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Review Article

Effectiveness of non-pharmacological interventions for chemotherapy-induced peripheral neuropathy–related pain: A systematic review and network meta-analysis

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ABSTRACT

Purpose: Chemotherapy-induced peripheral neuropathy (CIPN) is a common, distressing, adverse effect of neurotoxic chemotherapy that can persist post-treatment, and may affect therapy and daily functioning. Pharmacological options remain limited; therefore, non-pharmacological strategies are increasingly used. However, their comparative effectiveness remains unclear. We aimed to compare and rank the effectiveness of non-pharmacological interventions for CIPN-related pain.

Method: We conducted a systematic review and frequentist network meta-analysis (NMA) of randomised controlled trials (RCTs). PubMed, Web of Science, the Cochrane Central Register of Controlled Trials, PsycINFO, and CINAHL databases were searched through 23, May 2025. Interventions were grouped as acupuncture-based, electrical stimulation-based, exercise-based, psychological, cryotherapy, or control. Pairwise meta-analyses and random-effects NMA were performed. Treatments were ranked using P-scores. The risk of bias was assessed independently by reviewer pairs using RoB 2.0.

Results: Thirty-two RCTs (n = 1612) met the inclusion criteria, and 19 were used for NMA. Acupuncture-based interventions significantly reduced pain versus controls (standardised mean difference 0.66; 95% confidence interval 0.16–1.17). Treatment ranking based on P-scores suggested that cryotherapy ranked highest (P-score = 0.86), followed by exercise-based (P-score = 0.68), acupuncture-based (P-score = 0.54), and electrical stimulation–based (P-score = 0.42) interventions. No other intervention demonstrated a statistically significant reduction in pain compared with control conditions. Substantial heterogeneity was observed ($\tau^2 = 0.54$, $I^2 = 83.8\%$).

Conclusions: The effectiveness of cryotherapy and exercise remains unclear. However, our findings suggest that there is significant evidence to consider acupuncture as a supportive option for managing CIPN-related pain. Future well-powered RCTs are needed to support implementation in multidisciplinary oncology.

1. Introduction

Advances in cancer treatment have increased survival rates for many patients; however, the impact of treatment-related adverse effects on patients' quality of life (QoL) remains a significant challenge. Chemotherapy-induced peripheral neuropathy (CIPN) is a common and

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persistent adverse effect of neurotoxic chemotherapy characterised by symptoms such as numbness, burning pain, and sensory disturbances, resulting in functional impairment and psychological distress (Tofthagen et al., 2013). Furthermore, depending on the severity, dose reduction or discontinuation of chemotherapy may be required, potentially compromising the continuity and efficacy of cancer treatment (Bhatnagar et al., 2014). CIPN frequently occurs in response to specific chemotherapeutic agents, particularly taxanes (e.g., paclitaxel and docetaxel) and platinum-based agents (e.g., cisplatin and oxaliplatin), with an overall prevalence of approximately 68% (Seretny et al., 2014). Symptoms may persist for months to years after treatment completion, raising concerns about their long-term impact on daily living and social participation (Mols et al., 2014).

Various pharmacological therapies have been attempted for CIPN; however, evidence supporting their efficacy is scarce, and the treatments recommended by clinical guidelines are limited (Jordan et al., 2020; Loprinzi et al., 2020a,b). For instance, except for duloxetine, no standard therapeutic agent exists and issues regarding adverse effects and drug interactions have been reported. As such, there is growing interest in non-pharmacological interventions as safer and non-invasive alternatives (Greenlee et al., 2017). Non-pharmacological interventions for CIPN encompass a diverse range of approaches aimed at pain relief, including exercise therapy, acupuncture, massage, cognitive behavioural therapy (CBT), mindfulness, music therapy, and transcutaneous electrical nerve stimulation (TENS) (Jordan et al., 2020; Loprinzi et al., 2020a,b). While CIPN presents with multifaceted symptoms, including sensory and functional impairments, pain is a core symptom that significantly contributes to patient distress and functional impairment (Colvin, 2019; Mols et al., 2014) and directly affects treatment continuity (e.g., dose adjustment or discontinuation) (Bhatnagar et al., 2014). Consequently, numerous studies have evaluated pain relief using non-pharmacological interventions as the primary outcome. As the number of trials evaluating pain-specific outcomes has increased, there is a growing need to synthesise and compare the relative efficacy of these interventions to support evidence-based symptom management.

Recently, a network meta-analysis (NMAs) by Zhang et al. (2023) and Cai et al. (2026) evaluated non-pharmacological interventions for CIPN using a broad range of outcomes, including neurotoxicity scales, neuropathy symptom scores, and pain intensity measures. Although these studies provided valuable comparative evidence, pain outcomes were pooled together with composite neuropathy measures that included numbness, tingling, and functional impairment, rather than being synthesised as an independent construct. Importantly, these symptoms represent distinct clinical and pathophysiological constructs and may respond differently to interventions (Baron et al., 2010). Consequently, combining heterogeneous neuropathy outcomes may obscure the specific analgesic effects of non-pharmacological interventions for CIPN-related pain. Furthermore, prior reviews included multidimensional neuropathy and QoL instruments, which may lack sensitivity for detecting changes in pain intensity itself. To date, no NMA has exclusively synthesised evidence using validated pain-specific measures to clarify the comparative analgesic efficacy of non-pharmacological interventions for CIPN-related pain.

In this study, we conducted a network meta-analysis to clarify the comparative analgesic efficacy of non-pharmacological interventions for CIPN-related pain.

2. Materials and methods

2.1. Study design

This study was conducted as a systematic review and NMA to evaluate the efficacy of non-pharmacological interventions for CIPN-related pain, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses incorporating Network Meta-Analyses (PRISMA-NMA) guidelines (Hutton et al.). The study protocol was registered a priori in the Open Science Framework (OSF) (Registration DOI: 10.17605/OSF.IO/M9PXN). A protocol deviation should be noted: the registered protocol initially targeted cancer-related pain broadly; however, during the review process, we refined the scope to focus specifically on CIPN-related pain. This decision was made because cancer-related pain encompasses heterogeneous aetiologies (e.g., nociceptive, inflammatory, and neuropathic pain), whereas CIPN-related pain represents a distinct neuropathic pain condition with different pathophysiological mechanisms and potentially different responses to non-pharmacological interventions. Restricting the review to CIPN-related pain was therefore considered necessary to reduce clinical heterogeneity and improve the interpretability of the NMA. In addition, the registered protocol allowed studies reporting either pain or QoL outcomes. During the review process, the eligibility criteria were further refined to include only studies assessing CIPN-related pain using validated pain-specific instruments. Studies relying solely on QoL measures or multidimensional neuropathy scales were excluded. This decision was made to minimise clinimetric heterogeneity and improve the interpretability of treatment effects on CIPN-related pain.

2.2. Search strategy

A comprehensive literature search was conducted across five electronic databases: PubMed, Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL), PsycINFO, and CINAHL (Appendices A–E). The search covered all records from the inception of each database until 23 May 2025. Language restrictions were not imposed during the initial search. The search strategy combined Medical Subject Headings and free-text keywords related to ‘chemotherapy-induced peripheral neuropathy’, ‘non-pharmacological intervention’, and ‘cancer’. The search was limited to RCTs using database filters. No formal grey literature search was conducted.

2.3. Eligibility criteria

Studies were selected based on the following Population, Intervention, Comparison, Outcome, and Study Design (PICOS) criteria:

- Participants: Adults (aged ≥18 years) diagnosed with cancer and CIPN.
- Interventions: Non-pharmacological interventions aimed at improving CIPN-related pain (e.g., exercise, acupuncture, massage, CBT, and mindfulness). Interventions involving pharmacological therapies (e.g. chemotherapy and targeted therapy), herbal medicines, nutritional supplements, alcohol- or substance-based strategies, medical procedures (e.g., surgery and radiotherapy), or combinations thereof were excluded to minimise clinical heterogeneity and maintain conceptual consistency across intervention categories.
- Comparisons with usual care, waitlist, no intervention, sham intervention, or other non-pharmacological interventions. Comparisons with pharmacological treatments or invasive procedures were excluded.
- Outcomes: Studies that reported CIPN-related pain intensity as a primary outcome were included.
- Study Type: Only RCTs were included.
- Language: Only studies published in English were included.

The primary outcome was the intensity of chemotherapy-induced neuropathic pain. To ensure specificity and sensitivity of the analysis, we established strict criteria for outcome measurement instruments. First, studies were excluded if they assessed neuropathy solely using instruments that primarily measured general neuropathy symptoms (e.g., numbness, tingling, and motor dysfunction) or functional impairment rather than pain intensity (e.g., EORTC QLQ-CIPN20). This exclusion criterion was established because composite scores often

conflate sensory deficits (negative symptoms) with hypersensitivity (positive symptoms), which are pathophysiologically distinct entities (Baron et al., 2010). Similarly, studies assessing pain intensity solely as a subscale or domain of general QoL instruments (e.g., the pain domain of the EORTC QLQ-C30) were excluded, as these subscales may lack the sensitivity required to detect specific changes in neuropathic pain intensity compared with dedicated pain scales. Second, for the quantitative NMA, we restricted data synthesis to unidimensional scales specifically validated for pain intensity (i.e. the Brief Pain Inventory [BPI], Numeric Rating Scale [NRS], and Visual Analogue Scale [VAS]) to ensure clinimetric homogeneity. Studies using composite or multidimensional instruments that aggregate pain with other neuropathy symptoms (e.g., Chemotherapy-Induced Peripheral Neuropathy Assessment Tool) were excluded from the quantitative synthesis to maintain clinimetric homogeneity and outcome specificity. This distinction was applied to avoid the heterogeneity introduced by pooling pure pain intensity scores with multidimensional symptom burden scores.

