A Systematic Review of Dietary Lifestyle Interventions for Neuropathic Pain

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Introduction

- Leprosy is a neglected tropical disease affecting those residing in rural poverty[1]
- Therapies for chronic severe neuropathic pain (NP), a common consequence of leprosy, are associated with significant severe side effects and have limited effectiveness[1]
- Lifestyle interventions have become increasingly recognized as accessible and cost-effective strategies to reduce the burden and severity of neuropathic pain, particularly in type 2 diabetes
- Diets seeking to improve physiological nerve health, support gut barrier integrity, and decrease systemic inflammation have recently emerged as powerful tools conferring neuroprotective and anti-inflammatory effects, potentially reducing the neurological morbidity of multiple diseases[1]
- This systematic review seeks to understand and synthesize the literature reporting NP outcomes following dietary interventions compared to routine standard of care

Methods

- A comprehensive search strategy encompassing underlying neuropathic etiologies, lifestyle interventions, and stratifiers was conducted using 5 databases (Embase, Medline, Pubmed, Scopus, LILACS) from inception to Aug 2024
- Articles were screened independently by two reviewers and discrepancies were resolved by a tertiary arbitrator during title/abstract, and full-text screening
- The quality assessment tool GRADE (Grading of Recommendations, Assessment, Development and Evaluations) was implemented to assess the quality and bias of evidence
- Inclusion criteria: Randomized controlled trials, clinical trials, cohort studies, observational studies, case-control studies, case series & reports, no language restriction
- Exclusion criteria: Reviews, conference abstracts, editorials, animal studies, in vitro studies, trial descriptions
- Primary outcomes gathered: Efficacy by subjective pain and neuropathy severity (on physical exam and questionnaires), and objective nerve function (via quantitative sensory testing (QST), electrophysiology, biopsy, imaging, and physical exam); as well as safety & tolerability.

