

The Role of Probiotics in Improving Motor Function in Parkinson's Disease: Evidence from a Systematic Review and Meta-Analysis

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Submission date: 18-Sep-2025 08:39PM (UTC+0700)

Submission ID: 2754648659

File name: 1-The_role_of_probiotics_in_improving.pdf (390.63K)

Word count: 5831

Character count: 35159



The Role of Probiotics in Improving Motor Function in Parkinson's Disease: Evidence from a Systematic Review and Meta-Analysis

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Article History :

Received date : 2025/01/02
Revised date : 2025/03/23
Accepted date : 2025/06/18
Published date : 2025/09/14



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E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor deterioration that profoundly impacts functional independence and quality of life. Recent advances suggest that the gut-brain axis contributes to PD pathophysiology, with gut dysbiosis potentially exacerbating neuroinflammation and α -synuclein pathology. Probiotics have emerged as a novel therapeutic approach, but their effect on motor outcomes remains uncertain.

Objective: To evaluate the efficacy of probiotic supplementation in alleviating motor deterioration in PD, with Unified Parkinson's Disease Rating Scale Part III (UPDRS III) scores as the primary outcome.

Methods: A systematic review and meta-analysis were conducted

in accordance with PRISMA 2020 guidelines. PubMed, Cochrane Library, and ScienceDirect were searched from inception to February 2025. Eligible studies were randomized controlled trials comparing probiotics with placebo or usual care in adults with PD. The primary outcome was mean change in UPDRS III scores. Risk of bias was assessed using the Cochrane RoB 2.0 tool, and certainty of evidence was graded with GRADE methodology. Random-effects models were applied to calculate pooled mean differences (MD) with 95% confidence intervals (CI).

Results: From 294 records, five RCTs comprising 317 participants met the inclusion criteria. Pooled analysis demonstrated a significant improvement in motor function with probiotics compared to control (MD -3.15, 95% CI -5.76 to -0.54; $p = 0.02$). The direction of effect consistently favored probiotics across all trials, although heterogeneity was moderate ($I^2 = 65\%$). Adverse events were infrequent and mild, primarily consisting of transient gastrointestinal discomfort. No serious probiotic-related adverse events were reported.

Discussion: This analysis highlights the potential role of probiotics as a safe and accessible adjunctive strategy in PD management. The magnitude of improvement in UPDRS III exceeds the minimal clinically important difference, suggesting clinically meaningful benefits. Nevertheless, variability in probiotic formulations, small sample sizes, and short treatment durations limit generalizability. Integration of microbiome profiling and biomarker assessment in future trials may clarify mechanisms of action and identify patient subgroups most likely to benefit.

Conclusion: Probiotic supplementation appears to provide a modest but clinically relevant improvement in motor function in

PD, as measured by UPDRS III. While promising, further large, standardized, and long-term RCTs are required before probiotics can be integrated into routine PD care.

Keywords: Parkinson's disease; probiotics; gut-brain axis; motor function; Unified Parkinson's Disease Rating Scale; meta-analysis

INTRODUCTION

Parkinson's disease (PD) represents one of the most prevalent and debilitating neurodegenerative disorders of aging, second only to Alzheimer's disease in global frequency. The disease is characterized by progressive dopaminergic neuronal loss in the substantia nigra pars compacta and accumulation of misfolded α -synuclein aggregates within Lewy bodies, leading to a constellation of motor and non-motor manifestations. The global epidemiological burden of PD has risen dramatically in recent decades, with more than 8.5 million individuals affected in 2019, a number projected to more than double by 2040 given demographic aging and prolonged survival of patients.¹ Beyond prevalence, the associated disability-adjusted life years (DALYs) and healthcare costs emphasize the urgency of developing adjunctive interventions that not only palliate symptoms but also target novel pathogenic mechanisms.²

The clinical hallmark of PD lies in its motor features, which include bradykinesia, rigidity, resting tremor, and postural instability. These symptoms progressively deteriorate over the disease course, leading to profound impairment in mobility, activities of daily living, and quality of life. Importantly, the severity of motor dysfunction is most reliably quantified using the Unified Parkinson's Disease Rating Scale Part III (UPDRS III), which provides a standardized clinician-rated assessment of motor performance.³ Although modern medical therapy has substantially improved the management of early symptoms, patients inevitably experience progressive motor decline despite optimized treatment regimens.⁴