2.4. Study selection

Eight reviewers were divided into four independent pairs, and each pair independently screened the titles and abstracts of the retrieved records against the eligibility criteria. Subsequently, the full texts of potentially eligible articles were reviewed to determine the final inclusion criteria. Disagreements were resolved through discussion or consultation with a third reviewer. The study selection process is illustrated in a PRISMA flow diagram (Page et al., 2021).

2.5. Data extraction

Eight reviewers were divided into four independent pairs, and each pair independently extracted the data using a standardised data extraction form. Discrepancies were resolved by consensus or arbitration with a third reviewer. The following data items were extracted: (1) study characteristics (first author, year of publication, country); (2) participant characteristics (cancer type, age, sex, sample size); (3) intervention details (type, frequency, duration, provider); (4) comparator details; and (5) outcomes and results (pain intensity scores).

2.6. Risk of bias

The risk of bias for the included RCTs was assessed independently by each pair within four independent reviewer teams (eight reviewers in total) using the Cochrane Risk of Bias tool (RoB 2.0) (Sterne et al., 2019). Disagreements were resolved by consensus within each pair or consultation with a third reviewer.

2.7. Data analysis

Pairwise meta-analyses and frequentist NMAs were performed using a random-effects model. A frequentist NMA was conducted to synthesise direct and indirect comparisons across interventions. For continuous outcomes measured using different scales, standardised mean differences with 95% confidence intervals (CIs) were calculated. Inter-study heterogeneity was estimated using the restricted maximum likelihood method. NMA was performed using the netmeta package (version 3.2-0) in R (version 4.5.0; R Foundation for Statistical Computing, Vienna, Austria). Treatment ranking was assessed using P-scores. Significance was set at $P < 0.05$. Inconsistency was evaluated using local (node-splitting) and global approaches. Heterogeneity was quantified using the I^2 statistic. Planned sensitivity analyses based on risk of bias, type of outcome measure, and follow-up duration were not performed because of the limited number of eligible studies and the substantial methodological heterogeneity across the included trials.

The primary outcome was pain intensity. For studies reporting multiple pain-related outcomes, the most frequently used scale among the included studies was selected for NMA.

3. Results

3.1. Study selection

The database search identified 12,052 records. After removing 2489 duplicate records, the titles and abstracts of 9563 records were screened. After screening, 117 full-text articles were assessed for eligibility. Of these, 85 studies were excluded. The most common reason for exclusion was incorrect outcomes (n = 41), including studies that assessed general neuropathy symptoms (e.g., numbness) rather than pain intensity, or relied solely on pain items embedded within QoL instruments. Other reasons for exclusion were wrong population (n = 15), wrong publication type (n = 8), wrong study design (n = 7), wrong PICO (n = 5), non-English publication (n = 5), wrong intervention (n = 1), wrong study duration (n = 1), and other reasons (n = 2). Finally, 32 studies met the inclusion criteria and were included in this systematic review. Of these, 19 provided sufficient quantitative data and were included in the NMA (Fig. 1).

3.2. Study characteristics

The characteristics of the 32 studies included in the systematic review are summarised in Table 1 (Greenlee et al., 2016; Prinsloo et al., 2017, 2018; Rick et al., 2017; Griffiths et al., 2018; Knoerl et al., 2018, 2022; Kurt and Can, 2018; Izgu et al., 2019; Molassiotis et al., 2019; Andersen Hammond et al., 2020; Bao et al., 2020; Dhawan et al., 2020; Iravani et al., 2020; Loprinzi et al., 2020a,b; Lu et al., 2020; Smith et al., 2020; Song et al., 2020; Huang et al., 2021; Şimşek and Demir, 2021; D'Alessandro et al., 2022; Joy et al., 2022; Lopez et al., 2022; Stringer et al., 2022; Chan et al., 2023; Lagerstedt and Efverman, 2023; Langley-Brady et al., 2023; Elshinnawy et al., 2024; Eroğlu and Kutlutürkan, 2024; Kleckner et al., 2024; Wakolbinger-Habel et al., 2024; Jung et al., 2025). These studies were conducted in various countries, including the United States (n = 12), Turkey (n = 4), South Korea (n = 2), and China (n = 2). Participants were patients with various malignancies, most commonly breast, colorectal, and gynaecological cancers, who were experiencing or at risk of CIPN.

A total of 1612 participants were analysed across the 32 included studies. Among the studies reporting sex distribution, 1178 (73.1%) participants were female and 264 were male; sex was not reported in the remaining studies. Regarding age, the reporting methods varied across studies (e.g., mean, median, age range, or not reported). The weighted mean age, calculated from the studies reporting mean values (n = 624), was 57.4 years. In studies reporting median ages, the reported median values were generally in the late 50s to early 60s.

The non-pharmacological interventions evaluated in the included studies were diverse and categorised into six primary modalities. Acupuncture-based interventions, including manual acupuncture, electroacupuncture, auricular acupuncture, and intradermal needles, were the most frequently studied (n = 11; e.g., Bao et al., 2020; Huang et al., 2021; Jung et al., 2025). Since acupuncturists are licenced physicians in some countries and non-physician healthcare professionals in others, provider types were standardised and categorised as 'Physician' for analytical consistency. This was followed by electrical stimulation therapies (n = 8), which included diverse approaches such as Scrambler therapy, TENS, neurofeedback, and high-frequency electrical stimulation (e.g., Prinsloo et al., 2017; Smith et al., 2020; Song et al., 2020). Exercise-based interventions (n = 6) involved various programmes, including home-based combined aerobic and resistance training, yoga, and balance exercises (e.g., Andersen Hammond et al., 2020; Dhawan et al., 2020; Knoerl et al., 2022). Massage-based interventions (n = 3) included Swedish massage and reflexology (Kurt and Can, 2018; Izgu et al., 2019; Lopez et al., 2022), whereas cryotherapy/cold-based interventions (n = 3) used frozen gloves or socks to mitigate symptoms

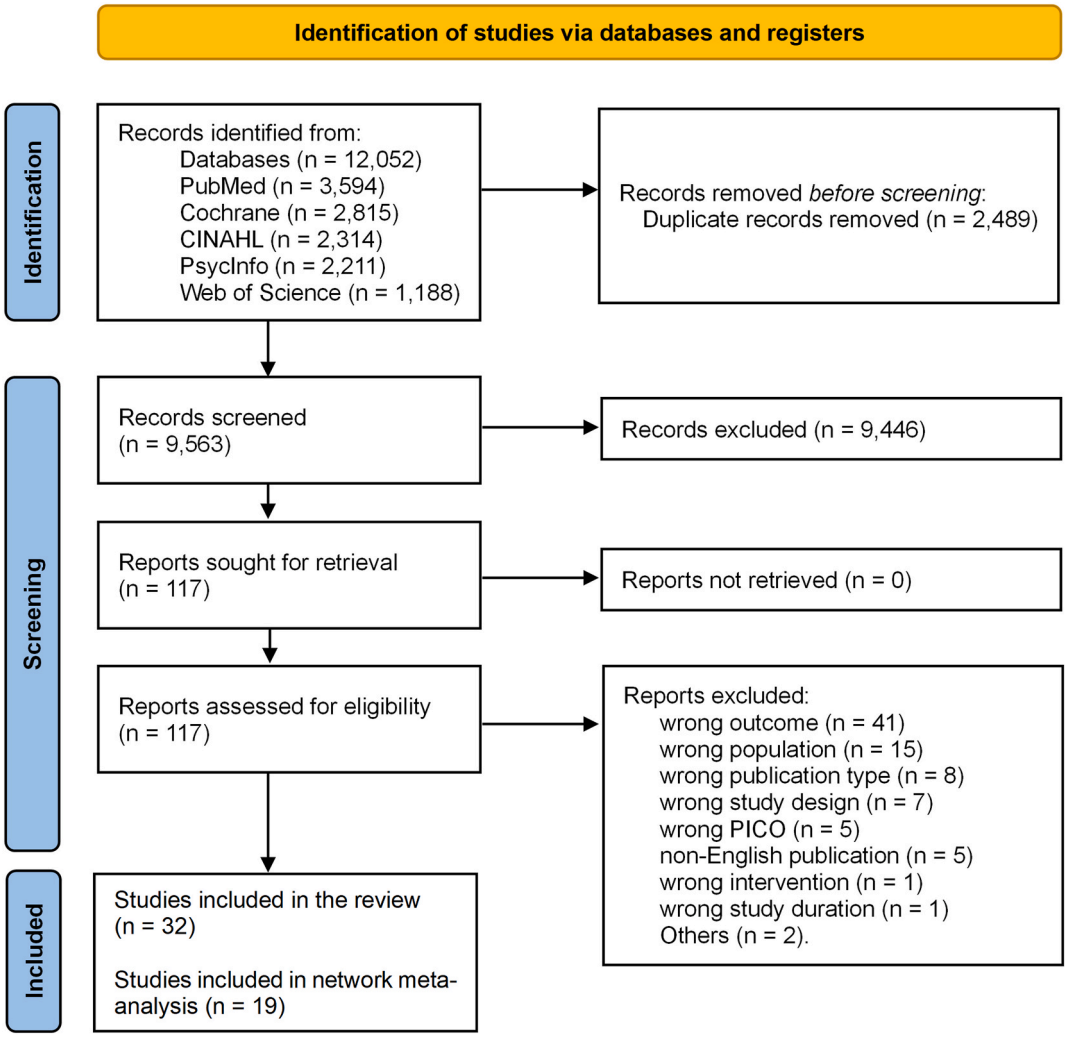

Fig. 1. PRISMA flow diagram
Flow diagram illustrating the study identification, screening, eligibility, and inclusion process for this systematic review and network meta-analysis. A total of 12,052 records are identified, 32 studies are included in the systematic review, and 19 studies are included in the network meta-analysis.

