Author’s response to reviews

Title: Osteopathic Manipulative Treatment for Low Back Pain: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Biomed Central

Dear Editorial Team:

We have completed the revisions to our manuscript (MS: 6646212565097155) entitled, “Osteopathic Manipulative Treatment for Low Back Pain: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.” The point-by-point responses to each of the reviewer comments are summarized below.

Reviewer: Dan Cherkin

Major Compulsory Revisions

1. Justify why it is believed that OMT is somehow different than other forms of spinal manipulation.

We believe that OMT is different than other forms of spinal manipulation for several reasons.

In the United States, OMT is delivered by fully licensed physicians who use it as a complementary treatment for low back pain, unlike other practitioners of spinal manipulation who use it as an alternative treatment for low back pain. The challenge to osteopathic physicians in the United States, as exemplified by Howell (Ref #14), has been to demonstrate how osteopathic practice is unique in comparison to allopathic practice. Studies such as ours are in response to this challenge. This information has been added to the background section of the revised manuscript on page 5.

Chiropractic trials have focused almost exclusively on high-velocity-low-amplitude techniques. This observation has been published in both the chiropractic (Nelson, Ref #12) and osteopathic literature (Mein, Ref #10). This information has been added to the background section of the revised manuscript on page 4. In contrast, osteopathic physicians use many manipulation techniques (Lesho, Ref #9), and this has been reflected in major trials of OMT (eg, Andersson, Ref #44 and Licciardone,
A major chiropractic trial of spinal manipulation for childhood asthma used a high-velocity-low-amplitude thrust as the primary treatment technique (Balon, Ref #11). In the control group, it used a sham manipulation technique that has been noted to closely resemble OMT (Mein, Ref #10 and Nelson, Ref #12). If chiropractic and osteopathic manipulation are similar, it is inconsistent that an osteopathic technique would be used as a sham control treatment in a chiropractic trial. This information has been added to the background section of the revised manuscript on page 4.

A recent major review of spinal manipulation cautioned against generalizing the findings of systematic reviews because differences in professional background and training lend themselves to diverse manipulation approaches (Bronfort, Ref #13). This information has been added to the background section of the revised manuscript on page 4.

2. Justify that the OMT trials are of adequate methodological quality to warrant inclusion in a meta-analysis.

The methodological quality of four of the six OMT trials was confirmed in a recent independent systematic review (Bronfort, Ref #13). Of the two remaining OMT trials, the Licciardone trial was not reviewed because it was published after the review's closing date. The Licciardone trial was subsequently identified as a rigorous and evidence-based trial in two subsequent publications (Ernst, Ref #48 and Margo, Ref #49). The Cleary trial was not reviewed because of small sample size. This information has been added to the methods section of the revised manuscript on page 7. The potential limitations of the Cleary trial were noted in the original manuscript and were addressed in sensitivity analyses, whereby the meta-analyses were repeated after excluding the Cleary trial.

3. Justify the use of meta-analysis of trials that are clearly very different in many ways. The fact that a statistical test didn’t provide evidence that these 6 trials were not heterogeneous does not prove that they are homogeneous. A quick look at their differences suggests they are very different.

We agree that there are some differences in the methodological aspects of the six OMT trials. Nevertheless, the “apples and oranges” criticism can be applied to virtually all meta-analyses. The trials included in our meta-analysis are potentially less heterogeneous than trials included in previous meta-analyses simply because they are all OMT trials rather than trials of various types of spinal manipulation.
We believe that potential heterogeneities among trials have been adequately handled by the stratified analyses and sensitivity analyses. These include analyses stratified according to country (United Kingdom vs United States), control group (active or placebo control vs no treatment control), and duration of follow-up (less than one month, one to less than three months, and three months or greater).

This approach is similar to that used a recent meta-analysis performed in collaboration with the Cochrane Back Review Group (Assendelft, Ref #31), in which forest plots were presented in a stratified fashion according to chronicity of low back pain (acute vs chronic), control group (five different control group interventions), and duration of follow-up (short-term vs long-term). This information has been added to the discussion section of the revised manuscript on page 15. It should also be noted that in their meta-analysis (Assendelft, Ref #31) there was considerable heterogeneity of trials, as manifested by five different types of control groups (vs two different types of control groups in our meta-analysis) and other heterogeneous trial characteristics as presented in their Appendix Table 1.

4. Provide an indication of the clinical significance of any observed effects of OMT.

The clinical significance of our observed findings is best portrayed in contrast to other common treatments modalities for low back pain. The best, recent comparison is a meta-analysis of nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors, for osteoarthritic knee pain (Bjordal, Ref #54). In this meta-analysis, based on more than 10,000 subjects, overall effect sizes of –0.23 and –0.32 were observed, depending on methodological assumptions. In either case, these observed pain reductions were comparable to the pain reduction attributed to OMT in our meta-analysis. The only available meta-analysis of nonsteroidal anti-inflammatory drugs specifically for low back reported relative risks for improvement, and concluded that these drugs are effective for short-term symptomatic relief during the acute stage of the condition (van Tulder, Ref #55). This information and the implications for use of OMT have been added to the discussion section of the revised manuscript on pages 13-14.

