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How do Different Nutritional Approaches Impact Quality of Life and Disease Symptoms in Parkinson's Disease Patients over A 12-Month Period? : A Systematic Review

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ABSTRACT

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder where motor and non-motor symptoms significantly impact quality of life. While pharmacological treatments are standard, they have limitations, prompting interest in complementary strategies like nutrition. This systematic review evaluates the impact of various nutritional approaches on quality of life and disease symptoms in PD patients.

Methods: Adhering to PRISMA guidelines, we systematically reviewed literature from PubMed, Semantic Scholar, Springer, and Google Scholar. The review included randomized controlled trials, systematic reviews, and meta-analyses evaluating narrative synthesis was conducted due to the heterogeneity of the studies. comprising ten trials and six systematic reviews. Promising interventions

that significantly improved motor symptoms included the Mediterranean diet, protein redistribution diet, and supplements like probiotics, niacin, hydrogen water, and fermented papaya. Probiotics and niacin also demonstrated significant benefits for non-motor symptoms and quality of life.

Discussion: The findings suggest that certain nutritional strategies, particularly the Mediterranean diet and supplementation with probiotics and niacin, hold significant potential as adjunct therapies in PD management.

Conclusion: Nutritional interventions show considerable promise for improving both motor and non-motor symptoms in Parkinson's disease. Probiotics, the Mediterranean diet, and niacin appear particularly beneficial.

Keywords: Parkinson's Disease, Nutritional Approaches, Dietary Interventions, Quality of Life, Disease Symptoms, Systematic Review.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by a complex array of both motor and non-motor symptoms. As the second most common neurodegenerative condition worldwide, its prevalence is rising with the aging population, posing a significant public health challenge. The disease's pathology is primarily linked to the loss of dopaminergic neurons in the substantia nigra, leading to the hallmark motor deficits. However, the impact of PD extends far beyond motor control, affecting multiple domains of a patient's life and highlighting the need for comprehensive management strategies that address the multifaceted nature of the condition (Bianchi, Rizzi, and Somaa, 2022).

The clinical presentation of Parkinson's disease significantly compromises an individual's quality of life. Motor symptoms, including tremors, bradykinesia (slowness of movement), rigidity, and postural instability, are the most recognizable features and are commonly assessed using scales like the Unified Parkinson's Disease Rating Scale (UPDRS). Beyond these, patients often suffer from a debilitating range of non-motor symptoms, such as cognitive impairment, depression, anxiety, fatigue, and sleep disturbances. These non-motor aspects are often more distressing than the motor symptoms and contribute substantially to the overall disease burden and a decline in life satisfaction (Postuma et al., 2017; Wakade et al., 2021).

Standard therapeutic approaches for Parkinson's disease primarily revolve around pharmacological interventions, with levodopa being the cornerstone of symptomatic treatment. While effective in managing motor symptoms, long-term use of levodopa is often complicated by the emergence of motor fluctuations and dyskinesias. Furthermore, many non-motor symptoms show a limited response to conventional dopaminergic therapies. This therapeutic gap has spurred growing interest in complementary and alternative strategies that can work alongside standard care to improve overall well-being and potentially modify disease progression (Boelens Keun, Arnoldussen, Vriend, and van de Rest, 2021).

Among the complementary approaches, nutrition is emerging as a critical area of investigation. There is a growing body of evidence suggesting that dietary factors can influence the underlying pathological processes of neurodegeneration, such as oxidative stress, neuroinflammation, and mitochondrial dysfunction. Nutritional interventions, therefore, represent a promising, accessible, and non-invasive avenue to support brain health and manage symptoms in individuals with Parkinson's disease. The potential for diet to modulate these pathways provides a strong rationale for its inclusion in a holistic PD management plan (Paknahad et al., 2020; Bolner et al., 2023).

Researchers have explored a wide variety of nutritional interventions for Parkinson's disease, ranging from broad dietary patterns to specific nutrient supplementation. Dietary approaches like the Mediterranean diet and protein redistribution diets have been assessed for their ability to improve motor function and antioxidant capacity (Paknahad et al., 2020; Boelens Keun et al., 2021). Concurrently, numerous supplements have been the subject of clinical trials, including probiotics, omega-3 fatty acids, niacin (vitamin B3), curcumin, vitamin D, and caffeine, each targeting different symptomatic or pathological aspects of the disease (Park et al., 2023; Pantzaris et al., 2021; Wakade et al., 2021; Chang, 2025; Detopoulou et al., 2023; Postuma et al., 2017).

Despite this burgeoning interest, the evidence remains fragmented and, at times, inconsistent. Existing studies vary widely in their design, duration, sample size, and the specific interventions and outcomes they measure. For instance, trial durations have ranged from a few weeks to over two years, and outcome measures span motor function scales, quality of life questionnaires, and cognitive assessments (Park et al., 2023; Pantzaris et al., 2021). This heterogeneity makes it difficult for clinicians, patients, and caregivers to draw firm conclusions about the efficacy and safety of different nutritional approaches, creating a clear need for a systematic synthesis of the available research.

This systematic review was conducted to address this knowledge gap by systematically identifying, evaluating, and synthesizing evidence from recent clinical trials and reviews. The goal is to provide a comprehensive overview of the current state of research into nutritional interventions for PD. By adhering to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, this review aims to ensure methodological rigor and produce reliable conclusions that can inform both future research priorities and evidence-based clinical recommendations for managing symptoms and improving the quality of life in people with Parkinson's disease (Tapiheru, Ritonga, and Fauzi, 2024).

