Reviewer's report

Title: Impact of oral melatonin on adult critically ill patients with ICU sleep deprivation: a study protocol and statistical analysis plan for a randomized controlled trial

Version: 2

Date: 1 July 2014

Reviewer: Erik Cobo

Reviewer's report:

I read the protocol trial paper from Hua-Wei Huang et al. about Melatonina for improving sleep quality in critically ill patients, and I think that it deserves publication in Trials.

However, in relation to the 4 questions Trials Journal address to me (1. Will the study design adequately test the hypothesis? 2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? 3. Is the planned statistical analysis appropriate? 4. Is the writing acceptable?), I would like to make some suggestions to the authors in order to clarify some points.

- Major Compulsory Revisions

To allow replication, the main analysis and the main variable should be clearly and fully specified. Based on previous experience you should already know if your main variable can be (approximately) represented by the Normal distribution. Please, consider improving your power by adjusting for baselines in the final analysis (see, for example, chapter 7 in “Statistical Issues in Drug Development”, by Stephen Senn, Ed Wiley).

In sample size, you correctly specify power and a two-sided alpha of 5%. But, instead of specifying the software, you should provide details about the statistical method and the expected difference (“delta”) under the alternative hypothesis (see Consort for examples). [Please, note that you open some further ambiguity because: (1) you employ median instead of mean to justify the expected effect; and (2) you specify 2 metrics, 5 hours and 59% percentage.]

In the first lines of page 13, you specify “they are regarded as the protocol violation and should drop out”. As you later specify that your main analysis will be by ITT, please note that you will need to have an outcome determination for those patients, and so they have to finish the follow up. See, for example, http://www.nap.edu/catalog.php?record_id=12955 or http://www.nejm.org/doi/full/10.1056/NEJMsr1203730

- Minor essential Revisions

Following Spirit 2013, please consider specifying your dissemination policy (item 31).

Please, consider specifying that your final report will be written in accordance
with the Consort statement.
- Discretionary revisions

Please, consider a statement like “a fully specified Statistical Analysis Plan will be provided prior to unmasking”. It should clarify all the details, such as, for example, the outcome imputation method for missing values (such as patients staying less than the full follow-up period).

My best wishes for the next phases of your meritorious work.
Erik Cobo

**Level of interest:** An article whose findings are important to those with closely related research interests

**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