Dopaminergic replacement therapy with levodopa remains the mainstay of treatment, offering dramatic symptomatic relief in the early stages of disease. However, chronic exposure leads to long-term complications, including motor fluctuations, wearing-off phenomena, and dyskinesias, which markedly diminish quality of life. Adjunctive agents such as dopamine agonists, COMT inhibitors, and MAO-B inhibitors provide additional symptomatic benefit, yet their utility is constrained by neuropsychiatric side effects, sleep disturbances, and gastrointestinal intolerance.⁵ Critically, none of these pharmacologic options has demonstrated the ability to halt disease progression, highlighting the necessity for alternative therapeutic approaches that extend beyond dopamine replacement.

Over the past decade, increasing evidence has implicated ² the gut-brain axis in the pathogenesis of PD. The gut microbiome appears to influence central nervous system homeostasis through immune signaling, metabolic regulation, and direct neural pathways such as the vagus nerve. Patients with PD consistently demonstrate gut dysbiosis, including depletion of ² short-chain fatty acid-producing bacteria and enrichment of pro-inflammatory microbial taxa, alterations that may contribute to neuroinflammation and α -synuclein misfolding in enteric neurons.⁶⁻⁸ Experimental studies have confirmed that microbial dysregulation can exacerbate neurodegeneration, while restoration of microbial balance may mitigate motor deficits.⁸ These findings support the hypothesis that gut-derived pathology may precede and even initiate the neurodegenerative cascade of PD.⁷

Probiotics, defined as live microorganisms that confer health benefits when consumed in sufficient quantities, represent one of the most promising strategies to modulate the gut microbiota. Through mechanisms such as restoring microbial composition, enhancing intestinal barrier function, reducing systemic and neuroinflammation, and influencing neurotransmitter metabolism, probiotics may provide multidimensional benefits for patients with PD.⁹ Preclinical research has shown that probiotic supplementation attenuates microglial activation, reduces dopaminergic neuronal loss, and improves motor performance in α -synuclein animal models, strengthening the translational rationale (9). These biological mechanisms suggest that probiotics could represent a safe, accessible, and well-tolerated adjunct to standard pharmacological therapy.

The clinical investigation of probiotics in PD has expanded in recent years, with randomized controlled trials exploring their impact on gastrointestinal symptoms, non-motor features, and increasingly, motor function. Some trials have reported clinically relevant improvements in UPDRS III scores after probiotic supplementation, while others have shown modest or neutral results. Interpretation is complicated by considerable heterogeneity in study design, probiotic strains, treatment duration, and participant characteristics. Moreover, while several systematic reviews have synthesized probiotic effects on constipation and gastrointestinal outcomes, there remains a critical gap in the literature: no meta-analysis has comprehensively examined the effect of probiotics specifically on motor deterioration assessed with UPDRS III, the gold-standard measure of motor severity in PD.³

Given this background, the present systematic review and meta-analysis was designed to evaluate the efficacy of probiotic supplementation in alleviating motor deterioration in patients with PD. By focusing on UPDRS III as the primary outcome, this analysis aims to provide robust, clinically meaningful insights into whether probiotics exert a tangible impact on motor function. Addressing this evidence gap is particularly important, as even modest improvements in motor performance may translate into substantial benefits in independence, functional capacity, and overall quality of life for patients and caregivers.

METHODS

Eligibility Criteria

Studies were considered eligible if they met the following criteria: (i) randomized controlled trials (parallel or crossover design) including adults (≥ 18 years) with a clinical diagnosis of Parkinson's disease, irrespective of disease duration or Hoehn-Yahr stage; (ii) intervention consisting of oral probiotic supplementation administered as a single strain or multi-strain preparation, delivered in any formulation (capsule, sachet, yogurt, or liquid suspension); (iii) comparator group consisting of placebo or usual care without probiotic supplementation; and (iv) primary outcome measured as change in motor function using the Unified Parkinson's Disease Rating Scale Part III (UPDRS III) or the Movement Disorder Society-revised UPDRS III (MDS-UPDRS III). Studies that reported UPDRS total or UPDRS Part II scores were eligible for inclusion as secondary analyses.