Results

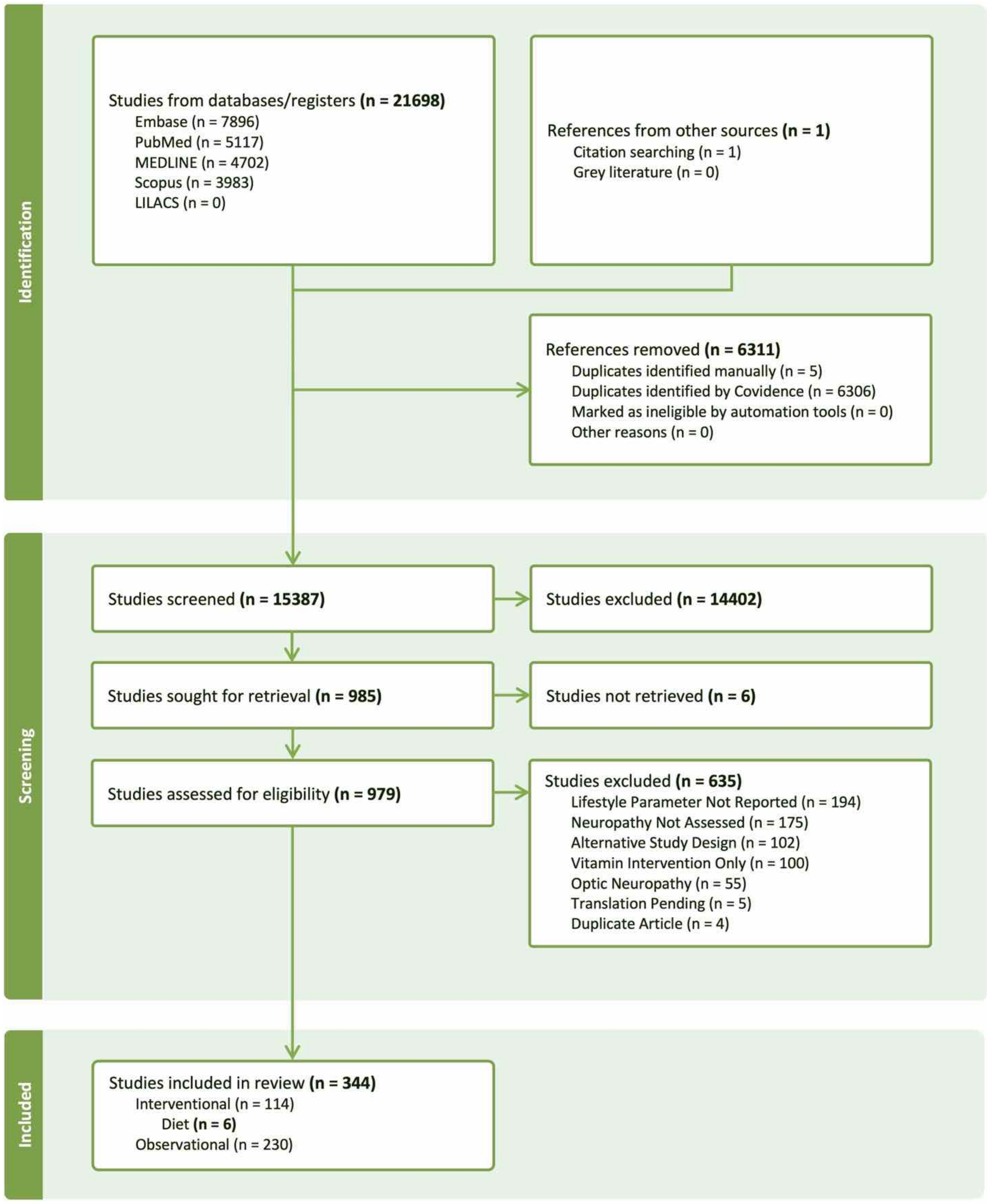

Figure 1. PRISMA Flowchart for all included lifestyle intervention papers for the indication of neuropathic

