Reviewer’s report

Title: Study protocol for a randomised controlled trial of nortriptyline in knee osteoarthritis (NortIKA Study)

Version: 1 Date: 25 August 2015

Reviewer: Kelli Allen

Reviewer’s report:

This manuscript describes the protocol to examine the effectiveness of nortriptyline for knee OA. The manuscript is generally well written, and in most places the detail is sufficient. I have the following recommendations to strengthen the paper:

Major compulsory revisions

Abstract
- In general, the abstract would be strengthened by a bit more detail, such as the specific primary outcome, duration of treatment, etc.

Background
- Please rephrase the statement that education and weight loss are “ineffective,” as this does not accurately reflect the evidence base or treatment guidelines. It is certainly true that many patients require pharmacotherapies as well as these interventions, to adequately manage pain. But that is different than stating that the behavioral approaches are ineffective.

Methods
- Please describe what is meant by the fact that duloxetine “is not funded,” as this concept may not be apparent to readers outside of NZ.

Methods
- Hypothesis 3 is not really stated as a testable hypothesis. Consider whether this could instead be described as a study aim, or phrase in terms of a testable hypothesis.
  - It would be helpful to include a bit more rationale for the study inclusion criteria. In particular, why were the ACR clinical criteria used instead of those including radiographs, and what are the potential limitations of this in terms of specificity of diagnosis? Also, describe what a WOMAC score => 20 means in terms of pain severity / level.

Minor essential revisions

Abstract
- Change “propose” as this seems like language associated with an application vs a protocol description

Methods
- In the dose adjustment section, please define what is meant by participants’ “response to the study drug” more specifically.
- There is overlap between the “final assessment” section and the prior sections on study outcomes. Please consolidate where possible.

Discretionary revisions
- Table 1 could be omitted as it is not central to the paper and is largely described in the text.
- Consider rephrasing the title of the section, “mechanisms of pain in OA” to something more specific, as this section focuses almost entirely on central processing (which is appropriate given topic of the study).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests