

# INPLASY PROTOCOL

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None declared.

## Is acupuncture effective and safety for chemotherapy-induced peripheral neuropathy? Evidence from an umbrella review of systematic review/meta-analysis of randomized clinical trials

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**Review question / Objective:** Acupuncture is empirically applied in CIPN. Previous evidence from evidence-based medicine demonstrated that acupuncture contributed to CIPN relief. In this study, the systematic review/meta-analysis (SR/MA) of RCT for the treatment of acupuncture in CIPN was re-evaluated to provide an evidence-based medicine basis for clinical use.

**Eligibility criteria:** Inclusion criteria: (1)Study subject: Patients diagnosed with CIPN. Nationality, race, gender, and course of illness are not limited. (2)Interventions: Patients treated with acupuncture therapy or in combination with other therapies, regardless of acupuncture materials, acupuncture techniques, stimulation methods. (3)Comparisons:Patients treated with comfort therapy or other therapies.(4)Outcome parameters No restrictions in the standard of effectiveness, and the standard of original included literatures was following. Exclusion criteria: (1)Non-English articles and grey literature; (2) duplicate literature; (3) Data is not publicly available; (4) systematic reviews of animal experiment; (5) protocol for systematic review.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 February 2023 and was last updated on 24 February 2023 (registration number INPLASY202320110).

### INTRODUCTION

**Review question / Objective:** Acupuncture is empirically applied in CIPN. Previous evidence from evidence-based medicine demonstrated that acupuncture

contributed to CIPN relief. In this study, the systematic review/meta-analysis (SR/MA) of RCT for the treatment of acupuncture in CIPN was re-evaluated to provide an evidence-based medicine basis for clinical use.

**Condition being studied:** Cancer is an ongoing threat to human health, and chemotherapy is the major therapeutic strategy. An increasing number of patients suffer from chemotherapy-induced peripheral neuropathy (CIPN), and significantly impaired quality of life. CIPN includes neuropathy comprised of autonomic, motor sensory nerve lesions as well as small fiber neuropathy. CIPN will occur in 60% at one month after the end of the treatment and 30% at 3 months. After chemotherapy, the symptoms of CIPN quickly stabilize and tends to become chronic, especially in the sensory peripheral neuropathy. As one of the most serious and common side effects of cancer chemotherapy, CIPN showed a dose-dependent response, and patients had to reduce their dosage or even stop therapy due to CIPN which hindered the implementation of the clinical treatment. So, it is highly necessary to seek effective strategies with low adverse reactions for CIPN relief.

The chemotherapy drugs are often a combination of multiple drugs, and additional medicines for CIPN increase the kidney-liver burden. An increasing number of non-pharmacological approaches, such as acupuncture, capsaicin patches, and exercise capture attention, and are available in the treatment of CIPN. Acupuncture is a component of traditional Chinese medicine (TCM) that may be traced back >2,500 years in China, the interest of Western countries in acupuncture has increased in recent decades. As an external therapeutic method, acupuncture has been used for the treatment of various kinds of neurological disorders. Acupuncture is of great concern for its economic feasibility and simplicity of operation, which are regarded as the potential approaches for the treatment of CIPN, and have been widely used in clinical practice. Several randomized controlled trials (RCTs) to date have examined the effects of acupuncture use on CIPN, and indicated its clinical efficacy for CIPN, based on which several systematic reviews/meta-analyses (SR/MA) was published. SR/MA is an evaluation method in evidence-based medicine and is

widely accepted as one of the most reliable tools in clinical analysis, whose conclusions contribute to clinical decision-making. However, there are differences in specific interventions, outcome measure as well as reporting quality and evidence level, thereby inconsistent conclusions were obtained. It is very necessary to perform a re-evaluation of available SR/MA.

## METHODS

**Participant or population:** Patients diagnosed with CIPN. Nationality, race, gender, and course of illness are not limited.

**Intervention:** Test groups: Patients treated with acupuncture therapy or in combination with other therapies, regardless of acupuncture materials, acupuncture techniques, stimulation methods.

**Comparator:** Control groups: Patients treated with comfort therapy or other therapies.

**Study designs to be included:** Systematic review/meta-analysis (SR/MA) of RCT for acupuncture in the treatment of CIPN.

**Eligibility criteria:** Inclusion criteria: (1)Study subject: Patients diagnosed with CIPN. Nationality, race, gender, and course of illness are not limited. (2)Interventions: Patients treated with acupuncture therapy or in combination with other therapies, regardless of acupuncture materials, acupuncture techniques, stimulation methods. (3)Comparisons:Patients treated with comfort therapy or other therapies. (4)Outcome parameters No restrictions in the standard of effectiveness, and the standard of original included literatures was following. Exclusion criteria: (1)Non-English articles and grey literature; (2) duplicate literature; (3) Data is not publicly available; (4) systematic reviews of animal experiment; (5) protocol for systematic review.

**Information sources:** The PubMed, Web of Science, Medline, and Embase databases were searched to collect SR/MA for acupuncture in treating CIPN. The time limit for searching is from the search beginning to February 2023. Search terms include: “acupuncture”, “chemotherapy-induced peripheral neuropathy”, “meta-analysis” and “systematic review”.

**Main outcome(s):** (1) efficacy rate; (2) functional assessment of cancer therapy/gynecologic oncology group-neurotoxicity (FACT/GOG-NTX); (3) brief pain inventory (BPI); (4) visual analogue scale (VAS); (5) numerical rating scale (NRS); (6) European organization for research and treatment of cancer quality of life questionnaire chemotherapy-induced peripheral neuropathy scale 30 (EORTC QLQ-C 30); (7) nerve conduction velocity (NCV).

**Quality assessment / Risk of bias analysis:** The methodological quality of the included studies was assessed using AMSTAR-2. The evidence of the outcome indicators was evaluated by the GRADE rating standards. Included articles were evaluated by the two independent investigators (C.L. and D.G.). The AMSTAR-2 included 16 questions, 2, 4, 7, 9, 11, 13, and 15 items are critical domains. Less than or equal to one key entry did not meet acceptable standards and their methodological quality was high. More than one key entry did not meet acceptable standards and their methodological quality was medium. one key entry did not meet acceptable standards with or without non-key item and their methodological quality was low. At least two key entries of each article did not meet acceptable standards and their methodological quality was extremely low. According to the GRADE criteria, RCT was regarded as high-level evidence. There are five factors that can reduce the quality of evidence: study limitations (risk of bias), inconsistency, indirectness, publication bias and imprecision. We started with a judgement for RCTs at high certainty and downgraded the evidence one level to moderate certainty, two levels to low

certainty, and three levels to very low certainty.

**Strategy of data synthesis:** The efficacy and safety of acupuncture in the CIPN were analyzed using standard methods of qualitative analysis.

**Subgroup analysis:** Not applicable.

**Sensitivity analysis:** Not applicable.

**Language restriction:** English.

**Country(ies) involved:** China.

**Keywords:** acupuncture; chemotherapy-induced peripheral neuropathy; umbrella review; randomised controlled trials; meta-analyses; systematic reviews.

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