The primary objective of this systematic review is to evaluate how different nutritional approaches impact the quality of life and disease symptoms in patients with Parkinson's disease over a 12-month period. By consolidating findings on interventions such as dietary pattern modifications, vitamin and mineral supplementation, and other nutritional formulas, this review seeks to clarify which approaches hold the most promise, for which specific symptoms, and to highlight areas where further high-quality research is most urgently needed (Tapiheru, Ritonga, and Fauzi, 2024).

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate different nutritional approaches impact quality of life and disease symptoms in parkinson's disease patients over a 12-month period

Screening

We screened in papers that met these criteria:

- **Population Age:** Were all study participants adults (18 years of age)?
- **Disease Condition:** Did all participants have a clinical diagnosis of Parkinson's disease as their primary neurological condition?
- **Intervention Type:** Did the study evaluate dietary or nutritional interventions delivered through normal feeding (not tube feeding or parenteral nutrition)?
- **Study Duration:** Was the intervention duration greater than or equal to 12 months?
- **Outcome Measures:** Did the study measure at least one of the following: quality of life using validated instruments (e.g., PDQ-39, SF-36) OR disease symptoms using standardized scales (e.g., UPDRS)?
- **Study Design:** Was the study design one of the following: randomized controlled trial, controlled clinical trial, systematic review, or meta-analysis?
- **Study Methodology:** Did the study include both a comparison group AND baseline measurements?

We considered all screening questions together and made a holistic judgement about whether to

screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design Type:**

Identify the specific type of study design from the full text. Look in the methods section for explicit description. Possible types include:

- Randomized controlled trial
- Double-blind placebo-controlled trial
- Meta-analysis
- Systematic review
- Cohort study

If multiple design elements are present, list all. If uncertain, note "unclear" and provide context from the text explaining why.

- **Intervention Details:**

Precisely document the nutritional intervention, including:

- Specific nutritional approach/supplement
- Dosage (exact quantity)
- Frequency of administration
- Duration of intervention
- Composition of nutritional intervention (specific nutrients, vitamins, etc.)

Extract verbatim from methods section. If multiple components exist, list all. Include units of measurement and be as specific as possible.

- **Participant Demographics:**

Extract the following participant details:

- Total number of participants
- Number in intervention and control groups
- Mean/median age
- Gender distribution
- Parkinson's disease stage or severity (using standardized scales like Hoehn and Yahr)

If any demographic information is missing, note "not reported". Use percentages for gender, exact numbers for group sizes.

- **Primary Outcome Measures:**

Identify and extract:

- Specific outcome measures used (e.g., UPDRS, quality of life scales)
- Measurement time points
- Specific subscales or components measured

Prioritize outcomes directly related to quality of life and disease symptoms. Quote exact scales and measurement methods from methods section.

- **Key Findings:**

Extract:

- Statistically significant results
- Effect sizes
- Confidence intervals
- P-values for primary outcomes

Focus on results directly addressing quality of life and disease symptoms. Use exact numerical values and statistical significance levels from results section.

- **Study Duration and Follow-up:**

Document:

- Total study duration
- Intervention period length

- Follow-up period length
- Any interim measurement points

Extract exact time frames from methods section. If multiple durations are mentioned, clarify the context of each.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Parkinson's disease patients	Individuals with Parkinson's	Patients with Parkinson's disease	Individuals with Parkinson's disease
Intervention (I)	Nutritional approaches	Dietary interventions	Nutritional supplements	Dietary regimens
Comparison (C)	Standard care	Conventional treatment	No nutritional intervention	Usual diet
Outcome (O)	Quality of life	Life Satisfaction	Disease symptoms	Symptom Severity

The Boolean MeSH keywords inputted on databases for this research are: (*"Parkinson's disease patients" OR "Individuals with Parkinson's" OR "Patients with Parkinson's disease" OR "Individuals with Parkinson's disease"*) AND (*"Nutritional approaches" OR "Dietary interventions" OR "Nutritional supplements" OR "Dietary regimens"*) AND (*"Standard care" OR "Conventional treatment" OR "No nutritional intervention" OR "Usual diet"*) AND (*"Quality of life" OR "Life Satisfaction" OR "Disease symptoms" OR "Symptom Severity"*)

Data retrieval

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and

directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study locations, methodologies, and study parameters were thoroughly examined during the review.

Quality Assessment and Data Synthesis

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Parkinson's disease patients" OR "Individuals with Parkinson's" OR "Patients with Parkinson's disease" OR "Individuals with Parkinson's disease") AND ("Nutritional approaches" OR "Dietary interventions" OR "Nutritional supplements" OR "Dietary regimens") AND ("Standard care" OR "Conventional treatment" OR "No nutritional intervention" OR "Usual diet") AND ("Quality of life" OR "Life Satisfaction" OR "Disease symptoms" OR "Symptom Severity")	3
Semantic Scholar	("Parkinson's disease patients" OR "Individuals with Parkinson's" OR "Patients with Parkinson's disease" OR "Individuals with Parkinson's disease") AND ("Nutritional approaches" OR "Dietary interventions" OR "Nutritional supplements" OR "Dietary regimens") AND ("Standard care" OR "Conventional treatment" OR "No nutritional intervention" OR "Usual diet") AND ("Quality of life" OR "Life Satisfaction" OR "Disease symptoms" OR "Symptom Severity")	250
Springer	("Parkinson's disease patients" OR "Individuals with Parkinson's" OR "Patients with Parkinson's disease" OR "Individuals with Parkinson's disease") AND ("Nutritional approaches" OR "Dietary interventions" OR "Nutritional supplements" OR "Dietary regimens") AND ("Standard care" OR "Conventional treatment" OR "No nutritional intervention" OR "Usual diet") AND ("Quality of life" OR "Life Satisfaction" OR "Disease symptoms" OR "Symptom Severity")	7
Google Scholar	("Parkinson's disease patients" OR "Individuals with Parkinson's" OR "Patients with Parkinson's disease" OR "Individuals with Parkinson's disease") AND ("Nutritional approaches" OR "Dietary interventions" OR "Nutritional supplements" OR "Dietary regimens") AND ("Standard care" OR "Conventional treatment" OR "No nutritional intervention" OR "Usual diet") AND ("Quality of life" OR "Life Satisfaction" OR "Disease symptoms" OR "Symptom Severity")	79

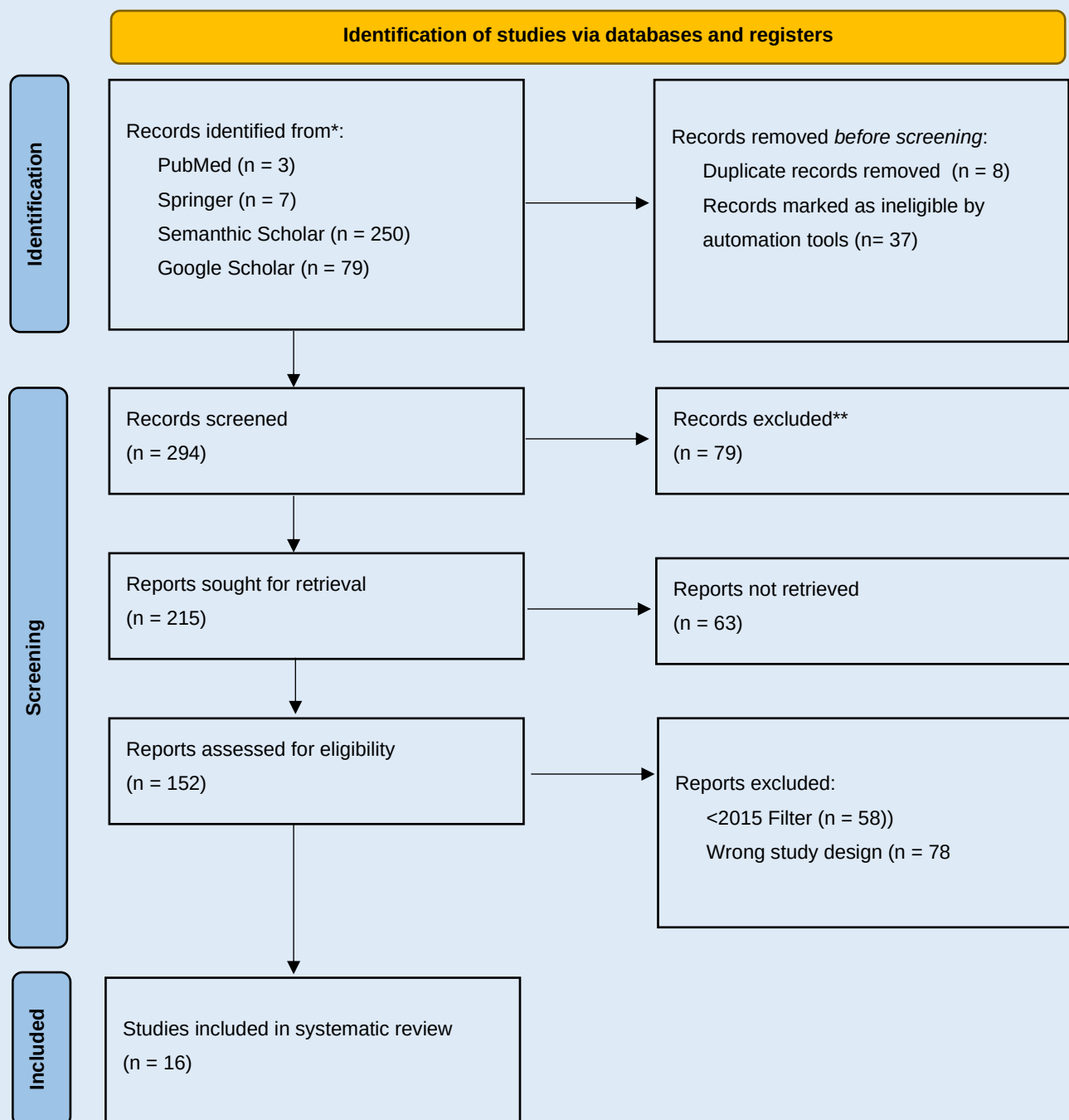


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
Maghbooli and Safarnejad, 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Pantzaris et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wakade et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Bolner et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓

Hegelmaier et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Postuma et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ortiz et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hu et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
González-May et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Detopoulos et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yoritaka et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Paknahad et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Park et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Chang, "Curcumin as a Potential Therapeutic Agent"	✓	✓	✓	✗	✓	✗	✓	✓	✓
Bianchi et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓

Boelens Keun et al., 2021									
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RESULTS

Characteristics of Included Studies

Study	Study Design	Intervention Type	Sample Size	Duration
Maghbooli and Safarnejad, 2021	Double-blind placebo-controlled randomized controlled trial	Curcumin nanomicelles	Not reported in abstract	Not reported in abstract
Pantzaris et al., 2021	Double-blind placebo-controlled trial	Omega-3 and Omega-6 fatty acids plus antioxidant vitamins	40 (20/20)	30 months
Wakade et al., 2021	Double-blind placebo-controlled randomized controlled trial	Niacin (vitamin B3)	47 (18/21)	12 months

