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In Reply:

We would like to thank Engel *et al.* and Manchikanti *et al.* for their astute comments regarding our recent systematic review and meta-analysis[1] and will address their comments in order. Regarding the first statement by Engel *et al.* that we combined data from different approaches and regions, we acknowledge that it is true that cervical epidural steroid injections (ESIs) may be not be *exactly* the same as lumbar ESI, as is true for image-guided *versus* blind procedures, and for the various approaches to access the epidural space. By the same logic, one could also conclude that combining spinal stenosis with herniated disc, pooling subjects with psychosocial factors with those without comorbid psychopathology, not separating elderly from young patients, including both high- and low-volume injections together, and failing to separate different types of steroids are also flaws. But, if we had only included studies with homogeneous patient populations that used the same technique, the number of subjects in our meta-analysis would have been so small as to preclude any meaningful comparisons, and the generalizability would be negligible. This criticism also fails to consider that the main reason that patients fail to improve with ESI and other interventions is poor patient selection (*i.e.*, greater disease burden, previous failed treatments, coexisting psychosocial factors), which outweighs by an order of magnitude the relative proportion that can be attributed to "technical failure."[2–5] To illustrate, a recent review article that stratified randomized trials by whether or not imaging was used found that a slightly higher proportion of studies in which the ESIs were done blindly had a positive result compared with those performed with image confirmation.[6]

The comment that the study by Ghahreman *et al.*,[7] which we agree was an excellent study, was the only study to prospectively address the questioning being explored is incorrect. Two other studies,[8,9] neither of which demonstrated a difference between the different control groups, also compared epidural nonsteroid injections (ENSIs) with nonepidural procedures. As for the authors' assertion that "the results showing the efficacy of transforaminal injection of steroid is significantly greater than that of transforaminal injection of nonsteroid happen to contradict the conclusions of the review," Engel *et al.* seem to reach the same false interpretation of our findings that the various lay press did. Our purpose was neither to prove, nor did our results show, that ENSIs are equally efficacious as ESIs, but rather that at the earliest available follow-up, ENSIs are superior to nonepidural injections. The authors also fail to appreciate that if well-conducted studies with more than 200 patients cannot reliably show a difference between ESI and a control treatment,[10] then a study that allocates between 27 and 37 patients per group[7] is incapable of detecting a difference between two ostensible "control" treatments.

The authors correctly point out that there is some evidence that shows that transforaminal ESI may be more effective than other approaches. If this is the case, then one could logically deduce that transforaminal nonsteroid solutions would be also be more effective than interlaminar or caudal nonsteroid injections, which renders this point moot. This statement, which is probably true, also fails to note that the studies that compare transforaminal ESI with other epidural injections are all underpowered and seriously flawed (*e.g.*,

Table 1. Updated Effect Estimates for Positive Response to Injection

	ESI *vs.* ENSI (Direct)		ENSI *vs.* NEI (Indirect)	
Effect Estimate (comparison)	Original	Reanalysis	Original	Reanalysis
Risk ratio (95% CI)	1.04 (0.96–1.13)	1.05 (0.97–1.13)	2.15 (1.85–2.50)	2.17 (1.87–2.53)
Risk difference (95% CI)	0.04 (–0.01 to 0.10)	0.05 (0.00–0.10)	0.26 (0.14–0.38)	0.27 (0.15–0.39)
Odds ratio (95% CI)	1.28 (0.98–1.67)	1.33 (1.03–1.73)	3.06 (2.28–4.10)	3.18 (2.37–4.27)

Data are given as effect estimate with 95% CI.

ENSI = epidural nonsteroid injection; ESI = epidural steroid injection; NEI = Nonepidural injection.

suspect blinding). How else can one explain that a higher proportion of studies comparing transforaminal ESI with other epidural injections demonstrate a difference than studies comparing any ESI with any control injection?

We agree that in an ideal setting, a randomized trial using standardized selection criteria comparing ENSI with nonepidural injections might yield more robust findings than a large meta-analysis comparing indirect findings, but a quick, *post hoc* power analysis we performed found that more than 2,500 patients would be required to a detect a 5% (30 *vs.* 25% success rate) difference in categorical treatment outcomes, which means that even the high-quality study by Ghahreman *et al.*[7] was underpowered by a factor of over 50. In terms of the last comment regarding the inclusion of epidural etanercept studies, our larger study published in 2012 included a comparison not only between transforaminal epidural etanercept and transforaminal ENSI[11] but also between transforaminal ESI and ENSI. The earlier pilot study did not include a steroid group but showed that transforaminal etanercept was superior to transforaminal ENSI.[12] Hence, if the results of this small study were excluded, it would strengthen our findings.

In response to Manchikanti *et al.*, their comment that we should have performed subgroup analyses (*e.g.*, local anesthetic *vs.* sodium chloride *vs.* sodium chloride plus steroid *vs.* steroid only *vs.* local anesthetic plus steroid, and so on) was considered as part of our original intention, but as noted above, there would have been too few patients to draw any meaningful conclusions. We are grateful for their assistance in accounting for the myriad studies by Manchikanti *et al.* which were appropriate for inclusion and exclusion in this analysis; however, because the results were so similar, no significant change in outcomes was found on reanalysis (table 1). With respect to the technical quality scale, any technical quality scale would be challenging to validate clinically due to the variable response rates to ESI, but it is important to emphasize that the technical quality score was shown to have no effect on our results or conclusions. The contention that one should not penalize studies that included patients with previous back surgery—and we assert that these studies were not excluded in our analysis—is in contradiction to Manchikanti's own study,[13] which reported a success rate of only 13% in this population with conventional ESI. The veracity of the statement that encountering patients with pain less than 6 months duration is "very unusual" of course depends on one's practice, but studies have shown longer duration of pain to be associated with failed ESI treatment in multivariate analysis.[14]

Competing Interests

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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