(Griffiths et al., 2018; Şimşek and Demir, 2021; Elshinnawy et al., 2024). Additionally, four studies that investigated the effects of photobiomodulation (light therapy), magnetic therapy, CBT, and aromatherapy-based interventions were categorised as other interventions (Rick et al., 2017; Knoerl et al., 2018; Joy et al., 2022; Langley-Brady et al., 2023).

Control conditions varied across studies and included sham/placebo, usual care, waitlist, behavioural or pharmacological controls, within-subject designs, and alternative interventions, or were not applicable.

Control conditions and outcome measures: The most frequent comparator was usual care (n = 15), which typically involved standard medical monitoring without specific rehabilitation. This was followed by sham or placebo interventions (n = 11), which were predominantly utilised in acupuncture and electrical stimulation trials. The remaining studies employed waitlist (n = 3) or active controls (n = 3) (e.g., health education).

In terms of outcome measurements, consistent with our selection criteria to minimise heterogeneity, most studies assessed pain intensity using three unidimensional scales: VAS (n = 12), BPI (n = 11), and NRS (n = 8).

3.3. Risk of bias assessment

The risk of bias assessment across the included studies is summarised in Figs. 2 and 3. The overall risk was predominantly classified as 'some concerns' or 'high risk', and no study was judged to be at overall low risk of bias.

Regarding the randomisation process (Domain 1), most studies were rated as 'low risk' or 'some concerns'. However, several trials did not provide sufficient information on allocation concealment. Missing outcome data (Domain 3) varied across studies. In several trials, attrition was reported and statistical approaches such as intention-to-treat analyses were applied.

Higher risk ratings were observed in domains related to blinding (Domains 2 and 4). Trials involving behavioural or sensory-based interventions, such as exercise (e.g., Şimşek and Demir, 2021; Kleckner et al., 2024), yoga (Knoerl et al., 2022), massage (Izgu et al., 2019), and cryotherapy (Griffiths et al., 2018), were frequently rated as 'high risk', particularly in Domain 2 (deviations from intended interventions) and Domain 4 (measurement of the outcome).

In contrast, trials utilising device-based interventions (e.g., Loprinzi et al., 2020a,b; Smith et al., 2020) or acupuncture (e.g., Huang et al., 2021; Bao et al., 2020) more frequently achieved 'low risk' ratings in Domain 2.

3.4. Network structure

Among the studies reporting pain outcomes, only those providing

Table 1
Characteristics of included studies
Summary of the characteristics of the included randomised controlled trials, including study design, participant characteristics, intervention details, comparator, outcome measures, and inclusion in the network meta-analysis.

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
Greenlee et al. (2016)	United States	n = 63; Female = 63; Age: 50 ± 11 years	Breast cancer	**Acupuncture-based intervention**	Individual electroacupuncture intervention (12 weekly sessions over 12 weeks; ~30 min/session) using low-frequency electrical stimulation at standardised upper- and lower-limb acupoints during taxane chemotherapy to prevent chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 31; Female = 31; Age: 51.8 ± 10.7 years	Sham/Placebo	n = 32; Female = 32; Age: 48.3 ± 12.0 years	BPI	Yes
Molassiotis et al. (2019)	China (Hong Kong)	n = 87; Female/Male = 63/24; Age: 57.1 ± 7.7 years	Breast cancer, colorectal cancer, ovarian cancer, head and neck cancer, myeloma	**Acupuncture-based intervention**	Individual manual acupuncture intervention (16 sessions over 8 weeks; ~30 min/session) using standardised bilateral needle insertion with manual de-qi stimulation at upper- and/or lower-limb acupoints to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 44; Female/Male = 35/9; Age: 56.3 ± 7.35 years	Waitlist	n = 43; Female/Male = 28/15; Age: NR	BPI	Yes
Bao et al. (2020)	United States	n = 75; Female/Male = 60/15; Age: median 59.7 (range 36.3–85.9) years	Breast cancer, colorectal cancer, other solid tumours	**Acupuncture-based intervention**	Individual acupuncture intervention (16 sessions over 8 weeks; ~30 min/session) using ear and body acupuncture with adjunct electroacupuncture to reduce chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 24; Sex: NR; Age: NR	Usual care	n = 21; Sex: NR; Age: NR	NRS	Yes
Iravani et al. (2020)	Iran; China	n = 38; Female/Male = 23/15; Age: NR	Breast cancer, ovarian cancer, prostate cancer, colorectal cancer, colon cancer, rectal cancer	**Acupuncture-based intervention**	Individual manual acupuncture intervention (12 sessions over 4 weeks; ~20 min/session) using standardised needling at bilateral upper- and/or lower-limb acupoints with de-qi stimulation to alleviate chronic chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 19; Female/Male = 12/7; Age: 57.95 ± 10.39 years	Pharmacological	n = 19; Female/Male = 11/8; Age: 58.79 ± 8.36 years	NRS	Yes
Lu et al. (2020)	United States	n = 40; Female = 40; Age: median 54 (range 26–71) years	Breast cancer	**Acupuncture-based intervention**	Individual acupuncture intervention (18 sessions over 8 weeks; ~30 min/session) using manual and electroacupuncture to alleviate chemotherapy-induced peripheral neuropathic symptoms and pain.	n = 20; Female = 20; Age: median 54.0 (range 32.0–68.0) years	Waitlist	n = 20; Female = 20; Age: median 53.5 (range 26.0–71.0) years	BPI	
Huang et al. (2021)	Taiwan	n = 20; Female = 20; Age: 49.60 ± 11.13 years	Breast cancer	**Acupuncture-based intervention**	Individual manual acupuncture intervention (15 sessions over 9 weeks; ~30 min/session) targeting chemotherapy-induced	n = 10; Female = 10; Age:	Sham Placebo	n = 10; Female = 10; Age:	BPI	Yes

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					peripheral neuropathy through stimulation of predefined acupoints on the abdomen and bilateral upper and lower limbs.	47.10 ± 11.07 years		52.10 ± 11.18 years		
D'Alessandro et al. (2022)	Brazil	n = 29; Female/Male = 17/12; Age: 57.68 years (range 41–82)	Breast cancer, gastrointestinal cancer, genitourinary cancer, haematological cancers	**Acupuncture-based intervention**	Individual manual acupuncture intervention (10 sessions over 5 weeks; ~30 min/session, twice weekly) delivered in addition to a rehabilitation programme, using symptom-tailored needling with a standardised core set of hand and foot yuan-source acupoints (LR3, SP3, KI3, HT7, PC7, LU9), SP9, and wrist–ankle acupuncture (areas 1–3) to alleviate chemotherapy-induced peripheral neuropathic sensory symptoms and pain.	n = 15; Sex: NR; Age: NR	Usual care	n = 14; Sex: NR; Age: NR	VAS	Yes
Stringer et al. (2022)	United Kingdom	n = 120; Sex: NR; Age: NR	Breast cancer, multiple myeloma, gastrointestinal cancer, gynaecological cancer	**Acupuncture-based intervention**	Individual manual acupuncture intervention (10 weekly sessions over 10 weeks; ~40 min/session) using a standardised protocol of bilateral upper- and lower-limb acupoint needling to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 61; Sex: NR; Age: median 61 (range 37–76) years	Usual care	n = 59; Sex: NR; Age: median 60 (range 29–79) years	NRS	Yes
Chan et al. (2023)	China	n = 55; Female/Male = 22/33; Age: NR	Colorectal cancer	**Acupuncture-based intervention**	Individual electroacupuncture intervention (12 sessions over 12 weeks; ~25–30 min/session) using low-frequency electrical stimulation at standardised upper- and lower-limb acupoints to alleviate oxaliplatin-induced peripheral neuropathic symptoms and pain.	n = 27; Female/Male = 9/18; Age: 60.0 ± 8.57 years	Sham/Placebo	n = 28; Female/Male = 13/15; Age: 62.5 ± 7.62 years	NRS	Yes
Lagerstedt and Efverman (2023)	Sweden	n = 12; Female/Male = 5/7; Age: NR	Colorectal cancer	**Acupuncture-based intervention**	Individual manual acupuncture intervention (10 sessions over 5 weeks; ~30 min/session) using standardised bilateral needle insertion with de-qi stimulation at facial, hand, and foot acupoints to alleviate chemotherapy-induced peripheral neuropathic pain and unpleasant sensations.	n = 6; Female/Male = 1/5; Age: median 68 (IQR 63–76) years	Sham/Placebo	n = 6; Female/Male = 4/2; Age: median 69 (IQR 64–70) years	VAS	Yes
Jung et al. (2025)	South Korea	n = 51; Female = 51; Age: NR	Breast cancer	**Acupuncture-based intervention**	Nurse-led auricular acupressure intervention (3 weekly sessions over 3 weeks; self-administered daily stimulation) using Vaccaria seeds applied to standardised ear acupoints to alleviate chemotherapy-induced	n = 25; Female = 25; Age: 49.24 ± 7.57 years	Sham/Placebo	n = 26; Female = 26; Age: 49.73 ± 5.19 years	NRS	Yes

