Decision Letter (JCQ-2025-0014.R1)

From: [redacted]

To:

CC:

BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0014.R1

Body: 1-Jun-2025

Dear Dr Chen:

Manuscript ID JCQ-2025-0014.R1 entitled "The Efficiency of Cryo or Compression Therapy in Preventing Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Network Meta-Analysis" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard Isaacs
Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author
This manuscript presents a well-structured and methodologically rigorous systematic review and network meta-analysis (NMA) on a clinically significant topic: the prevention of chemotherapy-induced peripheral neuropathy (CIPN) through cryotherapy, compression therapy, or cryocompression. The study offers timely insights into non-pharmacologic interventions for a common and often debilitating side effect of cancer treatment. However, several key issues need to be addressed.

Major 1The GRADE assessment indicates low certainty of evidence for the primary interventions, primarily due to risk of bias and imprecision. This limitation should be highlighted more explicitly in both the abstract and conclusion to avoid overstating the strength of the findings and recommendations.
Major 2There is substantial methodological heterogeneity across the included studies regarding design, intervention protocols, and outcome definitions. Additionally, the inclusion of self-controlled trials may introduce bias. A sensitivity analysis excluding these studies is recommended to assess the robustness of the results.
Major 3While the findings suggest that the combined intervention did not significantly outperform cryotherapy or compression alone, the conclusion implies potential promise. This interpretation may overstate the available evidence. Unless supported by subgroup analyses or higher-certainty evidence, the language in the conclusion should be tempered accordingly.
Minor 1The title's use of "efficiency" is not ideal in this context. "Effectiveness" would be more appropriate. Suggested revision: “The Effectiveness of Cryotherapy, Compression Therapy, or Cryocompression in Preventing Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Network Meta-Analysis.”
Minor 2Some awkward phrasing is present. For example, “There is an effective, evidence-based strategies…” should be revised to “There is a lack of effective, evidence-based strategies…”
Minor 3The word “Forthly” should be corrected to “Fourth.”

Reviewer: 2

Comments to the Author
This manuscript addresses a clinically essential and timely question through a systematic review and network meta-analysis of physical interventions for preventing chemotherapy-induced peripheral neuropathy (CIPN). The study is generally well-executed and provides valuable insights. However, several aspects require improvement to strengthen the overall reliability and applicability of the findings.
Although the manuscript outlines the databases searched and the general search terms used, the exact search strings are not provided. Including these—ideally in a supplementary appendix- would enhance transparency and reproducibility. Additionally, while the authors note that no language restrictions were applied, it remains unclear whether non-English studies were screened or included. Clarifying this would help assess the comprehensiveness of the review.
The inclusion of self-controlled trials is acknowledged, but no sensitivity analysis was conducted to assess their potential impact on the results. Given the higher risk of bias in these designs, a secondary analysis excluding them would provide a more robust evaluation. Similarly, the term "usual care" is variably defined across studies, which may introduce heterogeneity; this should be more explicitly discussed as a limitation.
Finally, while the manuscript touches on some logistical and tolerability issues related to cryotherapy, it lacks a formal summary of adverse events or dropout rates due to discomfort. Including such information would provide a more balanced assessment of the interventions’ clinical feasibility.

Date Sent: 1-Jun-2025

Journal of Clinical Question

Author's Response to Decision Letter for (JCQ-2025-0014.R1)

The Efficiency of Cryo or Compression Therapy in Preventing Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Network Meta-Analysis

Response to Reviewers

Dear Reviewers,
We would like to sincerely thank you for your thoughtful and constructive comments on our manuscript titled "The Effectiveness of Cryotherapy, Compression Therapy, or Cryocompression in Preventing Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Network Meta-Analysis." We appreciate the opportunity to revise our work and have addressed each of the points raised in detail below.

Reviewer 1:
Major Comment 1: The GRADE assessment indicates low certainty of evidence. This limitation should be highlighted more explicitly in both the abstract and conclusion.
Response: Thank you for your suggestion. We agree with the reviewer and have revised the abstract and conclusion to explicitly acknowledge the low certainty of evidence, in order to avoid overstating the strength of our findings and recommendations. As follows "Cryotherapy, especially continuous cooling and frozen gloves, emerged as the most effective non-pharmacological intervention for preventing CIPN. Compression therapy also showed potential as an alternative, though the certainty of evidence remains low."

