Reviewer's report

**Title:** Therapeutic Hypothermia for Perinatal Asphyxial Encephalopathy in a Low Resource Hospital Setting in Equatorial Africa: Pilot Randomized Controlled Trial of Cranial Ultrasound and Neurodevelopmental Follow up at 18-22 months

**Version:** 2  **Date:** 21 January 2011

**Reviewer:** Keith Wheatley

**Reviewer's report:**

This is a very good clear paper reporting a pilot RCT addressing an important health issue. All my comments are minor:

1. It would be good to have a reference for the epidemiological evidence (p4, l14) - two [17,18] are given for the experimental evidence but none for the epidemiological evidence, unless this is number [19] in which case the [19] should be moved forward.

2. Will patients included in the pilot trial also be analysed as part of any subsequent larger RCT (p6, l3)?

3. Pilot studies are often able to provide information to enable a more accurate sample size calculation for the main trial. Is this planned in the this case?

4. What does "<35 36" mean in exclusion criterion 1?

5. For the main trial, will it be possible to obtain sufficient patients if exclusion criterion 7 is still applied? If not, shouldn't the pilot have assessed the feasibility of accrual and follow-up of families who live more distantly by including them?

6. Did the parents of all eligible infants give consent? If not, what does "consecutive" mean (p7, l4)?

7. Change "will be" to "was" (p7, l6). The tense should be changed to past rather than future elsewhere also.

8. If the number of data loggers was a limitation (p7, l6), will this be a problem for a larger main trial?

9. What does "oOxygen mean (p7, l11)?

10. What is the 14.6 (p11, l6)? Standard deviation? Need to specify.

11. I don't like the use of the word "trend" to indicate a non-significant difference (p11, l15).

12. The risk ratio may have been large at 5.0 (p11, l16), albeit with a very wide CI, but what is the absolute difference? Absolute differences are usually more clinically relevant.

13. If there was an imbalance of severe NE (p11, l17), why not adjust for in the analysis?

14. Perhaps my most important comment is that I didn't really feel that the
discussion went into sufficient detail on whether the pilot study was considered a success and whether, and why, a larger trial was warranted. For example, the authors state that "these findings underline the importance of exerting caution in the application of therapeutic hypothermia in low and mid resource settings ..." (p11, l21), so it would have been nice for the future plans to have been discussed in relation to this sort of finding.

**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