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					peripheral neuropathic pain and symptoms.					
Prinsloo et al. (2017)	United States	n = 71; Female/Male = 62/9; Age: 62.5 ± 10.3 years	Breast cancer, gynecologic cancers, gastrointestinal cancers	**Electrical stimulation therapy**	Individual EEG neurofeedback intervention (20 sessions over up to 10 weeks; ~45 min/session) using visual and auditory feedback to train voluntary modulation of brainwave activity for alleviating chemotherapy-induced peripheral neuropathic pain.	n = 35; Female/Male = 31/4; Age: 62.0 ± 9.6 years	Usual care	n = 36; Female/Male = 31/5; Age: 63.0 ± 11.0 years	BPI	Yes
Prinsloo et al. (2018)	United States	n = 71; Female/Male = 62/9; Age: 62.5 ± 10.3 years	Breast cancer, gastrointestinal cancer, gynaecological cancer, other cancers	**Electrical stimulation therapy**	Individual EEG neurofeedback intervention (20 sessions over up to 10 weeks; ~45 min/session) using visual and auditory feedback–based training to facilitate voluntary modulation of brainwave activity for alleviating chronic chemotherapy-induced peripheral neuropathic pain and symptom burden.	n = 23; Sex: NR; Age: NR	Waitlist	n = 28; Sex: NR; Age: NR	BPI	Yes
Loprinzi et al. (2020)	United States	n = 46; Female/Male = 34/12; Age: NR	Various solid tumours	**i) Electrical stimulation therapy** **ii) Electrical stimulation therapy**	i) Individual Scrambler therapy intervention (10 consecutive daily sessions over 2 weeks; ~30 min/session) using transcutaneous electrical neuromodulation delivered via cutaneous electrodes placed proximal to painful areas to alleviate chronic chemotherapy-induced peripheral neuropathic pain and symptoms. ii) Individual TENS intervention (daily sessions over 2 weeks; ~30 min/session) using portable surface electrodes applied to the most symptomatic areas to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 24; Female/Male = 17/7; Age: median 61.5 (range 32–82) years	Not applicable	n = 22; Female/Male = 17/5; Age: median 61.0 (range 52–75) years	NRS	
Smith et al. (2020)	United States	n = 35; Female/Male = 26/9; Age: 59 ± 9 years	Colorectal cancer, breast cancer, myeloma	**Electrical stimulation therapy**	Individual scrambler therapy (10 sessions over 2 weeks; ~30 min/session) using transcutaneous electrical neuromodulation for chemotherapy-induced peripheral neuropathic pain.	n = 17; Female/Male = 11/6; Age: 59.71 ± 8.88 years	Sham/Placebo	n = 18; Female/Male = 15/3; Age: 58.94 ± 9.31 years	NRS	Yes
Song et al. (2020)	South Korea	n = 72; Female = 72; Age: 50.0 ± 8.85 years	Breast cancer	**Electrical stimulation therapy**	Individual low-frequency electrostimulation intervention (≥2 sessions daily over 2 weeks; ≥60 min/session, total ≥120 min/day) using a wearable wristband device delivering transcutaneous electrical	n = 36; Female = 36; Age: 49.9 ± 8.85 years	Sham/Placebo	n = 36; Female = 36; Age: 49.7 ± 8.24 years	NRS	Yes

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					stimulation at the PC6 acupoint to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.					
Wakolbinger-Habel et al. (2024)	Austria	n = 14; Sex: NR; Age: NR	Colorectal cancer	**Electrical stimulation therapy**	Home-based high tone therapy intervention (daily sessions over 3 weeks; ~60 min/session) using transcutaneous medium-frequency electrical stimulation applied to upper and/or lower extremities to alleviate chemotherapy-induced peripheral neuropathic symptoms and pain.	n = 7; Sex: NR; Age: median 54 (range 39–57) years	Sham/Placebo	n = 7; Sex: NR; Age: median 64 (range 53–75) years	NRS	
Andersen Hammond et al. (2020)	Canada	n = 48; Female = 48; Age: 61.5 years (range 37–78)	Breast cancer	**Exercise-based intervention**	Physical therapy–based home exercise and education intervention (four therapist-led visits at chemotherapy initiation with daily home practice throughout and after chemotherapy; ~5–10 min/session, three times daily) focusing on nerve gliding exercises, upper-limb stretching and range-of-motion training, and structured education for neuropathic symptom management to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 22; Female = 22; Age: 56.3 ± 9.9 years	Usual care	n = 26; Female = 26; Age: 53.0 ± 10.3 years	NRS	
Dhawan et al. (2020)	India	n = 45; Female/Male = 38/7; Age: NR	Ovarian cancer, cervical cancer, lung cancer, parotid ductal carcinoma, base of tongue cancer, retromolar trigone cancer	**Exercise-based intervention**	Home-based muscle strengthening and balance exercise intervention (daily sessions over 10 weeks; ~30 min/session) targeting chemotherapy-induced peripheral neuropathic pain and functional impairment.	n = 22; Female/Male = 18/4; Age: 50.5 ± 7.9 years	Usual care	n = 23; Female/Male = 20/3; Age: 52.5 ± 6.6 years	LANSS	
Şimşek and Demir (2021)	Turkey	n = 90; Female = 90; Age: 20–39: 17 (18.9%), 40–59: 50 (55.5%), ≥60: 23 (25.6%)	Breast cancer	**i) Exercise-based intervention** **ii) Cryotherapy/Cold-based intervention**	i) Home-based progressive exercise intervention (5 sessions per week over 12 weeks; ~15–30 min/session) consisting of strengthening, stretching, and balance exercises, supervised weekly and tailored to tolerance, to prevent and attenuate taxane-induced peripheral neuropathic pain and symptoms. ii) Localised cold application intervention (applied at each weekly taxane infusion and continued for 24 h over 12 weeks; ~30 min per application) using	n = 30; Female = 30; Age: NR	Usual care	n = 30; Female = 30; Age: NR	CIPNAT	

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					frozen cold packs to wrists and ankles before and during chemotherapy to prevent taxane-induced peripheral neuropathic pain and symptoms.					
Knoerl et al. (2022)	United States	n = 44; Female/Male = 42/2; Age: NR	Breast cancer, gastrointestinal cancer, gynaecological cancer, multiple cancers	**Exercise-based intervention**	Therapist-guided and self-guided yoga intervention (8 weeks; ~45 min/session) incorporating breathing exercises, stretching, and structured postures to alleviate chronic chemotherapy-induced peripheral neuropathic pain.	n = 28; Female/Male = 27/1; Age: median 60 (range 33–74) years	Usual care	n = 16; Female/Male = 15/1; Age: median 56.5 (range 40–79) years	NRS	Yes
Kleckner et al. (2024)	United States	n = 19; Female/Male = 10/9; Age: 64.6 ± 10.6 years	Bladder cancer, breast cancer, colon cancer, oesophageal cancer, multiple myeloma, pancreatic cancer, prostate cancer	**Exercise-based intervention**	Home-based combined aerobic and resistance exercise intervention (daily sessions over 12 weeks; ~30 min/day) consisting of moderate-intensity progressive walking and resistance-band training to attenuate chemotherapy-induced peripheral neuropathic symptoms and pain during neurotoxic chemotherapy.	n = 9; Female/Male = 5/4; Age: 57.1 ± 7.8 years	Behavioural control	n = 10; Female/Male = 5/5; Age: 71.1 ± 7.8 years	NRS	Yes
Eroğlu and Kutlutürkan (2024)	Turkey	n = 39; Female/Male = 14/25; Age: NR	Colorectal cancer	**Exercise-based intervention**	Hand–foot exercise programme intervention (home-based daily sessions throughout chemotherapy; ~15–20 min/day) consisting of a structured booklet- and video-guided exercise regimen using simple tools (tennis ball and towel) to improve mobility, sensory function, and neuropathic pain associated with chemotherapy-induced peripheral neuropathy.	n = 19; Female/Male = 8/11; Age: 60.84 ± 11.0 years	Usual care	n = 20; Female/Male = 6/14; Age: 60.45 ± 14.4 years	NRS	Yes
Kurt and Can (2018)	Turkey	n = 96; Female/Male = 28/32; Age: NR	Gastrointestinal cancer, breast cancer	**Massage-based intervention**	Foot reflexology massage intervention (twice-daily sessions over 6 weeks; ~20 min/session) applied to cervical-related reflex zones on the medial upper foot and the brain reflex area beneath the hallux using finger-based worm-like movements and pressure, delivered by a certified reflexologist or trained relatives to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 30; Female = 14 (46.7%); Age: 58.33 ± 11.24 years	Usual care	n = 30; Female = 14 (46.7%); Age: 57.86 ± 10.56 years	BPI	
Izgu et al. (2019)	Turkey	n = 40; Female = 40; Age: NR	Breast cancer	**Massage-based intervention**	Individual classical massage intervention (12 weekly sessions over 12 weeks; ~30 min/session) applied to hands and feet using	n = 19; Female = 19; Age: 44.5 ± 10.7 years	Usual care	n = 21; Female = 21; Age: 47.0 ± 9.6 years	S-LANSS	

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					standardised Swedish massage techniques prior to paclitaxel infusion to prevent chemotherapy-induced peripheral neuropathic pain and symptoms.					
Lopez et al. (2022)	United States	n = 71; Female/Male = 55/16; Age: 60.8 ± 9.8 years	Chemotherapy-induced peripheral neuropathy from: oxaliplatin, paclitaxel, and docetaxel	**Massage-based intervention**	Individual oncology (Swedish) massage intervention (2–3 sessions per week over 4–6 weeks; ≤30 min/session) applied to the lower extremities using a standardised protocol to alleviate chronic chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 47; Sex: NR; Age: NR	Alternate-site massage	n = 24; Sex: NR; Age: NR	PQAS	
Griffiths et al. (2018)	United States	n = 29; Female = 29; Age: 47.3 years	Breast cancer	**Cryotherapy/ Cold-based intervention**	Individual cryotherapy intervention (applied at each weekly paclitaxel infusion; ~210 min per infusion) using frozen gloves and socks worn before, during, and after chemotherapy to prevent paclitaxel-induced peripheral neuropathic pain and symptoms.	n = 7; Female = 7; Age: mean 47.3 (range 35–68) years	Within-subject	n = 7; Female = 7; Age: mean 47.3 (range 35–68) years	BPI	
Elshinnawy et al. (2024)	Egypt	n = 30; Female = 30; Age: NR	Breast cancer	**i)Cryotherapy/ Cold-based intervention** **ii) Electrical stimulation therapy**	i) Localised cold application intervention (three sessions per week over 12 weeks; ~30 min/session) using frozen cold packs applied to the ankles with protective gauze, delivered as two 15-min applications separated by a 45-min interval to prevent and attenuate chemotherapy-induced peripheral neuropathic pain and symptoms. ii) Individual TENS intervention (three sessions per week over 12 weeks; ~30 min/session) applied bilaterally to the lower limbs using low-frequency stimulation (15 Hz, 250 μs pulse width) at moderately strong intensity to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 15; Female = 15; Age: 50.93 ± 4.16 years	Not applicable	n = 15; Female = 15; Age: 52.67 ± 5.53 years	VAS	Yes
Rick et al. (2017)	Germany	n = 44; Female/Male = 31/13; Age: median 58 (range 28–73) years	Breast cancer, lymphoma, ovarian cancer, colorectal cancer, others	**Magnetic field therapy**	Individual magnetic field therapy intervention (twice-daily sessions over 3–12 weeks; ~5 min/session per affected extremity) using a hand-held low-frequency rotating magnetic field device (MAGCELL MICROCIRC®) applied to palms	n = 21; Female/Male = 15/6; Age: NR	Sham/Placebo	n = 23; Female/Male = 16/7; Age: NR	painDETECT questionnaire	

