Reviewer’s report

Title: The CASCADE trial: Effectiveness of ceramic versus PEEK cages for anterior cervical discectomy with interbody fusion; protocol of a blinded randomized controlled trial

Version: 1 Date: 25 April 2013

Reviewer: Carl J Lombard

Reviewer’s report:

This is an interesting and relevant study using the optimal design to establish equivalence/ non-inferiority of a new device.
I have the following specific comments starting at the beginning of the protocol.

First comment - no page numbers!

1. Methods. under this section it is stated that the blinding will be maintained for the full period of follow-up (24 months). Under the randomisation section it is stated that blinding will be maintained until 1 year. This does not make sense.

2. Was a fixed block size used for randomisation blocks? Were the envelopes numbered?

3. Surgical intervention. No information is given regarding the surgeons performing the procedures. What level of experience is required? is it a single surgeon per operation? Are there more than one surgeon?. How is this factor controlled for?

4. Main outcome: NDI. At what time point will the primary outcome be used for comparison - 24 months?. Is 24 months is moderate follow-up time for assessing the success of this procedure? il the NDI self administered?

5. Who sees the participant at each of the visits? il it the same person? What happens when a participant misses a visit?

6. What happens to the data?

7. What about safety of the patients? How is adverse events recorded and complications handled? Does the participants have insurance and who carries the risk of special investigations and long term care?

8. How is informed consent done ( not when and where).?

9. What is the involvement of the companies that produce the implants? Does the participant have to pay for their implant?

10. The safety and care aspects of the participants are lacking in the protocol

11. One of the major concerns of the protocol is that the sample size is based on a superiority hypothesis ( improvement) whereas it should have been formulated and calculated as a sample size for a non-inferiority hypothesis. It is not clear if the 7.5 NDI points is the equivalence limit specified. The study may therefore be underpowered.
12. The statistical inference outlined for evaluating equivalence does not make sense.

13. The repeated measures of NDI within participants can be of benefit in improving the precision of the estimated difference at say 24 months and using this improved precision in the confidence interval for the inference of non-inferiority. This will be an important issue since the study might be underpowered.

14. I would advise the study team to consult a medical statistician to ensure that the statistical section of this protocol is corrected.

15. It seems that the enrolment of participants have been completed. Could not calculated a revised sample size from the information provided in the protocol.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

'I declare that I have no competing interests'