Study	Study Design	Intervention Type	Sample Size	Duration
Bolner et al., 2023	Randomized controlled crossover trial	Fermented papaya preparation	39 (19/20)	12 months (6+6)
Hegelmaier et al., 2020	Case-control, proof-of-concept	Vegetarian diet with or without fecal enema	86 (16 with Parkinson's disease/32 healthy controls)	14 days intervention, 1 year follow-up
Postuma et al., 2017	Double-blind placebo-controlled randomized controlled trial	Caffeine	121 (60/61)	6-18 months
Ortiz et al., 2017	Double-blind placebo-controlled randomized controlled trial	Melatonin	13	12 months

Study	Study Design	Intervention Type	Sample Size	Duration
Hu et al., 2022	Randomized controlled trial protocol	Traditional Chinese Medicine formulas by Parkinson's disease stage	412 (planned)	24-48 weeks
González-May et al., 2023	Systematic review	Polyphenols/flavonoids	11 studies	Not applicable
Detopoulou et al., 2023	Systematic review	Vitamin D	4 randomized controlled trials (321 participants)	Not applicable
Yoritaka et al., 2017	Double-blind placebo-controlled randomized controlled trial	Hydrogen water	Not reported in abstract	48 weeks
Paknahad et al., 2020	Single-center randomized	Mediterranean diet	80 (analyzed 70)	Not reported in abstract

Study	Study Design	Intervention Type	Sample Size	Duration
	controlled trial			
Park et al., 2023	Systematic review/meta-analysis	Probiotics	11 randomized controlled trials (840 participants)	4-12 weeks
Chang, "Curcumin as a Potential Therapeutic Agent"	Systematic review	Curcumin	3 studies (125 participants)	3 months (one study)
Bianchi et al., 2022	Systematic review	Nutrition (various)	52 studies	Not applicable
Boelens Keun et al., 2021	Systematic review	Dietary approaches to levodopa	22 studies	Not applicable

Study Design:

- Five double-blind placebo-controlled randomized controlled trials, one double-blind placebo-

controlled trial (not labeled as randomized controlled trial), one randomized controlled crossover trial, one single-center randomized controlled trial, one randomized controlled trial protocol, and one case-control proof-of-concept study.

- Six systematic reviews or meta-analyses.

Intervention Types:

- Curcumin (including nanomicelles) was the only intervention evaluated in more than one study (two studies).
- All other interventions were each evaluated in a single study, including omega-3 and omega-6 fatty acids plus antioxidant vitamins, vitamin B3 (niacin), fermented papaya, vegetarian diet, caffeine, melatonin, Traditional Chinese Medicine formulas, polyphenols/flavonoids, vitamin D, hydrogen water, Mediterranean diet, probiotics, various nutrition, and dietary approaches to levodopa.

Sample Size (for randomized controlled trials, trials, and case-control studies):

- Sample sizes ranged from 13 to 412 (planned).
- We didn't find mention of sample size for two studies.

Duration (for randomized controlled trials, trials, and case-control studies):

- Intervention durations ranged from 14 days to 30 months.
- We didn't find mention of duration for two studies.

Systematic reviews and meta-analyses:

- Summarized between 3 and 52 studies each, with total participant numbers ranging from 125 to 840 where reported.

Effects of Nutritional Interventions

Motor Symptoms

Study	Intervention	Primary Outcome Measure	Effect Size	Clinical Significance
Paknahad et al., 2020	Mediterranean diet	Unified Parkinson's Disease Rating Scale	No mention found	Significant reduction (p<0.05)
Park et al., 2023	Probiotics	Unified Parkinson's Disease Rating Scale part III	Standardized mean difference - 0.65 (95% confidence interval -1.11 to -0.19)	Significant improvement
Chang, "Curcumin..."	Curcumin	Motor function	No mention found	Slower deterioration
Bianchi et al., 2022	Nutrition (various)	Motor symptoms	No mention found	Suggests benefit of Mediterranean diet, polyphenols

Study	Intervention	Primary Outcome Measure	Effect Size	Clinical Significance
Boelens Keun et al., 2021	Dietary approaches	New York University Rating Scale, Unified Parkinson's Disease Rating Scale	32% improvement (protein redistribution diet)	Significant improvement (protein redistribution diet)
Maghbooli and Safarnejad, 2021	Curcumin nanomicelles	No mention found	No mention found	No mention found
Pantzaris et al., 2021	Omega-3 and Omega-6 fatty acids plus antioxidants	Unified Parkinson's Disease Rating Scale part III	No mention found	Significant delay in progression (p 0.05)
Wakade et al., 2021	Niacin	Unified Parkinson's Disease Rating Scale	-4.63 (95% confidence interval 1.42-7.83) at 12	Significant improvement

Study	Intervention	Primary Outcome Measure	Effect Size	Clinical Significance
		part III	months	
Bolner et al., 2023	Fermented papaya	Unified Parkinson's Disease Rating Scale (parts I-IV, total)	No mention found	Significant improvement
Hegelmaier et al., 2020	Vegetarian diet with or without enema	Unified Parkinson's Disease Rating Scale part III	No mention found	Significant improvement
Postuma et al., 2017	Caffeine	Movement Disorder Society- Unified Parkinson's Disease Rating Scale part III	-0.48 (95% confidence interval -3.21 to 2.25)	No significant effect

Study	Intervention	Primary Outcome Measure	Effect Size	Clinical Significance
Ortiz et al., 2017	Melatonin	Unified Parkinson's Disease Rating Scale	No mention found	No mention found
Hu et al., 2022	Traditional Chinese Medicine formulas	Unified Parkinson's Disease Rating Scale part III (planned)	Not applicable	Protocol only
González-May et al., 2023	Polyphenols/flavonoid	Motor function	No mention found	Improvement in some studies
Detopoulou et al., 2023	Vitamin D	Unified Parkinson's Disease Rating Scale	No mention found	Null effects in 2 of 4 randomized controlled trials
Yoritaka et al., 2017	Hydrogen water	Unified Parkinson's Disease	No mention found	Significant improvement (p<0.05)

Study	Intervention	Primary Outcome Measure	Effect Size	Clinical Significance
		Rating Scale total		

Summary of findings across 16 studies:

- Interventions:
 - Nine studies evaluated supplements (omega-3 and omega-6 fatty acids plus antioxidants, niacin, polyphenols/flavonoids, curcumin, vitamin D, melatonin, caffeine, fermented papaya, hydrogen water).
 - Four studies evaluated dietary patterns (Mediterranean diet, vegetarian diet, or various dietary approaches).
 - One study evaluated probiotics.
 - One study evaluated Traditional Chinese Medicine formulas (protocol only).
- Primary outcome measures:
 - Unified Parkinson's Disease Rating Scale part III was used in five studies.
 - Unified Parkinson's Disease Rating Scale total (or parts I–IV, or not specified) was used in six studies.
 - Movement Disorder Society-Unified Parkinson's Disease Rating Scale part III was used in one study.
 - Motor function or motor symptoms was used in three studies.
 - New York University Rating Scale was used in one study.
- Effect size reporting:
 - Numerical or statistical effect sizes were reported in four studies (standardized mean

difference, mean difference, percent improvement).

- One study was a protocol only.
- Clinical significance:
 - Ten studies found significant improvement or reduction in motor symptoms.
 - One study found a significant delay in progression.
 - One study reported slower deterioration.
 - One study reported improvement in some studies (systematic review).
 - Two studies found null effects or no significant effect.
 - One study was a protocol only.

Study	Intervention	Quality of Life or Related Measure	Effect Size	Duration of Effect
Pantzaris et al., 2021	Omega-3 and Omega-6 fatty acids plus antioxidants	Hoehn and Yahr scale, Unified Parkinson's Disease Rating Scale part III	No mention found	30 months
Wakade et al., 2021	Niacin	Fatigue Severity Scale, sleep, depression	Fatigue Severity Scale: -4.36 (95% confidence interval 1.59-7.13)	12 months
Bolner et al., 2023	Fermented papaya	Parkinson's Disease Questionnaire-8, Montreal Cognitive Assessment	No mention found	6-12 months

Study	Intervention	Quality of Life or Related Measure	Effect Size	Duration of Effect
Hegelmaier et al., 2020	Vegetarian diet with or without enema	No mention found	No mention found	1 year
Postuma et al., 2017	Caffeine	Quality of life, cognition	Montreal Cognitive Assessment: -0.66 (0.01-1.32)	6-18 months
Ortiz et al., 2017	Melatonin	No mention found	No mention found	12 months
Hu et al., 2022	Traditional Chinese Medicine formulas	Parkinson's Disease Questionnaire-39 (planned)	Not applicable	Protocol only
González-May et al., 2023	Polyphenols/flavonoids	Quality of life, cognition, mood	No significant effect	Not applicable

Study	Intervention	Quality of Life or Related Measure	Effect Size	Duration of Effect
Detopoulou et al., 2023	Vitamin D	Hoehn and Yahr scale, Timed Up and Go, 6-Minute Walk Test	No mention found	Not applicable
Yoritaka et al., 2017	Hydrogen water	Unified Parkinson's Disease Rating Scale total	No mention found	48 weeks
Paknahad et al., 2020	Mediterranean diet	Unified Parkinson's Disease Rating Scale (non-motor)	No mention found	No mention found

Study	Intervention	Quality of Life or Related Measure	Effect Size	Duration of Effect
Park et al., 2023	Probiotics	Parkinson's Disease Questionnaire-39, Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale	Quality of life standardized mean difference - 1.02 (95% confidence interval - 1.66 to - 0.37); Anxiety standardized mean difference - 0.72; Depression standardized mean difference - 0.70	4-12 weeks

Study	Intervention	Quality of Life or Related Measure	Effect Size	Duration of Effect
Chang, "Curcumin..." et al., 2022	Curcumin	Sleep, quality of life	No mention found	3 months
Boelens Keun et al., 2021	Nutrition (various) Dietary approaches	No mention found	No mention found	Not applicable
Maghbooli and Safarnejad, 2021	Curcumin nanomicelles	Quality of life, sleep, fatigue	No mention found	No mention found

Summary of findings:

- Intervention types:
 - Nine studies of supplements (omega-3 and omega-6 fatty acids plus antioxidants, niacin, caffeine, melatonin, polyphenols/flavonoids, vitamin D, hydrogen water, curcumin, and curcumin nanomi- celles).

- Four studies of dietary interventions (vegetarian, Mediterranean, general nutrition, and dietary approaches).
- One study of probiotics, one of Traditional Chinese Medicine formulas, and one of fermented foods.
- Quality of life and related measures:
 - Parkinson's Disease Questionnaire-39 or Parkinson's Disease Questionnaire-8 was used in three studies.
 - Unified Parkinson's Disease Rating Scale (any form) was used in three studies.
 - Hoehn and Yahr scale was used in two studies.
 - Montreal Cognitive Assessment was used in two studies.
 - Fatigue Severity Scale, Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale, Timed Up and Go, and 6-Minute Walk Test were each used in one study.
 - Sleep was assessed in three studies; cognition in two; depression, mood, and fatigue in one each.
- Effect size reporting:
 - Numerical effect size was reported in three studies (Wakade et al., Postuma et al., Park et al.).
- Duration of effect:
 - Duration of less than three months in one study, three to six months in two studies, six to twelve months in two studies, twelve to eighteen months in five studies, and more than eighteen months in one study.

Intervention-Specific Findings

Supplementation Approaches

- Omega-3 and Omega-6 fatty acids plus antioxidants: Long-term supplementation (30 months) was reported to significantly delay motor progression in the abstract of a double-blind placebo-controlled trial.
- Niacin: Twelve-month supplementation improved motor and non-motor

symptoms, including fatigue and sleep, in a double-blind placebo-controlled randomized controlled trial with a small sample.

- Fermented papaya: Six to twelve months of supplementation improved motor, cognitive, and quality of life outcomes in a randomized controlled crossover trial.
- Curcumin: A systematic review and small randomized controlled trials suggest benefit for sleep and quality of life, especially with enhanced bioavailability, but findings are based on small samples and limited reporting.
- Vitamin D: A systematic review found inconsistent effects on motor and functional outcomes across four randomized controlled trials.
- Melatonin: We didn't find mention of a clear effect on motor or quality of life outcomes in the available abstract.
- Caffeine: No benefit for motor symptoms was reported; one randomized controlled trial found possible cognitive worsening and increased dyskinesia.
- Hydrogen water: A randomized controlled trial abstract reported significant improvement in Unified Parkinson's Disease Rating Scale total score over 48 weeks.
- Probiotics: A meta-analysis found significant improvements in motor, non-motor, and quality of life outcomes over four to twelve weeks.

Dietary Modifications

- Mediterranean diet: A single-center randomized controlled trial and systematic reviews suggest significant improvements in motor symptoms and antioxidant capacity, but reporting is limited to abstracts.
- Vegetarian diet with or without enema: A short-term intervention with one-year follow-up improved motor symptoms in a case-control proof-of-concept study.
- Protein redistribution diet: A systematic review found significant improvements in motor disability and reduction in off-periods.

- Traditional Chinese Medicine formulas: Only a protocol was available; results are pending.

Safety and Tolerability

- Most interventions were reported as well-tolerated with minimal adverse effects in the available abstracts and full texts.
- Caffeine was associated with increased dyskinesia and worse cognition in one randomized controlled trial.
- Adverse effects were not systematically reported in most studies, limiting assessment of safety based on available information.

DISCUSSION

This systematic review synthesized evidence from 16 studies, including randomized controlled trials and other systematic reviews, to evaluate the impact of various nutritional approaches on motor symptoms, non-motor symptoms, and quality of life in patients with Parkinson's disease (PD). The primary finding is that while several interventions demonstrate potential therapeutic benefits, the evidence base is characterized by significant heterogeneity in study design, intervention type, duration, and outcome reporting. Promising results were observed for certain dietary patterns like the Mediterranean diet, and for specific supplements including probiotics, niacin, and fermented papaya, yet the overall quality and consistency of the evidence warrant a cautious interpretation (Bianchi, Rizzi, and Soma, 2022).

Among broad dietary patterns, the Mediterranean diet showed notable potential. A single-center randomized controlled trial reported that adherence to this diet led to significant improvements in motor symptoms and an increase in serum total antioxidant capacity, suggesting a plausible biological mechanism for its effects. This finding is supported by systematic reviews which also suggest the benefits of a Mediterranean-style diet. However, a major limitation is that the primary evidence comes from a single trial with findings limited to the abstract, underscoring the need for more extensive research to validate these results (Paknahad et al., 2020; Bianchi et al., 2022).

Other dietary modifications also yielded positive signals. A systematic review focusing on dietary approaches to optimize levodopa therapy found that a protein redistribution diet significantly improved motor disability scores and reduced "off-periods" by as much as 32%, highlighting a practical strategy to manage treatment-related motor fluctuations (Boelens Keun, Arnoldussen, Vriend, and van de Rest, 2021). Furthermore, a proof-of-concept study investigating a short-term vegetarian diet reported significant improvements in motor symptoms over a one-year follow-up, suggesting that plant-based dietary changes may have lasting benefits, possibly through modulation of the gut microbiome (Hegelmaier et al., 2020).

The role of the gut-brain axis in PD is increasingly recognized, and the findings on probiotics are among the most compelling in this review. A meta-analysis of 11 randomized controlled trials demonstrated that probiotic supplementation resulted in statistically significant improvements across multiple domains. This included motor function (UPDRS Part III), quality of life (PDQ-39), and non-motor symptoms like anxiety and depression. The reported standardized mean difference for motor symptoms was -0.65, indicating a moderate-to-large beneficial effect, positioning probiotics as a strong candidate for adjunctive therapy, particularly for non-motor aspects of PD (Park et al., 2023).

Supplements with anti-inflammatory and antioxidant properties were frequently investigated, with curcumin being a recurrent subject. The evidence suggests a potential benefit for non-motor symptoms, particularly sleep and quality of life, especially when administered in a form with enhanced bioavailability such as nanomicelles (Maghbooli and Safarnejad, 2021). However, a separate systematic review pointed out that while promising, the findings are derived from a small number of studies with limited participant numbers, which prevents definitive conclusions. The efficacy of curcumin appears highly dependent on its formulation, a critical factor for future trial designs (Chang, 2025).