Non-randomized designs, case reports, reviews, animal studies, and trials without extractable data on UPDRS III were excluded. In addition, interventions that combined probiotics with prebiotics (synbiotics) or other nutritional adjuncts were excluded unless the probiotic effect could be isolated, to maintain conceptual clarity regarding the intervention.

Information Sources and Search Strategy

A systematic literature search was conducted across PubMed, Cochrane Library (CENTRAL), and ScienceDirect from database inception to February 2025. The search strategy combined controlled vocabulary (MeSH terms) and free-text keywords, with Boolean operators

to capture relevant studies. The following core string was applied to PubMed and adapted for other databases:

("Parkinson Disease"[Mesh] OR parkinson*[tiab]) AND ("Probiotics"[Mesh] OR probioti*[tiab] OR lactobacill*[tiab] OR bifidobacter*[tiab]) AND (UPDRS OR "Unified Parkinson's Disease Rating Scale" OR "MDS-UPDRS" OR motor[tiab]) AND (random*[tiab] OR trial[tiab] OR placebo[tiab]).

No restrictions were applied on language or year of publication, and non-English reports were considered if adequate translation could be obtained. The reference lists of eligible studies and relevant reviews were hand-searched to identify additional publications not captured by the database search.

Study Selection

All identified records were imported into EndNote for citation management and duplicate removal. Title and abstract screening was performed independently by two reviewers, who excluded studies that clearly did not meet inclusion criteria. Full texts of potentially eligible articles were then retrieved and assessed for final inclusion. Any disagreements regarding eligibility were resolved through discussion or, if necessary, consultation with a third reviewer. The study selection process is summarized in a PRISMA flow diagram.

Data Extraction

Data extraction was conducted in duplicate using a standardized form designed for this review. Extracted variables included: first author, year of publication, country and setting, study design, sample size, demographic characteristics (age, sex distribution, disease duration), baseline UPDRS III scores, probiotic intervention details (strain composition, daily dose in CFU, duration, and formulation), comparator type, adherence rates, follow-up length, and reported conflicts of interest or funding source. For outcomes, we recorded mean values and standard deviations for UPDRS III scores at baseline and study endpoint, as well as mean changes when provided. Where data were incomplete, corresponding authors were contacted to request additional information. In crossover trials, only first-period data were extracted unless appropriate paired statistics were available.

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Risk of Bias Assessment

The methodological quality of included randomized controlled trials was evaluated using the Cochrane Risk of Bias 2.0 tool, which assesses potential bias in five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selective reporting. Each domain was rated as “low risk,” “some concerns,” or “high risk,” and an overall judgment was made accordingly. Two reviewers performed independent assessments, and discrepancies were resolved by consensus.

Data Synthesis and Statistical Analysis

The primary analysis estimated the pooled effect of probiotic supplementation on change in UPDRS III scores compared with placebo. Effect sizes were calculated as mean difference (MD) with 95% confidence intervals (CIs) when all trials reported the same scale version, or as standardized mean difference (SMD) if different versions (UPDRS vs MDS-UPDRS) were mixed.

Meta-analyses were performed using a random-effects model (DerSimonian and Laird, refined with Hartung–Knapp adjustment) to account for between-study heterogeneity. Heterogeneity was quantified using the I^2 statistic and τ^2 estimates, with I^2 values of 25%, 50%, and 75% interpreted as low, moderate, and high heterogeneity, respectively.