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Table 1 (*continued*)

Author (Year)	Country	Participants (n, sex, age)	Cancer type	Intervention			Control		Measurement	Included in NMA
				Classification	Details	Participants (n, sex, age)	Control	Participants (n, sex, age)		
					and/or soles to alleviate chemotherapy-induced peripheral neuropathic symptoms and pain.					
Knoerl et al. (2018)	United States	n = 60; Female/Male = 45/15; Age: 61.15 ± 8.93 years	Breast cancer, gastrointestinal cancer, genitourinary cancer, lung cancer, multiple cancers, lymphoma	**Psychological intervention**	Self-guided online cognitive behavioural pain management intervention (8 weeks; flexible, self-paced use) delivering structured CBT-based modules targeting pain coping, relaxation, activity pacing, sleep hygiene, and cognitive restructuring to alleviate chronic chemotherapy-induced peripheral	n = 30; Female/Male = 23/7; Age: 58.93 ± 9.33 years	Usual care	n = 30; Female/Male = 22/8; Age: 63.37 ± 8.36 years	NRS	Yes
Joy et al. (2022)	Belgium	n = 32; Female = 32; Age: NR	Breast cancer	**Phototherapy/ Light-based intervention**	Individual photobiomodulation therapy intervention (twice-weekly sessions during taxane chemotherapy over 12–18 weeks; ~15–20 min/session) using near-infrared laser irradiation applied bilaterally to upper and lower limb peripheral nerve regions to prevent chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 16; Female = 16; Age: 51.88 ± 11.31 years	Sham/Placebo	n = 16; Female = 16; Age: 49.75 ± 11.25 years	NRS	
Langley-Brady et al. (2023)	United States	n = 26; Female = 26; Age: 60.31 years	Breast cancer	**Aromatherapy-based intervention**	Topical essential oil intervention (10% dilution; daily application using 5-mL doses supplied weekly) consisting of a 1:1 blend of essential oils diluted in jojoba oil, prepared and quality-controlled by a certified clinical aromatherapist, to alleviate chemotherapy-induced peripheral neuropathic pain and symptoms.	n = 13; Female = 13; Age: NR	Sham/Placebo	n = 13; Female = 13; Age: NR	VAS	

BPI, Brief Pain Inventory; CBT, cognitive behavioural therapy; CIPNAT, Chemotherapy-Induced Peripheral Neuropathy Assessment Tool; EEG, Electroencephalography; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs; NMA, network meta-analysis; NR, Not Reported; NRS, Numeric Rating Scale; PQAS, Pain Quality Assessment Scale; S-LANSS, Self-report Leeds Assessment of Neuropathic Symptoms and Signs; TENS, transcutaneous electrical nerve stimulation; VAS, Visual Analogue Scale.

sufficient quantitative data (mean, standard deviation, and sample size) for the validated pain intensity scales (BPI, NRS, or VAS) were included in the NMA. The NMA included six intervention categories: acupuncture-based interventions, electrical stimulation therapy, exercise-based interventions, psychological interventions, cryotherapy, and control conditions. Control conditions (usual care, sham, or waitlist) served as the most common comparator across the trials. Most interventions were compared with a common control group, forming a connected network that enabled indirect comparisons between interventions. Only one direct comparison between active interventions (cryotherapy vs. electrical stimulation therapy) was available (Fig. 4).

3.5. Primary outcome: pain

The results of the NMA are presented in Fig. 5. The NMA comparing non-pharmacological interventions for CIPN-related pain suggested a trend toward pain reduction across several modalities, although statistical uncertainty remained for many comparisons, as reflected by the wide CIs. Compared with the control conditions, acupuncture-based interventions demonstrated a significant reduction in pain intensity (standardised mean difference (SMD) 0.66, 95% CI 0.16 to 1.17). In contrast, exercise-based interventions (SMD 0.95, 95% CI: −0.03 to 1.94), electrical stimulation therapy (SMD 0.49, 95% CI: −0.28 to 1.26), psychological interventions (SMD 0.40, 95% CI: −1.18 to 1.98), and cryotherapy (SMD 1.64, 95% CI: −0.17 to 3.44) did not reach significance. Direct comparisons between the active interventions showed wide CIs, indicating substantial uncertainty in the relative treatment effects (Table 2).

Treatment ranking based on P-scores suggested that cryotherapy ranked highest (P-score = 0.86), followed by exercise-based ((P-score = 0.68), acupuncture-based (P-score = 0.54), and electrical stimulation ((P-score = 0.42) interventions (Table 3).

3.6. Inconsistency and heterogeneity

No evidence of inconsistency between the designs was observed in the global inconsistency test. Substantial heterogeneity was observed across studies ($\tau^2 = 0.54$, $I^2 = 83.8\%$, $Q = 86.58$, $P < 0.001$). Since most comparisons were conducted against a common control group, the network contained few closed loops, and a local inconsistency assessment using node-splitting was not feasible.

4. Discussion

4.1. Principal findings

This systematic review and NMA evaluated a broad range of non-pharmacological interventions for CIPN-related pain, including acupuncture-based interventions, electrical stimulation therapies, exercise-based interventions, massage therapies, cryotherapy, psychological interventions, and several emerging modalities such as photobiomodulation and aromatherapy. Among the interventions included in the NMA, only acupuncture-based interventions demonstrated a significant reduction in pain intensity compared with control conditions (SMD 0.66, 95% CI: 0.16 to 1.17). This finding is consistent with recent evidence highlighting the analgesic potential of acupuncture for CIPN (Li et al., 2024). Although current ASCO and ESMO guidelines do not provide strong recommendations for most non-pharmacological interventions for CIPN because of limited high-quality evidence, acupuncture has increasingly been recognised as a promising supportive care approach for neuropathic symptom management (Jordan et al., 2020; Loprinzi et al., 2020). Treatment ranking based on P-scores indicated that cryotherapy (P-score = 0.86) and exercise-based interventions (P-score = 0.68) ranked highest in the network; however, neither intervention demonstrated statistically significant superiority over control conditions, and both were associated with wide confidence intervals, indicating substantial uncertainty in the estimated treatment effects. Although cryotherapy and exercise-based interventions ranked highly in the NMA, their effects did not reach statistical significance, and evidence for psychological and other emerging interventions remained limited because of the small number of available trials.

4.2. Comparison with previous literature

In contrast to the recent NMAs by Zhang et al. (2023) and Cai et al. (2026), which evaluated non-pharmacological interventions for CIPN by pooling generalised neurotoxicity scales alongside specific pain measures, our study adopted a more targeted approach. By strictly limiting our inclusion criteria to trials that measured pain as an independent construct—using validated tools such as the VAS, NRS, and BPI—rather than as a subscale of composite neuropathy or QoL instruments, the current study substantially minimises clinimetric heterogeneity. Consequently, this methodological refinement provides a more precise and clinically meaningful estimate of pure analgesic efficacy compared to broader reviews.

4.3. Intervention modality

Distinct outcomes across modalities can be attributed to a combination of mechanistic pathways and methodological factors. Acupuncture was the sole intervention demonstrating significant pain reduction, likely due to its biological mechanisms, such as the activation of descending inhibitory pathways and neuroinflammatory modulation (Ma et al., 2022), which are central components in the pathophysiology of neuropathic pain (Streckmann et al., 2014), and the methodological rigour of sham-controlled trials that effectively minimise bias. Cryotherapy and exercise were ranked high in terms of potential efficacy; however, the results were not significant. The interpretation of cryotherapy is severely limited by the scarcity of eligible trials and the resulting small sample size, which directly accounts for the wide CIs. Similarly, while exercise may theoretically alleviate pain through improved microcirculation and central pain modulation (Streckmann et al., 2014; Kami et al., 2017; Sluka et al., 2018), the structural impossibility of blinding in these trials increases susceptibility to performance and detection biases. Finally, electrical stimulation therapies yielded mixed results, likely reflecting substantial heterogeneity in stimulation parameters including frequency, intensity, waveform, electrode placement, and treatment duration across studies, as documented in previous systematic reviews of neuromodulation in CIPN (Xu et al., 2024). In contrast, evidence for psychological interventions remains too limited to draw definitive conclusions. Overall, heterogeneity in risk of bias across studies appeared to be associated with differences in the feasibility of blinding across intervention modalities, rather than fundamental flaws in study design.

4.4. Strengths and limitations

A major strength of this study is that it is the first NMA to evaluate non-pharmacological interventions for CIPN by exclusively extracting data from validated pain intensity scales, thereby overcoming the clinical heterogeneity inherent in composite symptom scores. However, this study has some limitations. First, substantial statistical heterogeneity was observed across the network ($I^2 = 83.8\%$), likely driven by variations in intervention protocols, patient populations (e.g., cancer types), and control conditions among the included trials. Second, the network structure was inherently sparse, relying heavily on indirect evidence from common control groups. With only one direct comparison between active interventions (cryotherapy vs. electrical stimulation), there was a notable lack of closed loops. This sparsity precluded the use of the node-splitting method to evaluate the local inconsistency between direct and indirect evidence, necessitating cautious interpretation of the comparative rankings. Third, the control node included heterogeneous

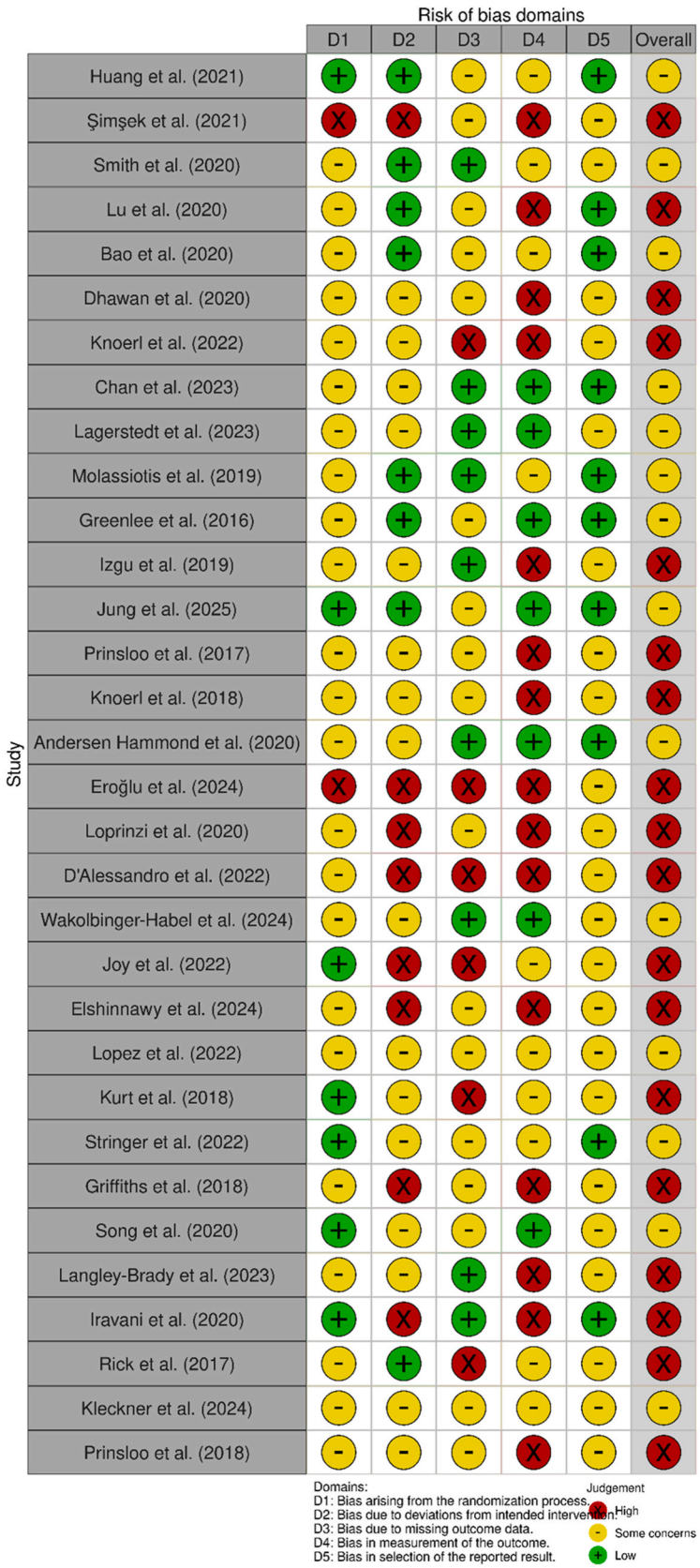

Fig. 2. Risk of bias summary for individual studies
Summary of the risk of bias assessments for each included study based on the Cochrane Risk of Bias 2.0 (RoB 2.0) tool. Each domain is rated as low risk, some concerns, or high risk of bias.

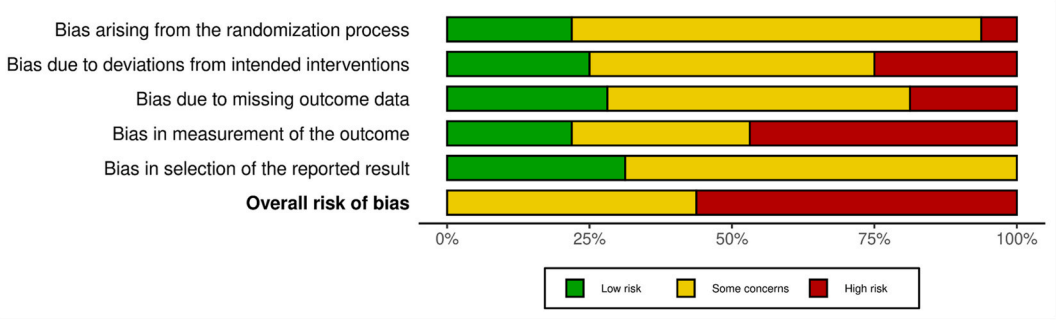

Fig. 3. Risk of bias graph
Graph showing the proportion of studies with low risk, some concerns, and high risk of bias across each domain, based on the Cochrane Risk of Bias 2.0 (RoB 2.0) tool.

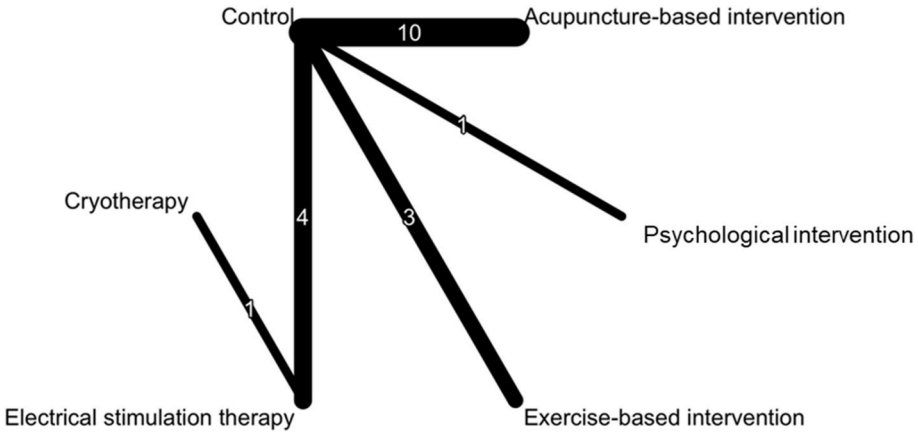

Fig. 4. Network plot of interventions
Network plot illustrating the comparisons among intervention categories included in the network meta-analysis. Nodes represent intervention categories, and edges represent direct comparisons between interventions. The size of each node and the thickness of each edge are proportional to the number of studies.

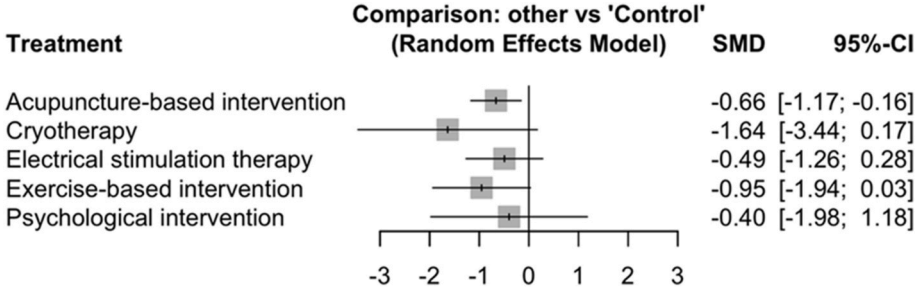

Fig. 5. Forest plot of network meta-analysis
Forest plot showing the effect estimates of non-pharmacological interventions on chemotherapy-induced peripheral neuropathy–related pain compared with control conditions. Effect estimates are presented as standardised mean differences (SMDs) with 95% confidence intervals (CIs).

comparator conditions, such as usual care, waitlist, sham interventions, and alternative non-pharmacological interventions. Because these comparators may differ in their degree of therapeutic activity, pooling them into a single control category may have influenced effect estimates and treatment rankings. Further stratified or sensitivity analyses, including analyses restricted to inert control conditions and analyses based on risk of bias, outcome measures, or follow-up duration, were not feasible because of the sparse network structure and the limited number of studies and direct comparisons available within each intervention category. Therefore, the impact of methodological heterogeneity on treatment rankings should be interpreted cautiously.

4.5. Clinical implications and future directions

Given the limited efficacy and potential adverse effects of the current pharmacological treatments for CIPN, our findings may help inform supportive care strategies for managing CIPN-related pain. Based on the synthesised evidence, acupuncture-based interventions have emerged as the most reliably supported non-pharmacological strategy for alleviating CIPN-related pain and should be considered a viable option in multidisciplinary oncology care. Cryotherapy and exercise-based interventions demonstrated promising potential in our rankings; however, their routine clinical recommendation specifically for pain management requires further substantiation. Future research must prioritise well-powered, rigorously designed, RCTs of these high-ranking modalities

Table 2
League table of network meta-analysis for pain outcomes (random-effects model)
League table presenting the comparative effects of non-pharmacological interventions on chemotherapy-induced peripheral neuropathy–related pain. Effect estimates are presented as standardised mean difference with 95% confidence intervals (CIs).

