Author's response to reviews

Title: A double blind randomized controlled trial in neonates to determine the effect of vitamin A supplementation on immune responses: The Gambia protocol

Authors:

Suzanna L. R. McDonald (Suzanna.McDonald@lshtm.ac.uk)
Mathilde Savy (mathilde.savy@ird.fr)
Anthony JC Fulford (Tony.Fulford@lshtm.ac.uk)
Lindsay Kendall (lkendall@mrc.gm)
Katie L Flanagan (katie.flanagan@dhhs.tas.gov.au)
Andrew M Prentice (Andrew.Prentice@lshtm.ac.uk)

Version: 2 Date: 27 March 2014

Author's response to reviews: see over
Dear Catherine Olino and Editors of BMC Pediatrics,

Please accept my sincere apologies for the length of time it has taken me to reply in full to this email.

I have addressed your queries from the email dated Thursday 13-Mar-2014 below.

**Power calculation:** As this study was exploratory, it was not possible to perform power calculations. Knowledge on the potential immunological sequelae of human NNVAS is so scarce that the foremost aim of this study is to seek indicative data on aspects of immunity likely to be affected by NNVAS which can then be subjected to adequately powered investigations where power can be calculated based on variances derived in this study (and its Bangladeshi counterpart). A sample size of 200 was based upon financial and feasibility constraints. Currently stated in the manuscript is the following: ‘A sample of size of 200 was based on previous similar immunological studies carried out in the same cohort[41], alongside logistical and financial factors. It is unknown whether this trial will be adequately powered to provide definitive answers to the primary and secondary hypotheses, although pooling data with the parallel Bangladeshi trial employing a very similar protocol will enhance power’. Please let me know if you require further clarification on this matter.

**Ethics and funding approval:** I confirm that the trial was funded by a Bill and Melinda Gates Foundation grant, awarded to the World Health Organisation (2010/98441-0) and further supported by the Medical Research Council (UK), through core funding to the MRC International Nutrition Group (MC-A760-5QX00). I have emailed copies of the trials ethical and funding approvals (as listed below) to BMCSeriesEditorial@biomedcentral.com.

Local ethics committee: Gambia Government/MRC Laboratories Joint EC (initial and final)
- LEC_SCC_1198_2010_05_03_Initial
- LEC_SCC1198_2011_08_29_Final
Sponsor: London School of Hygiene and Tropical Medicine (initial and final)
- LSHTM EC_5697_2010_06_28_Initial
- LSHTM EC_5697_2011_09_22_Final

Funder: World Health Organization (initial and annual continuing review)
- WHO EC_RPC 389_2010_07_15_Initial
- WHO EC_RPC 389_2011_08_09_Cont Rev
- WHO EC_RPC 389_2012_07_10_Cont Rev
- WHO EC_RPC 389_2013_07_02_Cont Rev

Funding approval:
- Bid Ref RFP-NHD-MNM-0101-Acceptance
- Bid Ref RFP-NHD-MNM-0101-Acknowledgement
- Bid Ref RFP-NHD-MNM-0101-Acceptance-Confidentiality

**Study status:** The trial is ‘ongoing’ in as much as the investigators are still analyzing data (we are partially unblinded). However, recruitment and follow-up visits have been completed.

**Related articles:**
I confirm no publications containing the results of this study have already been published or submitted to any journal.

Please find below a copy of the text from the original cover letter.

Please do not hesitate to contact me if you have any further questions or comments and please accept my apologies once again for the length of time taken to respond to your initial email.

Many thanks and best wishes,
Suzanna McDonald

---

Dear Editors of BMC Pediatrics,

The submitted manuscript is suitable for publication in this journal as it is a protocol for a double blind, randomised controlled trial, which was conducted in neonates.

As lead author, I apologise and accept responsibility for the late publication of the protocol, as follow-up has been completed before submission of this manuscript. Publishing this article late in the trial ‘life cycle’ was an oversight on my part and is for no other reason than I was not aware of the timing regulations pertaining to trial protocol publication. However, prior to participant recruitment, a brief poster on this trials study design and hypotheses was presented at an international conference (McDonald SLR, et al., ‘A randomized controlled trial in human neonates to determine the effect of vitamin A supplementation on immune responses.’ In: Keystone Symposia’s: Malnutrition, Gut-Microbial Interactions and Mucosal Immunity to Vaccines;
November 7 – 11, 2011; New Delhi, India). I am happy to supply a PDF of this poster to the editorial board/reviewers if required.

The trial is registered at clinicaltrials.gov, had ethical approval from LEC and IRB, written consent obtained for each participant prior to enrolment and was audited and monitored for ICH-GCP compliance throughout. Following database lock, I (the PI) have been partially unblinded (group level only, not allocation of placebo or intervention), and data analysis is still ongoing.

None of the authors declare any potential competing interests and I am happy to have the manuscript peer reviewed by any expert in the field, of your choosing.

Please do not hesitate to contact me if you have any questions or queries.

I look forward to hearing from you shortly,

Yours sincerely,

Suzanna McDonald