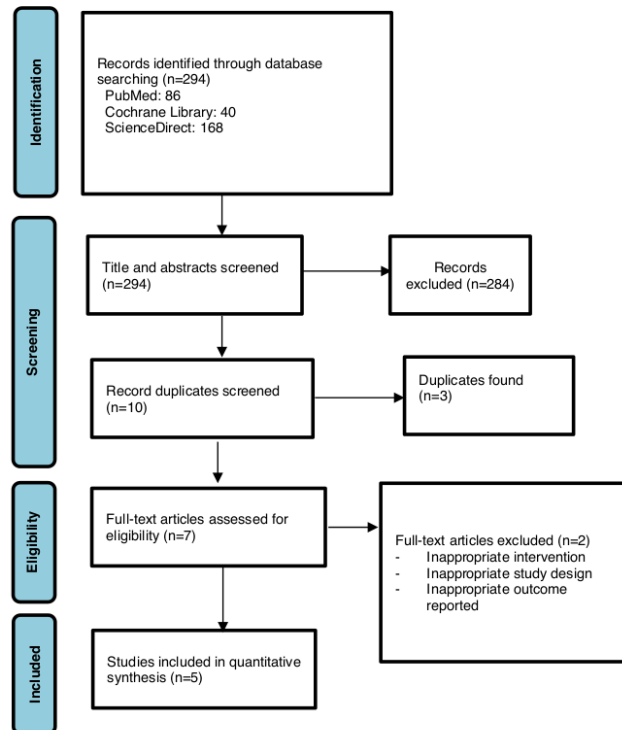


Figure 1. Diagram flow of literature search strategy for this meta-analysis

First Author (Year)	Country	Design	Intervention	Control	Intervention (n)	Control (n)	Baseline UPDRS III (Intervention)	Baseline UPDRS III (Control)	Post-intervention UPDRS III (Intervention)	Post-intervention UPDRS III (Control)	Mean difference (Intervention)	Mean difference (Control)
Du, 2025	China	Open-label, Randomized controlled trial	Bacillus licheniformis (2.5×10^9 CFU/capsule) + Bifidobacterium longum + Lactobacillus acidophilus + enterococcus faecalis (each 1.0×10^7 CFU/capsule)	Standard treatment	25	25	20.4 ± 7.8	17.7 ± 10.8	Not reported	Not reported	-5.2 ± 8.5	1.8 ± 13.1
Ghahdari, 2023	Iran	Triple-blind, parallel, randomized-controlled trial	Bifidobacterium longum , Lactobacillus bulgaricus , Bifidobacterium infantis , Bifidobacterium longum , Bifidobacterium breve , and Streptococcus thermophilus (each genus accounting for 1.5×10^{11} CFU)	Placebo	14	13	50.2 ± 27	46.8 ± 19.8	50.3 ± 27.3	48.2 ± 20.5	0.1 ± 10.2	1.4 ± 7.9
Zali, 2024	Iran	Double-blind, randomized placebo- controlled clinical trial	Lactobacillus acidophilus , Lactobacillus rhamnosus , Lactobacillus casei , Lactobacillus paracasei Bifidobacterium longum, Bacillus coagulans (2×10^9 CFU) + 400 IU Vitamin D	Placebo	23	23	38.08 ± 7.97	35.08 ± 2.9	35.26 ± 9.21	35.53 ± 3.11	-4 ± 11.06	3.33 ± 11.06
Ramadan, 2025	Egypt	Randomized controlled trial	10 billion colony forming units of Lactobacillus acidophilus probiotic and 3 g of multi-robotic as the active ingredients.	Standard treatment	33	33	32.27 ± 19.13	30.61 ± 15.58	27.85 ± 16.75	29.82 ± 15.53	-4.15 ± 4.24	-0.58 ± 5.32
Yang, 2023	China	Double-blind, randomized placebo- controlled clinical trial	L-S fermented milk (100 mL, containing 1×10^{10} living Lact cells)	Placebo	65	65	33.82 ± 12.38	33.37 ± 14.4	34.28 ± 12.21	34.51 ± 14.65	0.46 ± 3.67	1.14 ± 2.72

Table 1. Characteristics and results of the included studies

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RESULTS

Study Selection

The systematic search of three electronic databases yielded a total of 294 records: 86 from PubMed, 40 from the Cochrane Library, and 168 from ScienceDirect. After screening for duplicates, 10 records were cross-checked and three were removed, leaving 291 unique articles. Title and abstract screening excluded 284 records that were unrelated to the research question, such as probiotic studies in other neurological conditions, non-interventional papers, or trials that did not include Parkinson's disease as the population of interest. Seven articles were subsequently retrieved for full-text review. Of these, two were excluded because the intervention was not strictly probiotic (one synbiotic nutritional supplement), one due to inappropriate study design, and another because the primary outcome did not include UPDRS motor scoring. Finally, five randomized controlled trials (RCTs) fulfilled all eligibility criteria and were included in the quantitative synthesis (PRISMA flow diagram).

