

In Reply:

As investigators who are interested in the design and implementation of clinical trials, the divulging of disclosures has become nearly universally recognized as necessary. Therefore, we initiate our response to the questions raised by Manchikanti *et al.* by disclosing the fact that we fully expected their group to raise questions with our published article.¹ During the past 5 yr, Dr. Manchikanti's group has furnished insightful commentary on nearly all of our published work, especially our clinical trials, usually citing divergent work from their own publications.

The authors are correct in stating that we did not include one of their randomized studies evaluating cervical epidural steroid injections (ESIs) as a treatment for radiculopathy in the introduction.² What distinguishes their study from the other two we cited^{3,4} is that it was designed and promoted as a comparative-effectiveness study evaluating two different treatments rather than a placebo-controlled study. Their results in this study were almost identical to the results of the plenitude of studies they have published on ESI with the same exact study design.⁵ Although this may not seem like a major point, the manner in which a study is billed and presented to patients is likely to exert an enormous effect on treatment outcomes because expectations play a major role in the placebo effect,⁶ and the placebo effect probably comprises a majority of the treatment effect for pain interventions (*i.e.*, the average placebo response is greater than the difference between the active treatment and placebo in most clinical trials).⁷ It is therefore likely that the greater and longer-lasting results in the studies performed by Manchikanti *et al.* compared with other investigators are to a large extent attributable to their study design and patient population.^{8,9}

Manchikanti *et al.* go on to state that there is minimal benefit from using physical therapy and pharmacotherapy as stand-alone therapies. The results of studies evaluating pharmacotherapy and physical therapy for radiculopathy have indeed yielded mixed results,^{10–14} just as studies evaluating ESI have demonstrated conflicting findings.^{8,9} This likely indicates a small treatment effect size. We should also point out that in this multicenter study, the results of conservative treatment and ESI as stand-alone treatments were statistically comparable and that our decision to include three treatment groups was meant to reflect the real-world decisions faced by primary care providers. Many insurance companies will not even pay for spinal injections unless attempts at pharmacotherapy and physical therapy have been exhausted.

We were surprised that Manchikanti *et al.* seem to have misinterpreted the findings of a previous meta-analysis we performed.⁵ They wrote that we previously demonstrated that epidurally injected “nonsteroid solutions may be superior to steroid solutions,” whereas the conclusions of this review clearly state that “epidural nonsteroid solutions may provide improved benefit compared to nonepidural

injections....” In fact, if one were to remove all of the studies by Manchikanti *et al.* from our analysis,⁵ because they all point in the same direction, our conclusions might have been different.

Finally, the authors criticize our decision to not use local anesthetic in our ESI group. The results of Bicket *et al.*'s⁵ and other systematic reviews suggest that it is not the local anesthetic *per se*, but rather the volume of injectate, that leads to better treatment outcomes.¹⁵ The goal of comparative-effectiveness research is to determine which treatment is more effective for patients in routine clinical practice; hence, the selection criteria should be liberal, and the design should reflect real-life circumstances.¹⁶ In a study conducted 15 yr ago evaluating common practices for ESIs, Cluff *et al.*¹⁷ found that almost half of the academic centers did not administer local anesthetic during cervical ESI, mostly as a risk-mitigation strategy. In light of the concern over complications resulting from cervical ESI, this percentage has probably increased.

In summary, although we appreciate the time they took to write this letter (as well as a few of their insightful comments), Manchikanti *et al.* appeared to have missed the point on many of their criticisms.

Competing Interests

The authors declare no competing interests.

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