Author’s response to reviews

Title: Cord Pilot Trial, comparing alternative policies for timing of cord clamping before 32 weeks gestation: follow-up for women up to one year

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Author’s response to reviews:

Dear Editor-in-Chief,

RE: Re-submission `Cord Pilot Trial, comparing alternative policies for timing of cord clamping before 32 weeks gestation: follow-up for women up to one year`

Following the helpful reviewer comments on our paper, we have prepared a detailed response below. The manuscript has been revised with changes shown using track changes. Therefore we would like to resubmit our paper for consideration for publication in BMC Pregnancy and Childbirth.
Please let me know if you require anything further.

Yours faithfully,

Lucy Bradshaw

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Authors response to Reviewer reports:

Zachary A. Vesoulis (Reviewer 1):

Methods

-The authors later note that several of the infants died. Is this not exclusionary, particular when maternal maternal health is one of the measured outcomes?

Response:

This comment suggests the reviewer thought women were excluded if their baby died. However, all women were included regardless of the outcome for their baby. We have amended the methods text to make this clearer.
-What breastfeeding or lactation resources are available in the hospital/out of the hospital?

Response:

Women in the trial had access to usual care. As women in the trial had a preterm birth, they would have had access to breastfeeding/lactation support at the neonatal unit caring for their baby. We have added a sentence to the discussion to clarify this. No specific breastfeeding support was provided within the trial, which increases the generalisability of our data.

-Very sparse data is provided about the social determinants of health for the mothers beyond age at parturition. What is the mother's education level? What % are impoverished? What percentage received prenatal care? What about substance abuse during pregnancy, geographic location, race, language, etc?

Response:

We did not collect any information about the social determinants of health for the mother at the time of randomisation. Randomisation would have ensured that there was not bias in these factors between the allocated groups. However we do not know if any of these factors were associated with completion of the follow-up questionnaires.

-"median weeks to stopping breastfeeding" — is this weeks after discharge or weeks after birth?

Response:

Duration of breastfeeding is relative to birth and has been clarified throughout the manuscript.
Results

-The authors should have provided a statistical comparison between the two groups at both time points. While the initial recruitment was randomized and should have resulted in balanced groups, the significant drop out rate appears to have bias the group in some aspect, but the reader is not offered the ability to evaluate.

Response:

Table 1 shows characteristics at birth and outcomes at hospital discharge by allocated group for the women who responded at the two time points. Baseline characteristics according to questionnaire completion and allocated group are also given in the additional file. We agree that the loss to follow-up introduces potential for bias, particularly at one year; hence statistical comparisons between the two groups are potentially misleading. Also, the trial was not initially designed to compare clinical effects between the groups and, despite the extended recruitment, was not adequately powered to do so. Therefore we consider that presentation of descriptive statistics only is appropriate.

-Detail should be provided as the the normality of the distributions of the factors

Response:

The HADS anxiety and depression scores were reasonably normally distributed and this information has been added to the footnote in Table 2. The satisfaction scores were left skewed, i.e. the majority with high satisfaction scores and a small number with much lower scores, as described in the manuscript.
- The authors should either study a separate cohort of control term born infants, use historical controls, or provide normative data from prior studies, both for rates of breast feeding and scores on the questionnaires. The authors are undoubtably correct that the mother's of preterm infants experience more anxiety/depression, but how much more?

Response:

Our paper reports follow up of women recruited to a randomised trial, with the usual care group (in our study immediate cord clamping with neonatal care after clamping) providing the appropriate comparator for outcome in the intervention group. The study was not designed to compare outcome for women following preterm or term birth. The systematic review by Vigod et al in 2010 showed that estimates of how much more postpartum depression there is in mothers of preterm infants compared to term infants vary, which we have added to the discussion.


Conclusion

- What do the authors speculate is the reason for the INCREASE in percentage of infants receiving mother's milk at discharge?

Response:

As explained in the background, our hypothesis was that deferring cord clamping and providing immediate neonatal care, if needed, beside the mother might facilitate bonding. The slightly higher percentage of women who had ever breastfed or expressed milk in the deferred cord clamping group supports this hypothesis, and may be due to allowing women to share the first moments of their baby's life. We have added this to our discussion.
-It appears that breastfeeding ceased very close to the time of discharge, on average. Why was this the case? This goes back to the earlier question about availability of lactation resources.

Response:

Table 3 shows that the median number of weeks from birth was 16 weeks in the delayed clamping group and 12 weeks in the immediate clamping group, compared with median number of days to discharge in both groups in Table 1 of around 60 days. Table 1 also shows that around 60% of babies were continuing to receive breast milk at discharge. We apologise Table 1 did not make clear that duration of hospital stay was in days, and have now added this clarification.

-The authors repeatedly describe the different cohorts of women as having various outcomes or factors in "similar proportions" but there is no statistical testing to back up this assertion

Response:

See comment above

-Important acknowledgment by the authors about the limitation of followup rate

Response:

No response required.
It would be interesting to see how the responses vary when stratified by gestational age at birth. Perhaps (likely) that prematurity has a non-linear impact on maternal well being, with substantially greater stress for mothers of infants born < 26 weeks compared to those born at 32 weeks.

Response:

We agree that this is likely and would be interesting to study. However, as our study was not designed to assess this, and the sample size too small for any meaningful comparison by gestation at birth, we have not added anything to the manuscript.

The authors note that the difference in response rate may have been due to "disappointment" with allocated intervention or misunderstanding of randomization. It is not unusual for participants to have some confusion about randomization, but what evidence do the authors have that "disappointment" contributed to response rate?

Response:

As included in our discussion, this is based on our qualitative interviews with women in the trial to explore their views and experiences of the two alternative consent pathways. Some women allocated to immediate cord clamping reported feeling ‘disappointed’ they had not been randomised to the delayed clamping group and felt they had somehow ‘failed’ the trial. These interviews and the responses to questionnaire questions about participation in the trial suggest a strong preference amongst women for the intervention group, and disappointment for some if they were allocated the usual care of immediate clamping (paper submitted to BMC Trials). Based on these data we suggest that disappointment in the allocation and misunderstanding about randomisation may be factors in the lower response at one year for woman allocated immediate cord clamping.
Abstract: Was the median number of weeks of breast feeding significantly different? From the CIs, it would appear it was not but this should be clarified.

Response:

As noted above in the response to reviewer 1, the trial was not designed or powered to detect differences between the groups in clinical outcome at follow up, such as duration of breast feeding. Therefore we think that presentation of descriptive statistics only is most appropriate. We have updated the conclusion in the abstract around duration of breastfeeding to be consistent with the conclusion in the main text.

Line 136 the colon after if should be removed

Response:

This colon has been removed.

Table 1 - I could not find an explanation of the two stage/one stage consent pathway in either the text or Table legend.

Response:

Thank you for highlighting this. A footnote has been added to Table 1 to explain the two consent pathways.
Line 226 Breast feeding: as noted earlier, whether this result and the survival curves are significantly different should be spelled out.

Response:

See comment above.

Judith Mercer (Reviewer 3): Very well written, thoughtful paper. All details covered very well.

Thank you for your review and positive comment.