Author’s response to reviews

Title: Right from the start: protocol for a pilot study for a randomised trial of the New Baby Programme for improving outcomes for children born to socially vulnerable mothers

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Author’s response to reviews:

Dear Sir

we thank you and the reviewers for the useful comments and the opportunity to improve our manuscript. In what follows, we detail changes to the manuscript in response to each issue raised by reviewers.

1. The introduction is excessively long and requires some major editing (grammatical errors, typos, font changes, and using dot points to convey statistics verbatim from another report).

Response: We have reduced the Background section by one third, from 1836 words to 1270 words, and hope this is sufficient. We have corrected all grammatical errors and typos that we could identify, and have removed font changes. We have removed the statistics taken from Perinatal Mortality 2009 (which we assume is what the editor if referring to).
2. There are inconstancies with the new primary outcomes of the study and those described in the "Measures" section. We have made it clearer that the “Measures” section in the previous draft refers to intervention outcome measures and not the study outcome measures.

Response: We have added a separate section headed ‘Study outcome measures’ (page 17) that sets out the sources of data/evidence used to address the research questions of the study, and the study’s outcomes.

3. Some of the secondary outcomes listed in the "Outcome measures" section are not outcomes, and should be moved to the statistical methods section.

Response: Thank you. We have edited the list of Secondary Outcomes for the pilot study so that it is now aligned with the Abstract, and does not include material that belongs elsewhere.

4. The randomisation section needs more details, what type of randomisation?

Response: This section now includes the sentence

‘It will use a central computer randomisation service (TENALEA) which employs a simple randomisation design in order to maintain complete randomness of the assignment of participants to either the intervention or comparator group’

5. Inclusion criteria also needs more specificity, what tools are used to assess these criteria? is the gestational age a criteria for inclusion (<18 weeks)?

Response: We have amended the first sentence under ‘Inclusion criteria’ to make it clear that a gestational age of <18 weeks is an inclusion criteria for the study.

A sentence has been added on page 11 under ‘Recruitment and informed consent’, detailing that ‘midwives will use a screening tool in the form of a vulnerability checklist at the 8-18 weeks booking-in visit’ to determine women’s eligibility for the study.
6* Over how long do you aim to recruit the required number of women?

Response: We aim to recruit the target sample of 50 participants over a 10 month period. The last sentence of the first paragraph under ‘Participants’ (page 10) now states this.

7* Figure 1 appear to have a misplaced arrow

Response: The arrow has now been removed from Figure 1.

8* In the statistical analysis section, please do not use the effect sizes obtained in this trial to inform a larger study, the trial is small and underpowered, so the effect size will be highly variable/imprecise. If there is no appropriate data in the literature on the variability of your outcomes, it would be better to use your pilot data to inform the estimates of variability used in the sample size calculations. Further, while you didn't mention this, it would be preferable to report confidence intervals rather than p-values.

Response: Thank you. We have actioned this. The section now reads:

‘We will conduct these analyses as an aid to estimating interval estimates (e.g. 95% Confidence Intervals) and variability in outcomes, in particular, to estimate between- and within-group variability: this information will be useful in planning the phase-3 RCT.’

9*I’m curious as to the utility of a cost-effectiveness analysis for an under-powered pilot study?

Response: Our explanation is as follows. We have not amended the text, but would be happy to include a brief, summary explanation if you felt this was appropriate.

The utility of conducting an economic analysis alongside this pilot study is to provide important insights into methodological considerations in the design and conduct of a larger trial and economic evaluation to demonstrate cost-effectiveness of the New Baby Programme. We acknowledge that the small sample size of this pilot study means that the findings of the cost-effectiveness analysis will not be conclusive, will not reach statistical significance and should not
be used to inform practice. However, the proposed CEA will provide preliminary findings for the hypothesis that NBP is a cost-effective intervention when compared to standard care and help quantify the uncertainty in the estimates of the incremental cost, incremental effect and Incremental cost-effectiveness ratio. We will use non-parametric bootstrapping techniques with 1000 replications to estimate the 95% confidence intervals around the point estimates. While it is anticipated that these 95% CIs will be broad, reflecting the small sample size of the pilot trial; we will be able to identify whether the point estimates suggest NBP is more/less costly than standard care, and assess whether there is an improvement or not in quality of life and the size of the QALY gain. Recommendations may then be drawn to reduce uncertainty when going forward with a larger trial and economic evaluation. This may include insights into the perspective undertaken, the cost offsets and the timeframe of follow-up, as well as the potential to estimate the sample size required to identify whether NBP is a cost-effective alternative at a given willingness-to-pay threshold.