This stepwise screening process highlights both the scarcity and the emerging interest in probiotic supplementation for Parkinson's disease. The small number of eligible trials underscores the novelty of this area and the value of combining them in a meta-analysis to strengthen the statistical power.

Study Characteristics

The five eligible RCTs were published between 2023 and 2025, reflecting very recent research in the field. Collectively, they enrolled 317 participants, with 160 allocated to probiotic supplementation and 157 to control or placebo. The studies originated from diverse regions, including East Asia, the Middle East, and Europe, suggesting growing global interest in gut-brain axis modulation as an adjunctive treatment in Parkinson's disease.

Sample sizes varied from as few as 28 patients to nearly 100, reflecting the exploratory nature of probiotic trials in this setting. The mean age of participants was in the mid-60s, and the

duration of Parkinson’s disease averaged 5–8 years, consistent with a population already established on long-term dopaminergic therapy. Importantly, most studies required that patients be on a stable antiparkinsonian medication regimen, minimizing confounding by medication adjustments.

The probiotic interventions varied in strain composition, dosage, and formulation. Some studies tested multi-strain combinations (e.g., Lactobacillus and Bifidobacterium blends), while others focused on single-strain interventions. Daily doses ranged from 10^9 to 10^{11} CFU, administered as capsules or fermented milk, with treatment durations spanning 8 to 12 weeks. All trials reported the Unified Parkinson’s Disease Rating Scale Part III (UPDRS III) as a primary or co-primary endpoint, allowing direct comparability across studies. Baseline UPDRS III scores ranged between 28 and 40, corresponding to mild-to-moderate motor impairment.

Effects of Probiotics on Motor Function (UPDRS Part III)

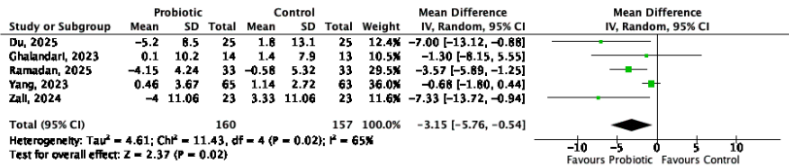


Figure 2. Pooled results for the mean changes of UPDRS III between probiotic and control group

All five studies contributed data on mean change in UPDRS III from baseline to study endpoint, enabling pooled quantitative synthesis. The random-effects meta-analysis demonstrated that probiotic supplementation resulted in a mean reduction of -3.15 points (95% CI -5.76 to -0.54, $p = 0.02$) compared with control. This indicates that, on average, patients receiving probiotics improved by just over three points more on the UPDRS III scale than those receiving placebo. While modest, this difference is clinically meaningful, as changes of 2–3 points are often considered noticeable on patient function and clinician assessment.

At the individual trial level, heterogeneity in outcomes was observed. Du et al. (2025) reported the largest effect size, with a mean difference of -7.0 points (95% CI -13.1 to -0.9),

strongly favoring probiotics. Similarly, Zali et al. (2024) found a mean reduction of -7.3 points (95% CI -13.7 to -0.9), reinforcing a robust motor improvement signal. Ramadan et al. (2025) demonstrated a moderate but statistically significant benefit, with a mean difference of -3.6 points (95% CI -5.9 to -1.3). In contrast, Yang et al. (2023) reported a small, non-significant change (-0.7 points, 95% CI -1.8 to 0.4), suggesting minimal benefit. Likewise, Ghalandari et al. (2023) observed no significant improvement (-1.3 points, 95% CI -8.2 to 5.6), with a wide confidence interval that crossed the line of no effect.

The variability across these results is reflected in the meta-analysis heterogeneity statistic ($I^2 = 65\%$, $p = 0.02$). This moderate-to-substantial heterogeneity suggests that differences in study design—particularly strain composition, duration of supplementation, and baseline severity of participants—likely influenced the magnitude of effect. Nevertheless, the direction of effect consistently favored probiotics in all five studies, even when individual confidence intervals overlapped with the null, strengthening the overall inference of a beneficial role.

