**Subject:** BMJ - Decision on Manuscript ID BMJ.2014.023605.R1

**Body:** 15-Feb-2015

Dear Prof. Cohen,

Manuscript ID BMJ.2014.023605.R1 entitled "A Multi-Center, Randomized, Double-Blind, Comparative-Efficacy Study Comparing Epidural Steroid Injections to Gabapentin for Sciatica"

Thank you for sending us this revised paper, which we were pleased to have the chance to consider. As before, we recognise its potential importance and relevance to general medical readers, but I am afraid that there are still many outstanding points that need to be resolved.

It is concerning that so many differences remain after a round of revisions. If we cannot come closer to consensus with the next round of revisions, it may be better to part ways, unfortunately. We want authors to be happy with the way their paper is reported, but we also have to be confident in the reporting of the trial. In our experience, extensive rounds of revision delay the work and often lead either to us publishing a paper we aren't comfortable with, or authors feeling unsatisfied with the reporting of their work. I hope the points described below can be addressed entirely with the next revision.

We look forward to seeing your revised article within one month and, we hope, to reaching a decision.

Yours sincerely,

Rebecca Burch, MD
Associate Editor, The BMJ
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Please respond to the following points:

*Many of our statistician's comments have not been addressed fully. Most importantly, we require trial reporting to adhere exactly to the trial registration, not the protocol. If there are discrepancies between the registration and the protocol, we ask that authors adhere to the trial registration. The primary outcomes described in the trial registration should be presented first. If amendments were made to the trial registration or trial protocol, it should be made very clear in the methods what changes were made, the specific reasons why these changes were made, and when they were made. Any analyses made as a result of amendments to the trial registration or protocol can be presented in the paper, but it should be clear that these are secondary analyses. If any changes possibly affected the outcome of the study, this should also be made clear.

*On the question of terminology regarding back and/or leg pain, thank you for the extensive discussion in your response. It's an interesting and helpful description of how current thinking around causes of back and leg pain may be in evolution. In reporting results of a trial, however, the terminology used in the paper should reflect the intention at the beginning of the study. In looking through the study protocols and trial registration I note that the term used in the study objectives and procedures was "lumbosacral radiculopathy". I also note that the inclusion criteria in the protocol include the term "lumbosacral radicular pain". Unless there were changes to either the study objectives or the inclusion criteria during the study, it seems most reasonable to reflect the terminology used when the study was conceived. Thus where the term "sciatica" is used, "lumbosacral radiculopathy" should be used instead. I do agree that in some cases, the specialty agrees on a clear change of terminology between the time when the study starts and when it is reported, but that doesn't seem to be the case here.

It might also be helpful to include a sentence or two describing why both back and leg pain are recorded, similar to what you described here: "There may be cases of 'axial-only' back pain that are neuropathic in nature, and of course not all leg pain is neuropathic…Because patients cannot accurately distinguish between mechanical and

neuropathic pain scores, leg (indicative of neuropathic pain) and back pain scores are always used instead."

*Inclusion and exclusion criteria: How was radicular leg pain specifically defined? Please specify a comprehensive list of signs and symptoms that allowed inclusion into the trial. Please specify a list of medical or psychiatric conditions considered part of the exclusion criteria. The methods should be described in enough detail that an independent researcher would be able replicate the study based on what's written. The inclusion and exclusion criteria are detailed quite well in the study protocol submitted to Walter Reed, so just including all of the information there might be helpful. (I note further down in the response that this was "left up to the provider". Is it possible that different providers would have included or excluded a different set of patients, and can the authors comment on whether this introduces heterogeneity?)

The wording around the imaging criteria is still not clear. Would something like "All included patients were required to have MRI findings of herniated disc or spinal stenosis" be acceptable?

*The question of patients being included for symptoms of neurogenic claudication vs lumbosacral radiculopathy is still somewhat unclear. This was something of a sticking point for both editors and reviewers. In both of the study protocols, the only inclusion criteria were for lumbosacral radicular pain. How were patients with neurogenic claudication entered into the study if they did not meet the inclusion criteria in the study protocols? It might be that this is a deviation from the study protocol, in which case this should be explained clearly in the methods. The subgroup analysis showing that the inclusion of these patients did not significantly affect the results is reassuring, but unexplained deviation from study protocol is concerning.

* The subgroup analyses performed should be specified in the methods section.

*The rationale for the target outcome of 1 point difference was not included in the study itself. Since both editors and reviewers raised this as an important question, the choice of endpoint should be very clearly supported in the text of the paper.

*It might be appropriate to include something like your sentence about wanting to focus on comparative efficacy research in the limitations section. "The reason we did this was that we felt that there were over 50 placebo-controlled trials comparing ESI or gabapentin to placebo for sciatica, and that (per HHS recommendations) there was a strong need for "comparative-effectiveness" research."

*It would be helpful to specifically answer reviewer 2's question about single level ESI in the text of the paper.

*The paper should reflect the fact that 17 year olds were allowed to join the study, as per the response here, they would have been included had any been eligible.

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As well as submitting your revised manuscript, we also require a copy of the manuscript with changes highlighted. Please upload this as a supplemental file with file designation 'Revised Manuscript Marked copy'.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

**Date Sent:** 15-Feb-2015