



COMMENT ON DUARTE ET AL.

Systematic Review and Network Meta-analysis of Neurostimulation for Painful Diabetic Neuropathy. *Diabetes Care* 2022;45:2466–2475

Behnam Sadeghirad,^{1,2,3}
Xiaoqin Wang,³ and
Jason W. Busse^{1,2,3}

Diabetes Care 2023;46:e112 | <https://doi.org/10.2337/dc22-2449>

Duarte et al. (1) reported the results of a network meta-analysis (NMA) that analyzes the effects of spinal cord stimulation (SCS) for painful diabetic neuropathy. They concluded that moderate-certainty evidence supports a large benefit in pain relief as a result of high- and low-frequency SCS compared with conventional medical management. This conclusion is misleading.

NMA can be a powerful tool to assess the comparative benefits and harms associated with interventions; however, this approach is likely to overestimate treatment effects when the indirect comparison is informed by only one trial for one of the two direct comparisons (2), which is the case in the comparisons of Duarte et al. (1). Most NMA analysts apply two rules of thumb in assessing the feasibility of performing NMA: first, availability of at least 7–10 trials for a network of treatments, and second, having more trials than number of number nodes (treatments) (3). The current review fails both criteria.

It is also concerning to see the authors indirectly acknowledging the power issue by downgrading the certainty of evidence two levels due to imprecision for all

comparisons from their pain responder analyses. However, for mean pain reduction at 6 months, which is based on the same set of data, the authors ignored the imprecision issue, which allowed them to keep the certainty of evidence as moderate. The results for pain reduction at 6 months of -5.20 (95% CI -5.77 to -4.63) and -3.13 (95% CI -4.19 to -2.08) for high- and low-intensity SCS compared with usual medical care were informed by 180 patients from one trial and 92 patients from two trials, respectively. These sample sizes do not meet the optimal information size suggested by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group (4), and both effects should have been rated as low-certainty evidence for imprecision. The associated 95% CI are misleadingly narrow because of the decision to pool using a fixed-effects model.

In addition, the authors acknowledge that the open-label design of the three small trials eligible for their review represents a source of potential bias, but they did not mention their recent review of SCS for chronic neuropathic pain that

showed no significant improvement in pain compared with a sham control (pooled mean difference -0.34 on a 10-cm visual analogue scale [95% CI -1.04 to 0.36]) (5). This finding suggests a large nonspecific effect associated with SCS.

To summarize, the questionable methodological and statistical approaches used in this review have distorted results and generated misleading conclusions.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

- Duarte RV, Nevitt S, Copley S, et al. Systematic review and network meta-analysis of neurostimulation for painful diabetic neuropathy. *Diabetes Care* 2022;45:2466–2475
- Mills EJ, Ghement I, O'Regan C, Thorlund K. Estimating the power of indirect comparisons: a simulation study. *PLoS One* 2011;6:e16237
- Thorlund K, Mills EJ. Sample size and power considerations in network meta-analysis. *Syst Rev* 2012;1:41
- Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence—imprecision. *J Clin Epidemiol* 2011;64:1283–1293
- Duarte RV, Nevitt S, McNicol E, et al. Systematic review and meta-analysis of placebo/sham controlled randomised trials of spinal cord stimulation for neuropathic pain. *Pain* 2020;161:24–35

¹Department of Anesthesia, McMaster University, Hamilton, Ontario, Canada

²Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

³Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada

Corresponding author: Xiaoqin Wang, wangx431@mcmaster.ca

All authors have contributed equally.

© 2023 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/journals/pages/license>.