Results

Author (Year)	Setting	N	Mean Age (SD)	Range	Sex N (F:M)	Etiology	Population	Lifestyle	Outcomes (mean ± SD)
Arnold (2017)	Australia	47	Int: 67; Con: 66	52-69	Int: 10:13; Con: 7:17	Chronic Kidney Disease	Stage 3/4 Chronic Kidney Disease	Potassium reduced diet (1 mmol/kg/day) including: energy (if BMI >30), sodium (<100 mmol/day), and phosphate (<1000 mg/day) restriction for 2 years	**Efficacy:** Improvement in the change in TNS (0.4±2.2 vs 2.8±3.3, p<0.01), and nerve excitability score (5.1±2.8 vs -2.3±2.2, p=0.04) between groups **Safety:** No AE observed. **Tolerability:** 8.7% L2FU in int. group & 12.5% L2FU in con. group.
Bunner (2015)	US	34	Int: 57 (6); Con: 58 (6)	-	Int: 8:9; Con: 11:6	Diabetes	T2DM + PN	Low-fat plant-based diet + 1000 mcg vitamin B12 /day including: omitting animal products, limiting fat intake to 20-30 g/day, and favouring low-glycemic index foods for 5 months	**Efficacy:** Improvement of pain on MPQ (22.6±11 vs 13.5±10, p<0.01), MNSI (7.5±2.5 vs 5.3±2.5, p<0.01), and NTSS (10.7±4.9 vs 6.8±4.5, p<0.01) within int. group, and in the change in MPQ (-9.1±11.4 vs -0.9±11.3, p=0.04), MNSI (-2.2±2.4 vs -0.6±1.5, p=0.03), and feet conductance (0.7±10.5 vs -11.7±13.2, p=0.03) between groups **Safety:** No AE observed. **Tolerability:** ~76% adherence.
Hadjivassiliou (2006)	UK	35	Int: 67.2 (2); Con: 70.9 (1.9)	-	-	Gluten Sensitivity (with 28% of participants demonstrating histopathological evidence of gluten enteropathy)	Gluten Sensitivity + PN	Gluten free diet including counselling from expert dietician for 1 year	**Efficacy:** Improvement in the change in sural sensory nerve action potential amplitude within the int. group (1.39±0.22 vs 2.15±0.43, p<0.001), con. group (1.39±0.47 vs 0.96±0.29, p<0.01), and between groups (0.76±0.31 vs -0.42±0.25, p<0.03) **Safety:** Not mentioned. **Tolerability:** High adherence.
Kender (2023)	Germany	31	Int: 66.6 (5.8); Con: 67.1 (5.9)	50-75	Int: 5:12; Con: 5:9	Diabetes	T2DM	Plant-based fasting-mimicking diet for 1 week / month for 6 months	**Efficacy:** Improvement in tibial motor nerve conduction velocity (37.23±2.38 vs 32.89±3.05, p<0.05), and HPT (-0.76±0.37 vs -1.10±0.30, p<0.05) within con. group, and tibial nerve compound muscle action potential (7.79±1.24 vs 9.21±1.45, p<0.05) within int. group **Safety:** Mentioned "low" but AEs not specified **Tolerability:** High adherence and no L2FU
Safari (2020)	Iran	96	Int: 39.67 (10.66); Con: 40.21 (10.46)	Int: 26-59; Con: 24-60	Int: 20:28; Con: 21:27	Chronic Sciatica	Chronic Sciatica + NP	Low calorie diet for 30 days	**Efficacy:** Improvement in MPQ sensory (6.73±1.41 vs 4.46±1.71, p<0.001), affective (0.98±0.64 vs 0.50±0.62, p=0.002), total (7.71±1.69 vs 4.96±2.02, p<0.001) scores, and PPI (2.23±0.47 vs 2±0.68, p=0.001) within int. group, PPI (2±0.68 vs 1.79±1.3, p=0.013) within con. group, and MPQ sensory (4.46±1.71 vs 5.74±2.11, p=0.015), affective (0.50±0.62 vs 0.87±0.85, p=0.002), total (4.96±2.02 vs 6.62±2.53, p=0.001) scores, and PPI (1.02±0.98 vs 1.79±1.3, p=0.006) between groups adjusted for baseline **Safety:** Not mentioned **Tolerability:** 100% adherence and no L2FU
Torlak (2020)	Turkey	60	Diet Group: 50.3 (1.64); Diet + PT Group: 54.30 (1.38); PT Group: 54.85 (3.81)	-	Diet Group: 10:10; Diet + PA Group: 10:10; PA Group: 10:10	Chronic Lower Back Pain	Chronic Lower Back Pain + NP	Intermittent high protein diet (2 days / week) and Mediterranean diet (5 days / week) for 5 weeks	**Efficacy:** Improvement in VAS (8.3±0.36 vs 4.7±0.41, p<0.001; 7.45±0.44 vs 4.7±0.42, p<0.001; 6.65±0.31 vs 3.1±0.59, p<0.001), and LANSS (4.8±0.88 vs 2.3±0.59, p<0.001; 10.6±0.88 vs 7.1±0.76, p<0.001; 5.1±0.42 vs 2.6±0.36, p<0.001) within diet group, diet + PT group, and PT group respectively **Safety:** Mentioned "low" but AEs not specified **Tolerability:** 100% adherence and no L2FU

Table 1. Study characteristics
Abbreviations: **AE:** adverse events; **BMI:** body mass index; **Con:** Control; **DM:** diabetes mellitus; **HPT:** heat pain threshold; **Int:** intervention; **L2FU:** loss to follow up; **LANSS:** leeds assessment of neuropathic symptoms and signs; **MNSI:** Michigan neuropathy screening instrument questionnaire; **MPQ:** McGill pain questionnaire; **NP:** neuropathic pain; **NTSS:** neuropathy total symptom score; **PN:** peripheral neuropathy; **PPI:** present pain intensity; **PT:** physical therapy; **T2DM:** type 2 diabetes mellitus; **TNS:** total neuropathy score; **VAS:** visual analog scale. *All outcomes reported as intervention group vs control group.*