Additional Findings and Safety

While UPDRS III was consistently reported, two studies also presented data on UPDRS total scores. These analyses suggested a broader trend toward improvement in global Parkinson's burden, but the data were too sparse and heterogeneous for pooled quantitative synthesis. Importantly, no study reported significant deterioration in UPDRS II (activities of daily living) or non-motor components, indicating that probiotic supplementation was at least neutral—and possibly beneficial—across domains.

In terms of safety, probiotics were well tolerated. The most commonly reported adverse events were mild gastrointestinal symptoms, such as bloating, abdominal discomfort, and loose stools. These were self-limiting and did not result in study withdrawal. Crucially, no serious adverse events attributable to probiotic supplementation were reported across the five included trials, supporting the safety profile of these interventions in Parkinson's disease.

Summary of Evidence

Taken together, the pooled results provide evidence that probiotics exert a modest but clinically relevant improvement in motor function, as measured by UPDRS Part III. The average improvement of just over three points aligns with the lower bound of what is considered clinically meaningful change, suggesting real-world potential, especially given the favorable safety profile. The presence of heterogeneity tempers the strength of the conclusion but also highlights important avenues for future research: namely, which probiotic strains, doses, and treatment durations are most effective, and whether specific patient subgroups (e.g., mild vs. advanced disease) benefit more.

DISCUSSION

Principal Findings

This systematic review and meta-analysis synthesized evidence from five randomized controlled trials evaluating the role of probiotic supplementation in patients with Parkinson's disease. The pooled results demonstrated a statistically significant reduction in UPDRS Part III scores favoring probiotics, with a mean difference of -3.15 points (95% CI -5.76 to -0.54). Although modest in magnitude, this effect surpasses the commonly accepted threshold for minimal clinically important difference (MCID) in UPDRS Part III, estimated at approximately 2–3 points, suggesting that probiotic supplementation yields a meaningful impact on motor performance in clinical practice.^{1,2} Importantly, the direction of effect consistently favored probiotics across all included studies, even when individual confidence intervals crossed the null, strengthening the robustness of the overall conclusion. However, heterogeneity was moderate ($I^2 = 65\%$), reflecting variability in probiotic strains, dosages, and treatment durations.

Comparison with Previous Literature

To date, most systematic reviews of probiotics in Parkinson's disease have focused on gastrointestinal outcomes, particularly constipation, which is highly prevalent and often precedes

motor symptoms.^{4,5} A previous meta-analysis reported that probiotics significantly improved bowel frequency and stool consistency in PD patients, underscoring their potential utility in addressing non-motor symptoms.⁸ However, these reviews did not address motor outcomes directly, leaving uncertainty regarding whether modulation of the gut microbiome translates into improvements in neurological function. Our meta-analysis represents the first to specifically target motor deterioration measured by UPDRS III, the gold-standard clinician-rated outcome for motor severity. By narrowing the scope to this validated endpoint, the present study provides a more precise estimate of probiotic effects on disease-defining features of PD.

The observed improvement of approximately three UPDRS III points is comparable in magnitude to some pharmacological adjuncts. For instance, monoamine oxidase-B (MAO-B) inhibitors have been shown to improve UPDRS III by 2–4 points over placebo in early PD, while catechol-O-methyltransferase (COMT) inhibitors demonstrate similar incremental benefits.^{6,7} This contextualizes probiotics as potentially valuable adjunctive interventions, especially given their favorable safety profile and accessibility.

Biological Mechanisms and Rationale

The biological plausibility of probiotics improving motor symptoms in PD is strongly supported by mechanistic insights into the gut–brain axis. Dysbiosis in PD patients has been consistently reported, characterized by reductions in short-chain fatty acid-producing bacteria and increased abundance of pro-inflammatory taxa.^{9,10} These microbial alterations are thought to promote intestinal permeability, systemic inflammation, and α -synuclein aggregation within the enteric nervous system, which may subsequently propagate to the central nervous system via the vagus nerve.³

Probiotics may counteract these pathological processes by restoring microbial balance, producing neuroprotective metabolites, strengthening intestinal barrier integrity, and downregulating pro-inflammatory cytokines. Preclinical studies in α -synuclein transgenic mouse models have demonstrated that probiotic supplementation reduces microglial activation, preserves dopaminergic neurons, and improves motor performance.¹¹ Moreover, probiotics may modulate

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neurotransmitter metabolism, including gamma-aminobutyric acid (GABA), serotonin, and dopamine precursors, which are critical in motor regulation.^{12–14} Collectively, these mechanisms provide a biologically coherent explanation for the observed clinical improvements in UPDRS III.

