Comments on "Relative Efficacy and Safety of Pharmacotherapeutic Interventions for Diabetic Peripheral Neuropathy: A Systematic Review and Bayesian Network Meta-Analysis"

To the Editor:

We have recently read the article " Relative Efficacy and Safety of Pharmacotherapeutic Interventions for Diabetic Peripheral Neuropathy: A Systematic Review and Bayesian Network Meta-Analysis" (1) published in *Pain Physician* in January 2021. The topic is of the foremost importance because up to 10% of patients with diabetes had neuropathic pain (2).

This network metanalysis performs a comprehensive literature search including a wide array of therapeutic alternatives. First, the authors perform a classical meta-analytic pairwise comparison between the alternatives, and then, they perform a network metanalysis which allows us to compare between different drugs even if there are no direct comparisons (3). Methodologically, the network metanalysis allows to evaluate the direct comparisons like a pairwise metanalysis, and then for those drugs without a direct comparison, it allows to make indirect comparisons if there are some shared comparisons. In the case of drugs with direct comparisons and indirect comparisons, the network technique allows us to calculate a global score merging direct and indirect comparison (network result) (4). Nevertheless, in the case of medications with only one clinical trial, there is only a direct comparison, and all the others are indirect comparisons.

While we read this metanalysis, we noted that for nortriptyline there was only one trial that compare it with duloxetine and it favours duloxetine (5). Using the league table for reduction of 50% of the pain is clear that Nortriptyline has an OR less than 1 in every comparison. This means that nortriptyline is less likely to achieve a reduction of pain of at least 50%. Then, when table 3 introduces the probability ranking it is stated that nortriptyline has the first ranking. This result seems like a mistake since nortriptyline is worst than all the other comparisons. The real interpretation of the table is the ranking of medications with fewer odds of achieving 50% pain reduction. We get the impression that the error was that usually an OR less than one is desirable because that means we are avoiding a negative outcome. But, in this case, an OR of more than one is the objective because we want to have more patients with pain reduction.

In our opinion, this challenge with the results should be addressed because the information from network metanalyses is being used by clinicians all around the world to formulate the best possible treatment (6).

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