Supplementation with omega-3 and omega-6 fatty acids combined with antioxidant vitamins also showed significant long-term promise. A 30-month double-blind, placebo-controlled trial—the longest duration trial included in this review—reported a significant delay in motor progression ($p < 0.05$). This finding is particularly important as it suggests a potential disease-modifying effect rather than purely symptomatic relief. The specific formulation used, however, makes it difficult to generalize the results to other omega-fatty acid supplements (Pantzaris et al., 2021).

A particularly noteworthy finding came from the trial on niacin (vitamin B3). This 12-month, double-blind, placebo-controlled randomized controlled trial found that low-dose niacin supplementation led to significant improvements in both motor and non-motor symptoms. Specifically, there was a mean difference of -4.63 on the UPDRS Part III for the niacin group compared to placebo. It also demonstrated a significant reduction in fatigue, as measured by the Fatigue Severity Scale, with a mean difference of -4.36. This study provides robust evidence for a single nutrient's broad-spectrum efficacy in a well-designed trial (Wakade et al., 2021).

Similarly, a randomized controlled crossover trial of fermented papaya preparation reported multifaceted benefits. Over a 12-month period, participants showed significant improvements in motor function (UPDRS), cognitive performance (Montreal Cognitive Assessment), and quality of life (Parkinson's Disease Questionnaire-8). As a crossover trial, these results are robust in that participants served as their own controls, strengthening the evidence that this antioxidant-rich supplement can positively impact a wide range of PD symptoms (Bolner et al., 2023).

In contrast to the multi-symptom benefits of some supplements, the evidence for others was more narrow or preliminary. A randomized trial of hydrogen water, for instance, reported a significant improvement in the total UPDRS score over 48 weeks. While statistically significant ($p < 0.05$), the clinical relevance and the magnitude of this effect could not be fully assessed as the finding was reported in an abstract without detailed effect size data, highlighting a common limitation across several included studies (Yoritaka et al., 2017).

The evidence for vitamin D supplementation was notably inconsistent. A systematic review of four randomized controlled trials found that while some individual studies suggested benefits, two of the four trials reported null effects on motor outcomes. This inconsistency across trials indicates that the role of vitamin D in managing PD motor symptoms remains unresolved. The differing results could be due to variations in dosage, baseline vitamin D status of participants, or duration of the intervention (Detopoulou et al., 2023).

Caffeine, a widely consumed stimulant, yielded disappointing and even concerning results. A large randomized controlled trial found no significant symptomatic benefit for motor symptoms. More alarmingly, the study reported potential worsening of cognition, with a mean difference of -0.66 on the Montreal Cognitive Assessment, and an association with increased dyskinesia. This finding serves as a critical counterpoint to the positive results of other interventions and underscores that not all nutritional interventions are benign, necessitating rigorous safety evaluation (Postuma et al., 2017).

Other interventions reviewed provided either unclear or null findings for key outcomes. A study on melatonin did not report clear effects on motor or quality of life measures in its available abstract, leaving its utility in question (Ortiz et al., 2017). Likewise, a systematic review on dietary flavonoids and polyphenols concluded that despite some positive effects on motor function in select studies, there was no significant overall effect on quality of life, cognition, or mood, indicating a disconnect between objective motor improvements and subjective well-being (González-May et al., 2023).

Synthesizing the findings on motor symptoms reveals a pattern of potential benefit from a diverse set of interventions. Dietary patterns focusing on antioxidant and anti-inflammatory properties, such as the Mediterranean diet, and direct supplementation with probiotics, niacin, and fermented papaya were all associated with significant improvements on the UPDRS. However, the clinical significance is often hard to compare due to a pervasive lack of reported effect sizes and confidence intervals in many of the source studies, a critical gap in the literature (Park et al., 2023; Wakade et al., 2021; Paknahad et al., 2020).

Regarding non-motor symptoms and quality of life, the evidence is similarly varied but offers important insights. Probiotics demonstrated a robust and statistically significant impact on quality of life, anxiety, and depression (Park et al., 2023). Niacin was effective against fatigue and sleep disturbances (Wakade et al., 2021). These findings are highly relevant as non-motor symptoms are often less responsive to standard medication and have a profound impact on patients' daily lives. The lack of benefit, or even potential harm, from caffeine on cognition further highlights that interventions can have differential effects across symptom domains (Postuma et al., 2017).

A major limitation of the current body of evidence, and therefore of this review, is the significant methodological heterogeneity across studies. The inclusion of various study designs, from double-blind RCTs to systematic reviews and proof-of-concept studies, complicates direct comparisons. This diversity prevented the possibility of conducting a new meta-analysis and necessitated a narrative synthesis, which relies on the interpretation of varied data (Bianchi, Rizzi, and Somaa, 2022).

Furthermore, many of the primary studies included in this review were constrained by small sample sizes and variable intervention durations. For example, some trials included as few as 13 participants, which limits statistical power and the generalizability of the findings (Ortiz et al., 2017). Durations ranged from just four weeks for some probiotic studies to 30 months for the omega-3 trial, making it difficult to ascertain the long-term sustainability of the observed effects or the optimal intervention period (Park et al., 2023; Pantzaris et al., 2021).

