Author's response to reviews

Title: Long-term health-related and economic consequences of short-term outcomes in evaluation of perinatal interventions.

Authors:

Margreet J. Teune (m.j.teune@amc.uva.nl)
Aleid G. van Wassenaer (a.vanwassenaer@amc.uva.nl)
Ben-Willem J. Mol (b.w.mol@amc.uva.nl)
Brent C. Opmeer (b.c.opmeer@amc.uva.nl)

Version: 5 Date: 14 June 2010

Author's response to reviews: see over
Amsterdam, 14 June 2010

Subject: Study Protocol “Long-term health-related and economic consequences of short-term outcomes in evaluation of perinatal interventions”.
ZonMW projectnumber: 80-82325-98-9010.

Dear Miss Titmus,

Thank your for your comments on our manuscript. These changes are the result of your input:

1. The reason to publish this protocol is not clear. A reason I can think of could be to get suggestions from the readers of original studies for the fist part… An explanation is now given in the response letter, and briefly at the end of “validation” para and of Discussion. These are unlikely places for the readers to find the motivation. It would be much clearer already in the introduction, modified to indicate this to be the reason to write this paper.

The motivation for writing this paper is now reported earlier in the paper (line number 141-145).

2. The background includes previous literature only on the 1st part. No previous literature on modeling and its possible benefits and difficulties … is given. Only one reference is now added. The rest of the references deal with statistical aspects (which may not be of so much interest). I would recommend having more literature on the benefits and drawbacks of modeling (in comparison to actual data).

More literature on benefits and drawbacks of modelling is now reported in this manuscript (line number 105-117).
3. The purpose of this paper is not given: to present a study plan addressing these and these issues. At the end of background “objectives of the study”, which are different from the objectives of the paper, are given.

See point 1 (line number 61-66).

4. Abstract is not very informative... The abstract is now changed. It contains more relevant data. Two problems: 1) it does not indicate the nature of the paper (see also comments 1 and 3), 2) Methods and Discussion are partly repetitive.

The abstract has been changed (line number 36-40, 61-66).

5. The authors do not explain why they start to look for studies on long term effects from the trials (on short term effects) from Cochrane library... This is now clearly explained in the response letter, but not as clearly in the paper itself.

We have added an explanation in the method session about why we searched for trials in the Cochrane library instead of PubMed (line number 151-156).

6. The short term outcomes (the predictive value of which for long-term outcomes will be modeled?) include very different types of phenomenon. The rationale of selecting the short-term outcomes is not given. This is now better formulated in the current text. In the response letter they say that the outcomes were selected “as the most often reported as outcomes in obstetric trials”. I am not a clinician, but some of the variables seem very rare (or the terms used are not customary). Could the reason be that these are the variables they have in their example case for modeling? Furthermore, the text on the page 6 on variables used in the prediction is contradictory. In the 2nd para the outcomes are listed, and in the “statistical analysis” “will be based on clinical expertise and plausibility”.

The selection of candidate predictors will be based on clinical expertise and plausibility, but also on the availability of these predictors in our database. Our plan is to develop prediction models for different long-term outcomes, so our selection of candidate predictors will be different for each prediction model (line number 190-192, 217)).

7. “Systematic review” in Methods: only trials “aimed to improve neonatal outcome” are included. Why this restriction? A perinatal intervention may have been evaluated e.g. by labor progress, and only later its long term infant effects are studied. The response letter explains that also interventions such as labor progress will be included. However, the text uses the formulation “interventions that aim to improve neonatal outcome”. There is a contradiction: will also interventions primarily looking other aspects than neonatal outcome be included?

Interventions primarily looking at other aspects than neonatal outcomes will also be included in our systematic review. We have changed the sentence “"interventions that aim to improve neonatal outcome” in the manuscript (line number 156-160).
8. Editorial request: Please provide your explanation, within the Methods section of the manuscript, why a power calculation is not possible at this stage.

We have added an explanation in the method section why a power calculation is not possible at this stage (line number 210-212).

We hope that our revised manuscript will be acceptable for publication. Do not hesitate to contact me if you have any further questions on our manuscript.

With best wishes,

Margreet Teune (corresponding author)

M.J. Teune, MD, MSc
Academic Medical Centre
Dept Obstetrics and Gynaecology, Room H4-140
Meibergdreef 9
1105 AZ Amsterdam
The Netherlands
E: M.J.Teune@amc.uva.nl, margreet@teune.nl
T: +31-(0)20-566199
M: +31-(0)6-47134234