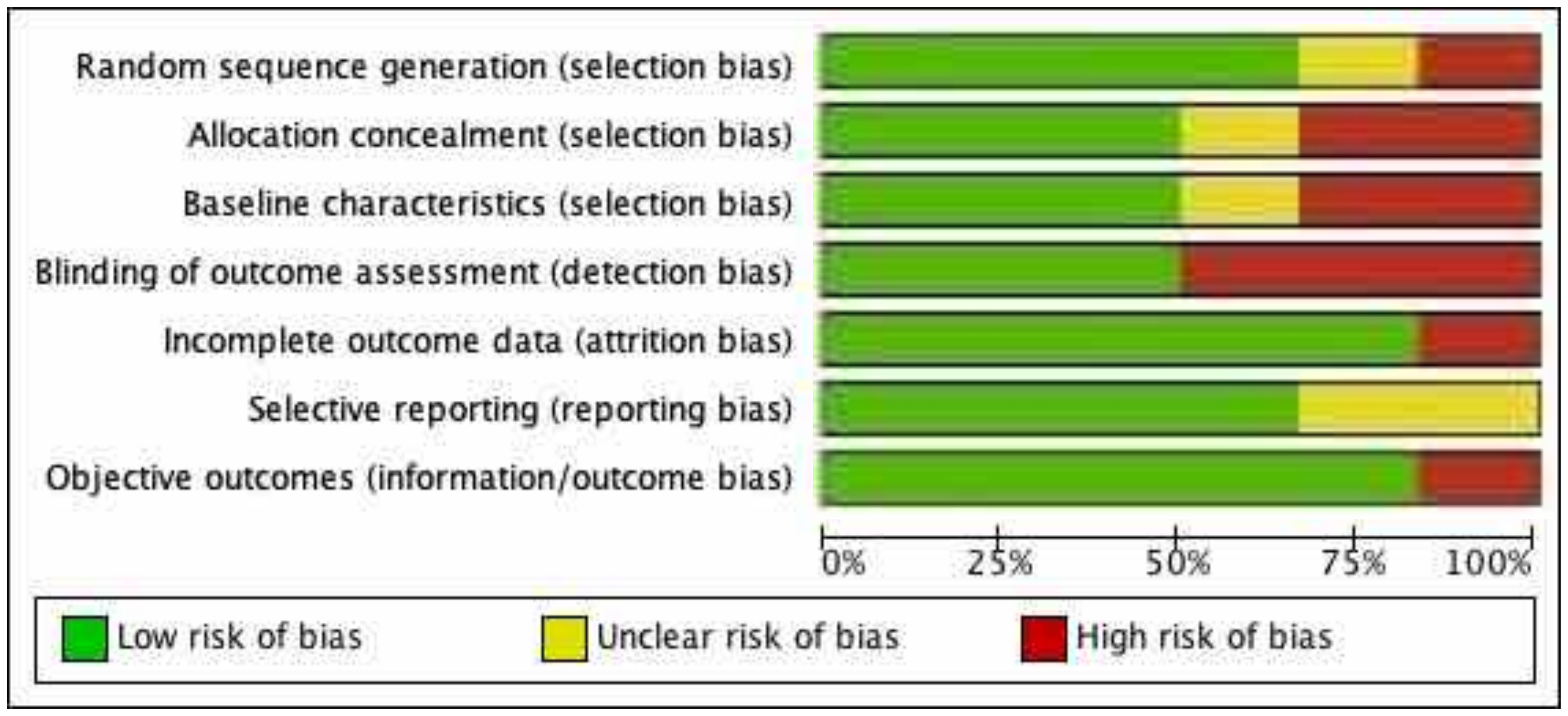

Figure 2. Summary of GRADE Risk of Bias Assessment

Discussion

- After screening, 344 articles were included; 114 were interventional trials, with 6 focused on dietary interventions (Figure 1)
- We synthesized evidence on the efficacy, safety, and tolerability of various dietary interventions, including low-fat plant-based, fasting-mimicking, Mediterranean, low-calorie, gluten-free, and potassium-reduced diets (Table 1)
- Our findings support the hypothesis that optimized dietary health may alter neuropathic pathophysiology, with some interventions showing significant improvements in NP
- Specific diets, such as low-fat plant-based and low-calorie, showed neuroprotective and anti-inflammatory benefits, improving NP severity in several populations via objective QST, electrophysiology, and subjective questionnaires.
- Overall risk of bias was moderate, with 64% of measures deemed low risk; the most common biases were detection, selection, and group allocation issues (Figure 2)
- Dietary interventions offer a low-risk, low-cost alternative for NP, especially in T2DM, but larger trials are needed to strengthen the evidence
- Future recommendations will depend on new data and updated evidence syntheses

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