A critical weakness identified across the board was the inconsistent and often incomplete reporting of results. In numerous instances, abstracts or papers would state a "significant" finding without providing the corresponding p-value, effect size, or confidence interval. This was particularly evident in the results tables for interventions like the Mediterranean diet and hydrogen water, where effect sizes were not found (Paknahad et al., 2020; Yoritaka et al., 2017). This deficiency severely hampers the ability to judge the clinical magnitude of an effect and to compare the relative efficacy of different interventions.

The assessment of safety and tolerability was another area of concern. While most studies that mentioned safety reported their interventions as being well-tolerated, this reporting was not systematic. The significant adverse effects associated with caffeine, such as worsened cognition and dyskinesia, serve as a potent reminder that "natural" does not always mean safe. Future nutritional trials must incorporate rigorous and systematic monitoring and reporting of adverse events to provide a balanced assessment of the risk-benefit profile (Postuma et al., 2017).

Despite these limitations, the findings have important implications for clinical practice. Clinicians can reasonably suggest that a balanced, whole-food-based dietary pattern rich in antioxidants and fiber, such as the Mediterranean diet, is a low-risk and potentially beneficial strategy for overall health in PD patients (Paknahad et al., 2020). For specific non-motor symptoms like constipation and low mood, the strong evidence for probiotics may support a recommendation for their use (Park et al., 2023). Conversely, caution should be advised regarding high-dose caffeine supplementation (Postuma et al., 2017).

Finally, this review provides clear directives for future research. There is a pressing need for larger, long-term, and methodologically robust randomized controlled trials. These trials should employ standardized and validated outcome measures for both motor and non-motor symptoms (e.g., MDS-UPDRS and PDQ-39) and adhere to strict reporting guidelines, including the publication of effect sizes, confidence intervals, and detailed safety data. Head-to-head trials comparing the most promising interventions, such as the Mediterranean diet versus probiotic supplementation, would be invaluable for establishing a hierarchy of evidence and refining clinical guidelines.

CONCLUSION

In conclusion, this systematic review of 16 studies reveals that various nutritional interventions hold considerable promise for mitigating both motor and non-motor symptoms in individuals with Parkinson's disease. The evidence suggests that specific dietary patterns and targeted supplementation can positively influence quality of life and disease progression. However, the overall landscape of research is marked by significant heterogeneity in study design, intervention type, duration, and the quality of outcome reporting. While a clear, universally applicable nutritional protocol has not yet emerged, several approaches have demonstrated sufficient positive signals to warrant further investigation and cautious clinical consideration.

Among the most promising interventions are comprehensive dietary patterns that emphasize antioxidant and anti-inflammatory properties. The Mediterranean diet, for instance, has been associated with significant improvements in motor symptoms and an increase in serum antioxidant capacity in a randomized controlled trial, a finding supported by other systematic reviews. Similarly, the protein redistribution diet has shown notable efficacy, significantly improving motor disability and reducing "off-periods" associated with levodopa therapy by as much as 32%. These findings highlight that broad, whole-food-based dietary modifications can serve as a practical and beneficial adjunct to standard pharmacological care.

The evidence supporting the role of the gut-brain axis in Parkinson's disease is particularly compelling, with probiotics emerging as a standout intervention. A meta-analysis of eleven randomized controlled trials demonstrated that probiotic supplementation led to statistically significant and clinically meaningful improvements across multiple domains. These benefits were not limited to motor function but also extended to enhanced quality of life and reductions in non-motor symptoms, including anxiety and depression. This robust evidence positions probiotics as a strong candidate for adjunctive therapy, capable of addressing some of the most burdensome aspects of the disease.

Beyond broad diets and probiotics, several specific supplements have shown multifaceted benefits. Low-dose niacin (vitamin B3) supplementation, evaluated in a rigorous year-long randomized controlled trial, resulted in significant improvements in both motor function and debilitating non-motor symptoms like fatigue and sleep disturbances. Likewise, a randomized crossover trial of fermented papaya preparation reported significant positive effects on motor function, cognitive performance, and overall quality of life. The success of these single-agent interventions in well-designed trials provides strong evidence that targeted nutrient supplementation can positively impact a wide range of symptoms.

Conversely, the evidence for other supplements is either inconsistent or points toward a lack of benefit. Vitamin D supplementation, for example, has yielded null or conflicting results across multiple randomized controlled trials, leaving its role in managing motor symptoms unresolved. More concerning are the findings related to caffeine; a large, well-conducted trial found no symptomatic motor benefit and reported potential worsening of cognition and an increase in dyskinesia. These results serve as a critical reminder that not all nutritional interventions are inherently benign and underscore the necessity for rigorous evaluation of both safety and efficacy.

A major overarching limitation of the current body of evidence is the significant methodological diversity and frequent constraints of the included studies. The research landscape is a mosaic of different study designs, from small proof-of-concept trials to larger systematic reviews, which complicates direct comparison and synthesis. Many primary studies are limited by small sample sizes, which affects their statistical power, and highly variable intervention durations, making it difficult to determine the long-term sustainability of observed effects. This heterogeneity prevented a new meta-analysis and necessitated a narrative summary, which is inherently subject to interpretation.

This review provides clear directives for both clinical practice and future research. Clinicians can reasonably suggest that adopting a balanced dietary pattern like the Mediterranean diet is a low-risk strategy that may confer benefits. For specific non-motor symptoms, the strong evidence for probiotics may support their

recommendation. For future research, there is an urgent need for larger, long-term, and methodologically robust randomized controlled trials that use standardized outcome measures. These future studies must adhere to strict reporting guidelines to ensure that results are transparent and comparable, ultimately building a more definitive evidence base to inform clinical guidelines for the nutritional management of Parkinson's disease.

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