Reviewer's report

**Title:** Effect of TENS on pain in relation to central sensitization in patients with osteoarthritis of the knee: protocol of a randomized controlled clinical trial

**Version:** 1  **Date:** 24 September 2011

**Reviewer:** Charlie Goldsmith

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The following comments are offered in an attempt to improve this protocol.

1. P(age) 2, p(aragraph) 4, l(ine) 39. Suggest including a [,] after [i.e.].
2. P 2, p 5, l 1. Also include the date of trial registration and include the date the first patient was randomized if that has already happened. If the trial is completed, state the date the last patient was randomized.
4. P 2, p 6, l 47. Should this not be [OAk] rather than [OA]? Also l 48 on the same P.
5. P 3, p 1, l 60. Should [osteoarthritis] not be [OA] since it is already defined?
6. P 3, p 2, l 72 and 82. Should [WDR] on l 82 not be [WRD] as defined on l 72 as well as P 11, l 307?
7. P 3, p 2, l 77. [TS] is defined here but left out of the list on P 11.
8. P 4, p 1, l 87. Suggest adding [s] at the end of [appear] to read [appears].
9. P 4, p 3, l 94. Suggest adding a [,] after [i.e.]. Also P 10, p 3, l 274.
10. P 4, p 4, l 107 to 11. Given that this variable is not yet standardized, should not a study of the measurement tool be conducted before doing a trial? As a primary outcome measure this tool should have stated reliability, validity and responsiveness in the hands of the people who are being used to measure outcomes of patients in this trial.
11. P 5, p 4. What about patients who have had recent uses of hyaluronic acid products such as Synvisc or Durolane?
12. P 6, p 1, l 148. How many and what are the age strata?
13. P 6, p 2, l 156, 159, 160, 162, 163 should all use [.] rather than [,] to represent the decimal place.
14. P 6, p 2, l 163. To properly inflate the size of 42 by a loss of 15%, you should divide by 0.85 to get 49.4 and round up to 50 per group. In addition you have not accommodated the loss of degrees of freedom for the two stratification variables of age and sex. For sex you should increase the total sample size by 1 and the increase for age will depend on the number of strata that you plan to use. See 12 above. Consider adding the two groups sample sizes and state the total sample size to be recruited.
15. P 6, p 4, l 174. Suggest dropping [OA] since osteoarthritis is already part of
the [WOMAC] name. Also P 8, p 4, l 229.

16. P 7, p 1, l 177. Delete [in order] in front of [to] as the words are redundant in
English. Also P 7, p 3, l 190. Also P 7, p 4, l 199. Also P 10, p 5, l 280.

17. P 7, p 1, l 177 to 179. What is the experience of the investigators in using the
sensitization instrument? Provide data if you can.

18. P 7, p 2, l 186. Suggest replacing [average] by [mean].

19. P 7, p 3, l 195. Do you have a reference for this choice?

20. P 7, p 4, l 201. Insert a space to read [30 s].

21. P 8, p 1, l 207. Suggest replacing [parameters] by [settings]. Also P 8, p 2, l
213, 215, l 217.

22. P 8, p 3, l 22. Replace [parameter] by [variable]. A parameter is a
characteristic of a distribution of a variable in a population; not another name for
a variable in a sample. Also P 9, p 2, l 235.

23. P 8, p 1, l 208. Insert a space to read [100 Hz]. Also P 8, p 2, l 213.

24. P 8, p 3, l 225. Replace [score] by [scale]. Also provide a reference to this
method. Also P 11, p 2, l 300.

25. P 8, p 4, l 227. Replace [parameters] by [variables]. Also replace the [u] by [o]
to read [Secondary].


27. P 9, p 6, l 249 and 250. The sample size is too small for the KS test of
normality. Consider trying one of the other ones that work with small sample
sizes such Shapiro-Wilk and indeed it is important to test residuals from models,
not basic data from groups. So this sentence should be modified.

28. P 9, p 6, l 250. It is not necessary to test baseline values. It is more important
to measure the randomization integrity. Any differences in baseline variables
should be due to chance. See Dore and Altman where this is discussed in detail.

29. P 9, p 6, l 251. You should consider replacing the Student’s t test by ANOVA
since you should be taking the stratification factors into account in your analysis.
Also for the logistic regression in l 257.

30. P 9, p 7, l 254. Suggest inserting a space to read [6 w].

31. P 9, p 7, l 256. Rewrite as [0.05].

32. P 9, p 7, l 257 and 258. Suggest inserting [:] after [state] and replacing
[dependent] by [independent].

33. P 10, p 4, l 279. Why did you mention cost effectiveness? You have not
proposed measuring any costs so how can this be done? Consider dropping this.

34. P 11, p 1, l 292. Since no subgroups are identified as yet, consider dropping
this from your protocol. Subgroups should be defined in advance ideally with a
literature reference as to why it should be considered, have power to be
statistically significant in one subgroup and not the others, and have the ability to
detect an interaction between the subgroups and the treatment factor.
35. P 11, p 2, l 307. WRD is defined differently here than on P 3, l 72.

A random sample of R(eference)s was checked for citation accuracy. Also, this reviewer likes to see issue numbers added as they help to find the article when a reader wants to read the R.
36. P 12, R 4, l 1. Delete [(Oxford)].
37. P 12, R 7 appears correct.
38. P 12, R 9, l 1. Delete [(80-)] and on l 2, insert [(694)] after [150].
39. P 12, R 10, l 2. There should be a location and city for this type of R.
40. P 12, R 12, l 1. Replace [p] by [Panel] as the author; and on l2, insert [(10)] after [81].
41. P 12, R 14. There is now a 5th edition of this classic book, and is also available online. It appears to also be Chapter 1. Should these issues be considered for a reader?
42. P 13, R 20, l 4. insert [(10)] after [59].
43. P 13, R 22, l 2. Insert [(1-2)] after [129].
44. P 13, R 23, l 3. Insert [(1-2)] after [109].
45. P 13, R 26, l 3. Insert [(2)] after [15].
46. P 13, R 28 appears to be correct.
47. P 13, R 30, l 2. Insert [(4)] after [24].
48. P 14, R 38, l 2. While [tens] is lower case in the database used for checking, you have used [TENS] in its conventional form in the rest of the text. What does the actual paper do? Also insert [(2)] after [35].

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.