IN REPLY

In reply: Pain exposure physical therapy in complex regional pain syndrome: promising enough to warrant further investigation

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To the Editor,

We thank Dr. Staal *et al.*¹ for their interest in our review article² on complex regional pain syndrome (CRPS) and for bringing to our attention a trial that had escaped the literature search.³

We have read the three trials^{3–5} discussed by Staal *et al.*¹ and would like to present readers with a more cautious interpretation. First, in Barnhoon *et al.*'s study, an *intention-to-treat* analysis clearly showed no benefit associated with pain exposure physical therapy (PEPT) compared with conventional treatment.⁴ Staal *et al.*¹ argue that more “nuanced” (i.e., positive) findings could be derived from a *per protocol* analysis. We respectfully disagree as the scientific gold standard remains *intention-to-treat* and not *per protocol* analysis.⁶ In fact, introducing the latter confers inherent bias (rather than “nuance”), particularly as the authors might not have conducted a *per protocol* analysis had the *intention-to-treat* analysis revealed a treatment effect. For example, in Barnhoon *et al.*'s secondary analysis of the healthcare costs incurred during the first nine months of treatment,⁵ the *intention-to-treat* analysis revealed that conventional treatment was 64% more expensive than PEPT. This led the authors to

immediately conclude that cost differences favour PEPT without resorting to the “nuanced” *per protocol* analysis to confirm or disprove these findings. Second, den Hollander *et al.*² have indeed reported that, compared with conventional treatment, exposure *in vivo* resulted in decreased self-reported disability, pain intensity, pain catastrophizing, perceived harmfulness of activities, and increased health-related quality of life. However, den Hollander *et al.*³ specifically recruited subjects with documented pain-related fear, whereas Barnhoon *et al.*⁴ did not triage for such a subset of patients. Despite this important distinction, Staal *et al.*¹ draw a parallel between the two trials because they “share the theory of exposure to pain and stimulated use of the affected limb”. Such an argument is flawed—it would be akin to stating that, since root canal therapy is indicated for dental cavities complicated by abscesses, it should also be performed for all cavities.

In summary, based on our reading of the literature, we respectfully disagree with the assertion that PEPT “deserves a place in the treatment of CRPS”. We concede that the current evidence supports its role in patients with pain-related fear. However, the available trials do not (yet) support its use in other subsets of CRPS patients. Nonetheless, they highlight the need for further randomized investigation with proper *intention-to-treat* analysis.

Conflicts of interest None declared.

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