Reviewer: Dave Baxter

Major Compulsory Revisions

1. The case for the current review needs to be more clearly articulated, and the relevance of its findings more fully discussed. What is ‘distinctive’ about osteopathic manipulation (apart from the clinical or practice context as outlined in the review), and how is this different from that performed by chiropractors, physical therapists, etc? This is particularly pertinent in the light of the recent
publication of the UK BEAM trial (in BMJ) which suggested no difference between manipulation performed by these three groups. Several of these questions have already been addressed, as indicated above in response to Cherkin, Items 1 and 4.

With respect to the UK BEAM trial, it has been noted that the professional associations representing osteopaths, chiropractors, and physiotherapists in the United Kingdom developed a spinal manipulation package consisting of three common manual techniques (Harvey, Ref #6). However, there are no data reported in the UK BEAM trial to indicate that profession-specific outcomes using these common techniques are comparable (UK BEAM Trial Team, Refs #7,8). This information has been added to the background section of the revised manuscript on page 4. It does not appear that profession-specific outcomes will be forthcoming from the UK BEAM Trial Team, as Harvey (Ref #6, page 46 [summary]) states, "...the trial design specifically precluded comparison of the effect between the professions..."

Moreover, we are unaware of comparable agreements between the professional associations representing osteopathic physicians and those representing chiropractors or physical therapists in the United States. This may reflect that osteopathic physicians are fully licensed physicians in the United States, unlike chiropractors or physical therapists.

As noted above, OMT extends beyond the three common techniques used in this UK BEAM trial package (Lesho, Ref #9) and a recent review has cautioned against generalizing spinal manipulation results because of differences in professional background and training (Bronfort, Ref #13). In fact, the American Academy of Osteopathy's Outpatient Osteopathic SOAP Note Form has check boxes for 14 OMT methods, including the three in the UK BEAM trial package and 11 others.

2. The outcome measure used for the current review was pain. Particularly in the primary care setting (the focus of the current review), this would appear less important than some of the other outcomes recommended by Bombardier. What were reported findings for alternative outcome measures in the six studies reviewed and were these as consistently positive?

Because the alternative outcome measures were not consistently reported in the OMT trials, it was not feasible to perform meta-analysis on these outcomes. This information has been added to the discussion section of the revised manuscript on pages 16-17.

3. What defined osteopathic manipulation: e.g. manipulation reported as performed by an osteopath? Was any detailed consideration given to the relevance or appropriateness of the OMT performed in trials? This is relevant for several
reasons, not least including potential bias in inclusion/exclusion and potential under-reporting of negative trials.

Osteopathic manipulation was considered to consist of manipulation performed by osteopaths, osteopathic physicians, or osteopathic trainees. This information has been added to the methods section of the revised manuscript on page 6. Based on the reported inclusion/exclusion criteria, OMT was considered to be an appropriate treatment in each of the OMT trials.

We performed a post-hoc analysis to address the issue of potential under-reporting of negative OMT trials. File drawer analysis was used to compute the fail-safe N (Wolf, Ref #60). For this analysis, it was assumed that an effect size ≥ -0.10 would represent insignificant clinical benefit. Actually, an effect size of -0.10 may exceed 40% of the pain reduction attributed to nonsteroidal anti-inflammatory drugs (Bjordal, Ref #54). Thus, it should be noted that this is a conservative (i.e., low) estimate of the fail-safe-N not only on clinical grounds, but also from a statistical perspective because the null hypothesis suggests that an effect size of 0.00 would indicate no benefit.

This analysis demonstrated that 16 unpublished trials, with effect size averaging ≥ -0.10, would be needed to obviate the significance of our findings. Based on historical funding of complementary and alternative medicine research, this appears very unlikely. This information has been added to the discussion section of the revised manuscript on page 16.

Minor Essential Revisions

4. Some comment on where most of articles were sourced would be useful (i.e. Medline?).

Five of the six OMT trials were identified through MEDLINE. The Cleary trial was identified only in the Cochrane Central Register of Controlled Trials. This information has been added to the methods section of the revised manuscript on page 6.

Discretionary Revisions

5. The differences between osteopathic training and practice in the UK and the USA are worthy of some discussion. E.g. if there is no difference between findings (effectiveness) in the two countries, does this not suggest that osteopaths need not be trained as physicians to successfully treat low back pain with OMT?

As this is a discretionary revision, we have elected not to address it in the current manuscript. We believe this is a complex question that is beyond the scope of our
study’s purpose, and that cannot be adequately discussed within the context of this manuscript. We shall consider this question for future research.

We thank the reviewers for their comments. We believe that the revisions described above are responsive to these comments and have enhanced the quality of our manuscript.

Sincerely,

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On behalf of all the authors