Reviewer's report

Title: Effects of light-emitting diodes on muscle fatigue and exercise tolerance in patients with COPD: a randomized clinical trial

Version: 3 Date: 17 December 2012

Reviewer: Charlie Goldsmith

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This protocol needs to answer the following issues and possibly revised before it can be published.
The pages were numbered from 1 to 23.
1. P(age) 5, p(agraph) 2, l(ine) 1. The sample size if 30 here while it is 35 on P 2, l 5 as well as P 10, p 4, l 3. Make them all agree.
2. P 5, p 2, l 1 and 2. Rewrite as [… FEV1 # 70% predicted)…].
4. P 5, p 3, l 2. Insert the date that the trial was registered.
5. P 5, p 4. Multiple outcome measures are listed and just one can be the primary. Which one is the primary? Each outcome measure should have its scale stated, the MCID for it and some idea how long it takes to administer each measure as well as all of them. The sample size justification on P 10 does not state which outcome measure this is computed to handle. If multiple outcome measures are to be analysed, and tested, how will the conclusion be handled if there is conflict in the statistical significance of the multiplicity of measures?
6. P 5, p 4, l 3. Replace [parameters] by [variables]. A parameter is a characteristic of a distribution of a variable in a population of patients and not another name for a variable in a sample. Also P 8, p 3, l 2.
7. P 6, p 2, l 10. What happens of the variability is > 5%?
8. P 7, p 3. There are too few R(eference)s to the methods used here. Each one should have a R.
9. P 7, p 3, l 11. Who has validated the program? Is it published anywhere?
10. P 8, p 1, l 18. Was this modified as well? Should R 23 be cited here?
11. P 9, p 1, l 6, 7, 8. Insert the company and city where these can be obtained.
13. P 10, p 2, l 2. Rewrite as [1 h].
14. P 10, p 3. The details of the randomization are not adequate. See CL Meinert's clinical trials book on P 86 for how to do it. Stratification is mentioned in Figure 1. What is the stratification factor and how many levels does it have? This does not appear to have been considered in the sample size calculation below and is not mentioned in the statistical analysis section.
15. P 10, p 5, l 1. Rewrite as [Assuming a Type 1 error rate of 0.05 and a Type 2 error rate of 0.2 ...]. What is the justification for these choices? Also why is the MCID chosen as 55 sec and the sd of 79? Was the R 31 study done the same as you plan to do? Do you have any local pilot data to back these up? Was any software used to calculate this sample size? Document it. Does this apply to the other outcomes besides DET of the many listed on P 5? How has stratification been considered? Is this to be a one or two tailed test? What will you do if there are missing data? What about sample size for P 11, p 1 on endurance time?


17. P 11, p 1, l 5. Rewrite as [… paired Student’s t-test.]

18. P 11, p 2, l 5. Rewrite as [… for normal distributions and Spearman’s correlation will be used for non-normal distributions.]

19. P 11, p 2, l 6 and 7. Rewrite as [The level of significance will be set at 0.05.] P values are compared to the level and if they are < than the level they are declared to be statistically significant. What do you plan to do about multiplicity from the multiple outcomes? What do you plan to do about missing data if there are any? What software do you plan to use for data management and the statistical analyses?

20. p 13, p 1, l 5 to 7. Where are the Rs to justify this statement.

21. P 14. [SIC] is missing from the list of short forms. See P 22, Figure 2.

22. P 14, last p. Given the number of statistical issues that were not used correctly in this protocol, you might consider adding a statistical consultant to your list of authors.

A random sample of 10 Rs was checked for citation accuracy. Also this reviewer likes to see issue number as you used in the Rs as they make finding the Rs much easier in many databases.

23. P 15, R 4 appears to be correct.

24. P 16, R 11, 12 and 18 appear to be correct.

25. P 16, R 10, l 2. The author is [De Necochea-Champion R].

26. P 17, R 20 and 212. Both of these were not verifiable and should be translated into English with the translation in [square brackets]. At the end of the citation enclose the (language) in round brackets.

27. P 17, R 23 appears to be correct.

28. P 17, R 26, l 3. Insert [(4-5)] after [87].

29. P 18, R 30, l 3. Delete [S] to read [LED].


31. P 20, R 44 and 47 appear to be correct.

32. P 20, last l. Replace [Parameters] by [Settings]. Also P 23 l 1.

33. Figure 2. Why is there a double randomization? Where does stratification take place?