symptoms, probiotics may be cautiously considered as an adjunct to standard care. While one of the three included RCTs reported improvement in pain-related outcomes, the overall evidence remains inconclusive and of low certainty. High-quality studies with adequate statistical power are needed before probiotics can be considered part of the standard of care for this indication.

## Conclusion

This systematic review found no evidence of the efficacy of probiotics as monotherapy for pain in fibromyalgia due to heterogeneity of the current findings and methodological limitations. Future randomized controlled trials should prioritize the use of standardized and validated pain outcome tools, incorporate strain-specific analyses to better characterize probiotic efficacy, and include longer follow-up periods to assess sustained clinical benefit and reduce heterogeneity. Additionally, adequately powered sample sizes are essential to ensure findings are both robust and generalizable to the broader fibromyalgia population.

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## Conflicts of Interest

The authors declare no conflict of interest.

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