Major Comment 2: Substantial methodological heterogeneity. A sensitivity analysis excluding these studies is recommended.
Response: Thank you for this important suggestion. We conducted a sensitivity analysis, excluding self-controlled trials, to assess the robustness of the findings. We added contents in the result section as follows "A sensitivity analysis including all RCTs was conducted, with the network graph presented in Figure S4. Four studies compared frozen gloves with usual care. Among all interventions, frozen gloves demonstrated the greatest efficacy, with an OR of 0.22 (95% CI: 0.05–1.06), followed by surgical gloves (OR: 0.29; 95% CI: 0.02–4.42), compression gloves (OR: 0.40; 95% CI: 0.03–5.23), ice bag (OR: 0.48; 95% CI: 0.01–16.47), continuous cooling (OR: 0.50; 95% CI: 0.03–7.40), and surgical gloves with ice bags (OR: 0.78; 95% CI: 0.01–64.72). The results of the NMA are summarized in Table S1. No treatment demonstrated clearly superior efficacy over the others. The ranking of interventions is illustrated in Figure S6. Among the assessed treatments, frozen gloves had the highest SUCRA value (0.705), followed by surgical gloves (0.594), compression gloves (0.543), continuous cooling (0.496), ice bag (0.495), surgical gloves with ice (0.392), and control (0.275)."
Major Comment 3: The conclusion implies potential promise. The language should be tempered unless supported by subgroup analyses or higher-certainty evidence.
Response: We appreciate the reviewer's comment on this point. In response, we have added a statement regarding the certainty of evidence and revised the conclusion accordingly. The updated conclusion now reads:
"This NMA suggests that cryotherapy, particularly continuous cooling and frozen gloves, may be among the more effective non-pharmacological options for preventing CIPN; however, the certainty of evidence is low. Compression therapy also showed potential benefit and might be considered when cryotherapy is not feasible. Given the limitations in the current evidence base, these findings should be interpreted with caution. Further high-quality, adequately powered trials are needed to confirm these results and guide clinical implementation."We have revised the conclusion to adopt more cautious language, ensuring that any statements regarding the promise of combined interventions are now clearly qualified by the limitations in evidence quality. We refrained from speculative interpretation without subgroup analyses or high-certainty evidence.

Minor Comment 1: Replace "efficiency" with "effectiveness" in the title.
Response: Thank you for the suggestion. We have revised the title accordingly to: "The Effectiveness of Cryotherapy, Compression Therapy, or Cryocompression in Preventing Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Network Meta-Analysis."

Minor Comment 2: Awkward phrasing: "There is an effective, evidence-based strategies" should be revised.
Response: Thank you for the suggestion. We have corrected this phrasing to "There is a lack of effective, evidence-based strategies..." as suggested.

Minor Comment 3: Correct "Forthly" to "Fourth."
Response: Thank you for the suggestion. We have corrected the term "Forthly" to "Fourth" to ensure proper usage.

Reviewer 2
Comment 1: The exact search strings are not provided. Including these in a supplementary appendix would enhance transparency.
Response: Thank you for highlighting this point. We have added the full search strategies for each database as a supplementary appendix to enhance transparency and reproducibility.

Comment 2: Clarify whether non-English studies were screened or included.
Response: We appreciate the reviewer's suggestion. We have clarified in the Methods section that non-English studies were screened and included if they met the eligibility criteria. This update ensures clarity regarding the comprehensiveness of our search strategy.

Comment 3: No sensitivity analysis excluding self-controlled trials was conducted.
Response: Thank you for your valuable comment. As noted in our response to Reviewer 1, we have conducted a sensitivity analysis excluding self-controlled trials. The findings have been incorporated into the revised Results section and discussed in both the Limitations and Discussion sections.

Comment 4: "Usual care" is variably defined... this should be discussed as a limitation.
Response: We appreciate this observation. We have revised the Limitations section to explicitly address the variability in how "usual care" was defined across studies. The updated text reads: "Definitions of 'usual care' differed across studies and were often inadequately described, complicating comparisons between interventions and control groups."

Comment 5: The manuscript lacks a formal summary of adverse events or dropout rates.
Response: Thank you for this important point. We have updated the Limitations section to reflect the lack of standardized reporting of adverse events and dropout rates across studies, with the following addition: "Adverse events and dropout rates were inconsistently reported, precluding a comprehensive summary of safety and treatment adherence."

Once again, we thank the reviewers for their valuable feedback, which has helped us improve the clarity, rigor, and transparency of our work. We hope that the revised manuscript meets your expectations and remains suitable for publication.

Sincerely,
Hao Chen
On behalf of all authors

1. Response letter.pdf PDF