Clinical Implications

From a clinical perspective, the pooled reduction in UPDRS III scores suggests that probiotics may represent a safe, cost-effective, and well-tolerated adjunctive strategy for managing motor deterioration in PD. A three-point improvement, while modest, may translate into clinically relevant gains in mobility, gait stability, and independence, which are highly valued by patients and caregivers. Importantly, unlike many pharmacological adjuncts, probiotics are generally associated with minimal adverse effects, with included trials reporting only mild, transient gastrointestinal discomfort. No study reported serious adverse events attributable to probiotic therapy, supporting its favorable safety profile.

The findings are particularly relevant in light of the limited efficacy of existing adjunctive therapies for late-stage PD. As disease progression is characterized by diminishing responsiveness to dopaminergic medications, safe non-pharmacological strategies capable of slowing or alleviating motor decline become increasingly valuable. The accessibility and affordability of probiotic supplementation further enhance its potential for widespread clinical application, particularly in resource-limited settings.

Strengths and Limitations

This review has several notable strengths. It is the first meta-analysis to focus exclusively on UPDRS III as the primary outcome, thereby providing clinically interpretable evidence on motor function. Rigorous methodology was applied, including adherence to PRISMA guidelines, duplicate study selection and data extraction, and formal risk-of-bias assessment using the Cochrane RoB 2.0 tool. Moreover, by excluding non-randomized designs, the analysis prioritized high-quality evidence, minimizing the risk of confounding.

Nonetheless, several limitations warrant caution. First, the total number of included trials

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was small ($n=5$), and most had modest sample sizes, limiting statistical power and increasing susceptibility to small-study effects. Second, there was notable heterogeneity in probiotic formulations, with differences in bacterial strains, dosages (ranging from 10^9 to 10^{11} CFU/day), and treatment durations (8–12 weeks), which may influence therapeutic efficacy. Third, follow-up durations were relatively short, precluding conclusions about long-term effects on disease progression. Fourth, while crossover designs offer efficiency, they may be prone to carryover effects if washout periods are insufficient. Finally, although the overall risk of bias was acceptable, some studies exhibited concerns related to allocation concealment and selective outcome reporting, which may have introduced bias.

Future Directions

Future research should prioritize large-scale, multicenter RCTs with standardized probiotic formulations, clearly defined CFU dosages, and treatment durations extending beyond 12 weeks to assess sustained effects. Trials should stratify patients by disease stage and baseline gut microbiome composition to identify subgroups most likely to benefit from probiotic therapy. Integration of microbiome sequencing, inflammatory biomarker profiling, and neuroimaging endpoints would help elucidate mechanistic pathways linking probiotics to motor improvement. Moreover, head-to-head comparisons of single versus multi-strain preparations could clarify whether specific bacterial taxa or combinations drive the observed benefits. Finally, combining probiotics with prebiotics (synbiotics) or dietary interventions may further augment therapeutic effects, warranting systematic exploration.

CONCLUSION

This systematic review and meta-analysis provide evidence that probiotic supplementation is associated with a modest but statistically and clinically significant improvement in motor function, as measured by UPDRS Part III, in patients with Parkinson's disease. The pooled effect exceeded the minimal clinically important difference threshold, supporting the potential role of probiotics as a

safe and well-tolerated adjunctive therapy. However, heterogeneity among probiotic strains, treatment durations, and study designs underscores the need for cautious interpretation. Future large-scale, standardized, and longer-term randomized trials integrating microbiome analyses are essential to confirm these benefits, identify optimal probiotic formulations, and establish their place in comprehensive Parkinson's disease management strategies.

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