	Control	Acupuncture-based intervention	Electrical stimulation therapy	Exercise-based intervention	Psychological intervention	Cryotherapy
Control	—	0.66 [0.16; 1.17]	0.49 [−0.28; 1.26]	0.95 [−0.03; 1.94]	0.40 [−1.18; 1.98]	1.64 [−0.17; 3.44]
Acupuncture-based intervention	−0.66 [−1.17; −0.16]	—	−0.17 [−1.09; 0.75]	0.29 [−0.82; 1.40]	−0.26 [−1.92; 1.39]	0.97 [−0.90; 2.85]
Electrical stimulation therapy	−0.49 [−1.26; 0.28]	0.17 [−0.75; 1.09]	—	−0.46 [−1.71; 0.79]	0.09 [−1.66; 1.85]	1.14 [−0.49; 2.78]
Exercise-based intervention	−0.95 [−1.94; 0.03]	−0.29 [−1.40; 0.82]	−0.46 [−1.71; 0.79]	—	−0.55 [−2.41; 1.30]	0.68 [−1.37; 2.74]
Psychological intervention	−0.40 [−1.98; 1.18]	0.26 [−1.39; 1.92]	0.09 [−1.66; 1.85]	0.55 [−1.30; 2.41]	—	1.24 [−1.16; 3.64]
Cryotherapy	−1.64 [−3.44; 0.17]	−0.97 [−2.85; 0.90]	−1.14 [−2.78; 0.49]	−0.68 [−2.74; 1.37]	−1.24 [−3.64; 1.16]	—

Table 3
Treatment ranking based on P-scores in the network meta-analysis
Ranking of non-pharmacological interventions for chemotherapy-induced peripheral neuropathy–related pain based on P-scores.

Intervention	P-score
Cryotherapy	0.86
Exercise	0.68
Acupuncture	0.54
Electrical stimulation	0.42
Psychological	0.39
Control	0.1

P-scores range from 0 to 1, with higher values indicating a greater probability of being the most effective intervention.

to reduce structural uncertainty and narrow CIs. To overcome the clinimetric heterogeneity highlighted in this review, it is highly recommended that future trials standardise their outcome assessments by consistently measuring pain as an independent construct, even when broader neuropathy or QoL instruments are concurrently employed. Building a methodologically robust evidence base will ultimately contribute to the establishment of more targeted and effective management strategies for patients with CIPN.

5. Conclusions

This NMA, which uniquely evaluated pain as an independent construct to minimise clinimetric heterogeneity, demonstrated that acupuncture-based interventions provided the most reliable and significant reduction in CIPN-related pain among non-pharmacological therapies. To build a more robust evidence base, it is essential for future research to consistently employ validated pain-specific scales to facilitate the establishment of targeted and effective symptom management strategies for patients with CIPN.

Ethical approval

Ethical approval was not required, because this study was based exclusively on previously published data.

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None.

CRediT authorship contribution statement

Masamitsu Kobayashi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Jun Kako:** Conceptualization, Investigation, Methodology, Resources, Software, Supervision, Writing – review & editing. **Hideaki Sakuramoto:** Data curation, Formal analysis, Investigation, Resources, Software, Visualization, Writing – review & editing. **Takahiro Kakeda:** Investigation, Resources, Software, Writing – review & editing. **Yoshiyasu Ito:** Investigation, Resources, Software, Writing – review & editing. **Kohei Kajiwara:** Investigation, Resources, Software, Writing – review & editing. **Michihiro Tsubaki:** Investigation, Resources, Software, Writing – review & editing. **Makoto Yamanaka:** Investigation, Resources, Software, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejon.2026.103254.

Data availability

Data sharing is not applicable to this article, as no datasets were generated or analysed during the current study.

References

Andersen Hammond, E., Pitz, M., Steinfeld, K., Lambert, P., Shay, B., 2020. An exploratory randomized trial of physical therapy for the treatment of chemotherapy-induced peripheral neuropathy. Neurorehabil. Neural Repair 34, 235–246. https://doi.org/10.1177/1545968319899918.

Bao, T., Patil, S., Chen, C., Zhi, I.W., Li, Q.S., Piulson, L., Mao, J.J., 2020. Effect of acupuncture vs sham procedure on chemotherapy-induced peripheral neuropathy symptoms: a randomized clinical trial. JAMA Netw. Open 3, e200681. https://doi.org/10.1001/jamanetworkopen.2020.0681.

Baron, R., Binder, A., Wasner, G., 2010. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. Lancet Neurol. 9, 807–819. https://doi.org/10.1016/S1474-4422(10)70143-5.

Bhatnagar, B., Gilmore, S., Goloubeva, O., Pelser, C., Medeiros, M., Chumsri, S., Tkaczuk, K., Edelman, M., Bao, T., 2014. Chemotherapy dose reduction due to

