Reviewer’s report

Title: The effect of Spinal Manipulative Therapy on Heart Rate Variability and pain in patients with chronic neck pain: A Randomized Controlled trial

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Reviewer: Richard Hooper

Reviewer's report:

The manuscript presents a protocol for a trial of spinal manipulative therapy (SMT) plus stretching compared with stretching alone for patients with recurrent and persistent neck pain.

More detail/clarity is needed in some places:

1. The primary outcome measure is not clearly defined. The website cited on page 5 is presented in lay language and does not go into detail on measures of heart rate variability, and the reference cited with the sample size justification (Hallman et al) presents a number of different measures - all leading to different required sample sizes (the proposed sample size of 60 makes me think you are planning to use the log of root mean squared successive differences in RR intervals, as measured by the firstbeat device).

2. Randomisation is presumably stratified by clinic, since a separate sequence of opaque envelopes is presumably distributed to each clinic - this needs to be stated.

3. Some variation in the intervention delivered to different participants is allowed by the protocol. This is fine for a pragmatic trial, but I still find the detail of the intervention a little sparse ("a variety of techniques … which will be decided on and described by the participating clinicians"), and this would make replication of the trial difficult. Is any heterogeneity in the effect of the intervention anticipated between clinics (since clinicians at different clinics may use different approaches), and will this be addressed in the analysis?

4. The assessment of conditioned pain modification (CPM) is unclear. "CPM consists of the evaluation of a painful test stimulus followed by a second evaluation either at the same time as a distant, painful conditioning stimulus or in series after the painful conditioning stimulus has been withdrawn": which of these methods will be used, and how will pain be evaluated?

5. There is no description of how the secondary aim of the trial (to investigate whether CPM is a predictor of treatment outcome) will be addressed. I would expect this be analysed by looking at the statistical interaction between CPM and SMT. It is not sufficient just to say that "possible interaction effects on the outcomes will be checked for". (The precise research questions addressed by the multiple regression analyses and path analyses are unclear.)
6. The discussion explains that a pilot study will be conducted prior to commencing the full-scale study. Presumably this has already happened - please make this clear: if there were any changes made as a result of this pilot work these should now be part of the protocol.

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