RESPONSE TO COMMENT ON DUARTE ET AL.

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

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Sharan et al. (1) and Sadeghirad et al. (2) raise important points regarding the data sets used in our article (3) and whether a network meta-analysis (NMA) is appropriate. We appreciate the opportunity to respond.

We agree that it would have been preferable for our NMA to follow an intention-to-treat (ITT) approach. Although we are aware of the publicly available ITT analysis for the study of high-frequency spinal cord stimulation (SCS), ITT analysis was only available for 50% pain reduction at the 3-month follow-up. Comparable outcome data were not available for the studies of low-frequency SCS at the 3-month follow-up. Therefore, we were unable to compare the studies based on an ITT approach for any outcome. The results and conclusion are based on the available data.

No long-term data are available that are appropriate to inform comparisons in the NMA, since crossover was allowed at 6-month follow-up in the included trials.

Furthermore, Sadeghirad et al. (2) highlight the results of another subgroup analysis. The results of the primary comparison of SCS to placebo/sham showed significant improvements in pain (pooled mean difference −1.15 [95% CI −1.75 to −0.55, P = 0.001]) (4). This review, however, was conducted in a different population.

The probabilities that each treatment is the "best" (i.e., the largest effect size) (5) for each outcome are presented in Supplementary Table 1, and the footnote explains that these are calculated in the NMA. Importantly, our analysis shows that both forms of SCS provide better outcomes than conventional medical management (CMM) in a population with painful diabetic neuropathy (PDN).

The choice between fixed-effects and random-effects NMA was made a priori based on the anticipated similarity of population, trial design, outcomes, etc., for the research question. A fundamental issue for these analyses is that only a small number of trials with small sample sizes have been performed, as SCS currently is not commonly used in PDN treatment. We agree with Sadeghirad et al. (2) about power in NMA; however, it will likely be many years before 10 trials are published with the "optimal information size." Do Sadeghirad et al. suggest we wait until then to do an NMA? Until a direct head-to-head comparison is available, indirect comparison, despite its limitations, is currently the only evidence available to inform clinician choice.

We have acknowledged and downgraded all outcomes due to imprecision, and the certainty of evidence was downgraded further for 50% reduction in pain because although the outcome of 50% pain reduction is based on pain intensity score, the dichotomization into <50% and ≥50% pain reduction resulted in very small patient numbers in the CMM groups. The same does not apply to the evaluation of pain intensity as a continuous outcome.

In conclusion, we consider that the methods, interpretation, and conclusions made are justified and supported by the results presented. As we state in our article, there are limitations in the evidence base of SCS for patients with PDN, and a head-to-head trial of LF-SCS and HF-SCS would provide greater clarity on which intervention provides better outcomes for patients with PDN (3).

Duality of Interest. R.V.D. has received consultancy fees from Mainstay Medical, Medtronic, and Saluda Medical, all unrelated to this work. He is an employee of Saluda Medical. R.S.T. has received consultancy fees from Medtronic, Nevro Corp., and Saluda Medical, all unrelated to this work. He is due to serve on a Medtronic advisory board on

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SCS for PDN and is a co-investigator for the Comparison of 10 kHz SCS Combined With CMM to CMM Alone in the Treatment of Neuropathic Limb Pain (SENZA-PDN) trial. S.E. has received consultancy fees from Abbott, Boston Scientific Corp., Mainstay Medical, and Medtronic, all unrelated to this work. He has received department research funding from the National Institute of Health Research, Medtronic, and Nevro Corp. No other potential conflicts of interest relevant to this article were reported.

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