chemotherapy induced peripheral neuropathy in breast cancer patients receiving chemotherapy in the neoadjuvant or adjuvant settings: a single-center experience. SpringerPlus 3, 366. https://doi.org/10.1186/2193-1801-3-366.
Cai, L., Lin, L., Xue, J., Sun, S., Chen, Q., Wang, Y., Li, L., Shen, Y., 2026. Efficacy of non-pharmacological interventions for chemotherapy-induced peripheral neuropathy: a systematic review and network meta-analysis for randomized controlled trials. Support. Care Cancer 34, 174. https://doi.org/10.1007/s00520-026-10316-7.
Chan, K., Lui, L., Lam, Y., 2023. Efficacy and safety of electroacupuncture for oxaliplatin-induced peripheral neuropathy in colorectal cancer patients: a single-blinded, randomized, sham-controlled trial. Acupunct. Med. 41, 268–283. https://doi.org/10.1177/09645284231166765.
Colvin, L.A., 2019. Chemotherapy-induced peripheral neuropathy (CIPN): where are we now? Pain 160 (Suppl. 1), S1–S10. https://doi.org/10.1097/j.pain.0000000000001540.
D'Alessandro, E.G., Nebuloni Nagy, D.R., de Brito, C.M.M., 2022. Acupuncture for chemotherapy-induced peripheral neuropathy: a randomized controlled pilot study. BMJ Support. Palliat. Care 12, 64–72.
Dhawan, S., Andrews, R., Kumar, L., Wadhwa, S., Shukla, G., 2020. A randomized controlled trial to assess the effectiveness of muscle strengthening and balancing exercises on chemotherapy-induced peripheral neuropathic pain and quality of life among cancer patients. Cancer Nurs. 43, 269–280. https://doi.org/10.1097/NCC.0000000000000693.
Elshinnawy, A.M., Eraky, Z.S., Abdelaziz, S.S., Abd-Elrahman, N.A.F., 2024. Effect of cold application versus transcutaneous nerve stimulation on chemotherapy induced diabetic peripheral neuropathy post mastectomy. Physiother. Res. Int. 29, e2051. https://doi.org/10.1002/pri.2051.
Eroğlu, İ., Kutlutürkan, S., 2024. The effect of hand-foot exercises on chemotherapy-induced peripheral neuropathy-related pain, falls, and quality of life in colorectal cancer: a randomized controlled trial. Eur. J. Oncol. Nurs. 71, 102641. https://doi.org/10.1016/j.ejon.2024.102641.
Greenlee, H., Crew, K.D., Capodice, J., Awad, D., Buono, D., Shi, Z., Jeffres, A., Wyse, S., Whitman, W., Trivedi, M.S., Kalinsky, K., Hershman, D.L., 2016. Randomized sham-controlled pilot trial of weekly electro-acupuncture for the prevention of taxane-induced peripheral neuropathy in women with early stage breast cancer. Breast Cancer Res. Treat. 156, 453–464. https://doi.org/10.1007/s10549-016-3759-2.
Greenlee, H., DuPont-Reyes, M.J., Balneaves, L.G., Carlson, L.E., Cohen, M., Deng, G., Hershman, D.L., Kamen, C., Keefe, D.M.K., Mao, J.J., Mumber, M., Sood, A.K., Smith, R.A., Wenner, C.A., 2017. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J. Clin. 67, 194–232.
Griffiths, C., Kwon, N., Beaumont, J.L., Paice, J.A., 2018. Cold therapy to prevent paclitaxel-induced peripheral neuropathy. Support. Care Cancer 26, 3461–3469.
Huang, C.C., Ho, T.J., Ho, H.Y., Chen, P.Y., Tu, C.-H., Huang, Y.-C., Lee, Y.-C., Sun, M.-F., Chen, Y.-H., 2021. Acupuncture relieved chemotherapy-induced peripheral neuropathy in patients with breast cancer: a pilot randomized sham-controlled trial. J. Clin. Med. 10, 3694. https://doi.org/10.3390/jcm10163694.
Hutton, B., Salanti, G., Caldwell, D. M., Chaimani, A., Schmid, C. H., Cameron, C., Ioannidis, J. P. A the PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann. Intern. Med. 162, 777–784. https://doi.org/10.7326/M14-2385 ..
Şimşek, N. Yükseltürk, Demir, A., 2021. Cold application and exercise on development of peripheral neuropathy during taxane chemotherapy in breast cancer patients: a randomized controlled trial. Asia Pac. J. Oncol. Nurs. 8, 255–266. https://doi.org/10.4103/apjon.apjon-2075.
Iravani, S., Kazemi Motlagh, A.H., Emami Razavi, S.Z., Shahi, F., Wang, J., Hou, L., Sun, W., Afshari Fard, M.R., Aghili, M., Karimi, M., Rezaeizadeh, H., Zhao, B., 2020. Effectiveness of acupuncture treatment on chemotherapy-induced peripheral neuropathy: a pilot, randomized, assessor-blinded, controlled trial. Pain Res. Manag. 2020, 2504674. https://doi.org/10.1155/2020/2504674.
Izgu, N., Metin, Z.G., Karadas, C., Ozdemir, L., Cetin, N., Demirci, U., 2019. Prevention of chemotherapy-induced peripheral neuropathy with classical massage in breast cancer patients receiving paclitaxel: an assessor-blinded randomized controlled trial. Eur. J. Oncol. Nurs. 40, 36–43. https://doi.org/10.1016/j.ejon.2019.03.002.
Jordan, B., Margulies, A., Cardoso, F., Brice, P., Buske, C., 2020. Systemic anticancer therapy-induced peripheral and central neurotoxicity: ESMO–EONS–EANO clinical practice guidelines for diagnosis, prevention, treatment and follow-up. Ann. Oncol. 31, 1306–1319. https://doi.org/10.1016/j.annonc.2020.07.014.
Joy, L., Jolien, R., Marithé, C., 2022. The use of photobiomodulation therapy for the prevention of chemotherapy-induced peripheral neuropathy: a randomized, placebo-controlled pilot trial (NEUROLASER trial). Support. Care Cancer 30, 5509–5517.
Jung, M.S., Kim, M., Sohn, E.H., Lee, J.S., 2025. The effectiveness and safety of nurse-led auricular acupressure on chemotherapy-induced peripheral neuropathy among patients with breast cancer: a randomized, double-blind, sham-controlled trial. Cancer Nurs. 48, E64–E74.
Kami, K., Tajima, F., Senba, E., 2017. Exercise-induced hypoalgesia: potential mechanisms in animal models of neuropathic pain. Anat. Sci. Int. 92, 79–90.
Kleckner, I.R., Manuweera, T., Lin, P.J., Chung, K.H., Kleckner, A.S., Gewandter, J.S., Culakova, E., Dunne, R.F., Loh, K.P., Mohile, N.A., Kesler, S.R., Mustian, K.M., 2024. Pilot trial testing the effects of exercise on chemotherapy-induced peripheral neurotoxicity (CIPN) and the interoceptive brain system. Support. Care Cancer 32, 677. https://doi.org/10.1007/s00520-024-08855-y.
Knoerl, R., Giobbie-Hurder, A., Berfield, J., 2022. Yoga for chronic chemotherapy-induced peripheral neuropathy pain: a pilot, randomized controlled trial. J. Cancer Survivors 16, 882–891.
Knoerl, R., Smith, E.M.L., Barton, D.L., Sloan, J.A., 2018. Self-guided online cognitive behavioral strategies for chemotherapy-induced peripheral neuropathy: a multicenter, pilot, randomized, wait-list controlled trial. J. Pain 19, 382–394.
Kurt, S., Can, G., 2018. Reflexology in the management of chemotherapy induced peripheral neuropathy: a pilot randomized controlled trial. Eur. J. Oncol. Nurs. 32, 12–19.
Lagerstedt, K., Efverman, A., 2023. A randomized sham-controlled mixed methods pilot study of the feasibility of acupuncture for chemotherapy-induced neuropathy: lessons learned from patient experiences in integrative cancer care. Integr. Cancer Ther. 22, 15347354231178877. https://doi.org/10.1177/15347354231178877.
Langley-Brady, D.L., Campbell, R.T., Maihle, N.J., Barnes, V.A., Bratton, A.R., Zadinsky, J.K., 2023. A pilot randomized controlled trial evaluating essential oils for chemotherapy-induced peripheral neuropathy. Pain Manag. Nurs. 24, 289–298. https://doi.org/10.1016/j.pmn.2022.12.008.
Li, L., Huang, Y., An, C., et al., 2024. Acupuncture in the treatment of chemotherapy-induced peripheral neuropathy: a meta-analysis and data mining. Front. Neurol. 15, 1442841.
Lopez, G., Eng, C., Overman, M., 2022. A randomized pilot study of oncology massage to treat chemotherapy-induced peripheral neuropathy. Sci. Rep. 12, 19023. https://doi.org/10.1038/s41598-022-23060-5.
Loprinzi, C., Le-Rademacher, J.G., Majithia, N., 2020. Scrambler therapy for chemotherapy neuropathy: a randomized phase II pilot trial. Support. Care Cancer 28, 1183–1197.
Loprinzi, C.L., Lacchetti, C., Bleeker, J., Cavaletti, G., Chauhan, C., Hertz, D.L., Kelley, M. J., Lustberg, M.B., Paice, J.A., Schneider, B.J., Smith, M.L., Smith, T.J., Ta, L.E., 2020. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American society of clinical oncology guideline update. J. Clin. Oncol. 38, 3325–3348. https://doi.org/10.1200/JCO.20.01399.
Lu, W., Giobbie-Hurder, A., Freedman, R.A., 2020. Acupuncture for chemotherapy-induced peripheral neuropathy in breast cancer survivors: a randomized controlled pilot trial. Oncologist 25, 310–318.
Ma, X., Chen, W., Yang, N.N., et al., 2022. Potential mechanisms of acupuncture for neuropathic pain based on somatosensory system. Front. Neurosci. 16, 940343.
Molassiotis, A., Suen, L.K.P., Cheng, H.L., Mok, T.S.K., Lee, S.C.Y., Wang, C.H., Lee, P., Leung, H., Chan, V., Lau, T.K.H., Yeo, W., 2019. A randomized assessor-blinded wait-list-controlled trial to assess the effectiveness of acupuncture in the management of chemotherapy-induced peripheral neuropathy. Integr. Cancer Ther. 18, 1534735419836501. https://doi.org/10.1177/1534735419836501.
Mols, F., Beijers, T., Vreugdenhil, G., van de Poll-Franse, L.V., 2014. Chemotherapy-induced peripheral neuropathy and its association with quality of life: a systematic review. Support. Care Cancer 22, 2261–2269. https://doi.org/10.1007/s00520-014-2255-7.
Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., et al., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372, n71. https://doi.org/10.1136/bmj.n71.
Prinsloo, S., Novy, D., Driver, L., Lyle, R., Ramondetta, L., Eng, C., Lopez, G., Li, Y., Cohen, L., 2018. The long-term impact of neurofeedback on symptom burden and interference in patients with chronic chemotherapy-induced neuropathy: analysis of a randomized controlled trial. J. Pain Symptom Manag. 55, 1276–1285. https://doi.org/10.1016/j.jpainsymman.2018.01.010.
Prinsloo, S., Novy, D., Driver, L., Lyle, R., Ramondetta, L., Eng, C., McQuade, J., Lopez, G., Cohen, L., 2017. Randomized controlled trial of neurofeedback on chemotherapy-induced peripheral neuropathy: a pilot study. Cancer 123, 1989–1997. https://doi.org/10.1002/cncr.30649.
Rick, O., von Hehn, U., Mikus, E., Dertinger, H., Geiger, G., 2017. Magnetic field therapy in patients with cytostatics-induced polyneuropathy: a prospective randomized placebo-controlled phase-III study. Bioelectromagnetics 38, 85–94. https://doi.org/10.1002/bem.22005.
Seretny, M., Currie, G.L., Sena, E.S., Ramnarine, S., Grant, R., MacLeod, M.R., Colvin, L. A., Fallon, M., 2014. Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. Pain 155, 2461–2470. https://doi.org/10.1016/j.pain.2014.09.020.
Sluka, K.A., Frey-Law, L., Hoeger Bement, M., 2018. Exercise-induced pain and analgesia? Underlying mechanisms and clinical translation. Pain 159, S91–S97.
Smith, T.J., Razzak, A.R., Blackford, A.L., 2020. A pilot randomized sham-controlled trial of MC5-A scrambler therapy in the treatment of chronic chemotherapy-induced peripheral neuropathy (CIPN). J. Palliat. Care 35, 53–58.
Song, S.Y., Park, J.H., Lee, J.S., Kim, J.R., Sohn, E.H., Jung, M.S., Yoo, H.-S., 2020. A randomized, placebo-controlled trial evaluating changes in peripheral neuropathy and quality of life by using low-frequency electrostimulation on breast cancer patients treated with chemotherapy. Integr. Cancer Ther. 19, 1534735420925519. https://doi.org/10.1177/1534735420925519.
Sterne, J.A.C., Savović, J., Page, M., Elbers, R.G., Blencowe, N.S., Boutron, I., Cates, C.J., Chen, H.-Y., Corbett, M.S., Eldridge, S.M., Emberson, J.R., Hernán, M.A., Hopewell, S., Hróbjartsson, A., Junqueira, D.R., Jüni, P., Kirkham, J.J., Lasserson, T., Li, T., McAleenan, A., Reeves, B.C., Shepperd, S., Shrier, I., Stewart, L.A., Tilling, K., White, I.R., Whiting, P.F., Higgins, J.P.T., 2019. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 366, l4898. https://doi.org/10.1136/bmj.l4898.
Streckmann, F., Zopf, E.M., Lehmann, H.C., et al., 2014. Exercise intervention studies in patients with peripheral neuropathy: a systematic review. Sports Med. 44, 1289–1304.
Stringer, J., Ryder, W.D., Mackereth, P.A., Misra, V., Wardley, A.M., 2022. A randomised, pragmatic clinical trial of acupuncture plus standard care versus

standard care alone for chemotherapy-induced peripheral neuropathy (ACUFOCIN). Eur. J. Oncol. Nurs. 60, 102171.
Tofthagen, C., Visovsky, C.M., Hopgood, R., 2013. Chemotherapy-induced peripheral neuropathy: an algorithm to guide nursing management. Clin. J. Oncol. Nurs. 17, 138–144. https://doi.org/10.1188/13.CJON.138-144.
Wakolbinger-Habel, R., Reinweber, M., Alakraa, M., et al., 2024. Home-based high tone therapy May alleviate chemotherapy-induced neuropathic symptoms in patients with colorectal cancer: a randomized double-blind placebo-controlled pilot evaluation. Support. Care Cancer 32, 134.
Xu, R., Yu, C., Zhang, X., et al., 2024. The efficacy of neuromodulation interventions for chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. J. Pain Res. 17, 1423–1439.
Zhang, X., Wang, A., Wang, M., Li, G., Wei, Q., 2023. Non-pharmacological therapy for chemotherapy-induced peripheral neurotoxicity: a network meta-analysis of randomized controlled trials. BMC Neurol. 23, 433. https://doi.org/10.1186/s12883-023-03485-z.