Author's response to reviews

Title: Mortality and major morbidities in very preterm infants born from assisted conception or naturally conceived. Results of the area-based ACTION study.

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Version: 4 Date: 16 May 2014

Author's response to reviews:

Dear Editor,

Please find attached a revised version of the paper:

Ref. MS: 1730835641103601

Mortality and major morbidities in very preterm infants born from assisted conception or naturally conceived. Results of the area-based ACTION study.

Carlo Corchia, Monica Da Fre', Domenico Di Lallo, Luigi Gagliardi, Franco Macagno, Virgilio Carnielli, Silvana Miniaci and Marina Cuttini.

The paper has been modified according to the reviewer’s comments.

We thank the reviewer for the pertinent comments, that helped us to improve the paper. The manuscript has been modified according to his advises.

The point-by-point responses to the reviewer are as follows:

- “The current description of statistical models in the Statistical analysis section is completely inadequate”.

The multivariable method used in the analysis has been specified in more detail, that is multivariable logistic regression models with robust variance and standard error estimates of regression parameters, to account for the intra-group correlation of observations within NICUs. A relevant reference has been added.
- “Even more important is the fact that the paper interprets lack of significant difference between AC and non-AC groups as a kind of evidence for them being ‘similar’. This is exactly in the spirit of much criticized ‘absence of evidence being taken as evidence of absence’”.

We agree with the reviewer’s comment, and want to thank him for having advised us about this criticism. Several sections of the manuscript have been modified accordingly, in particular results’ presentation, discussion, mainly in the paragraph about criticisms, and conclusions. In the new version the term “similar” was not any longer employed. Consequently, also the abstract has been modified.

- “The findings presented in the paper should be supplemented with some power calculations”.

This has been done, a relevant reference has been added, and findings have been included in the results’ section.

- “If the power would be small, the paper could still be published, but with a strong, explicit warning about the danger of premature no-difference conclusion. In fact, in such a case a new, larger study would be called for. And the current one can serve as a suitable pilot”.

Due to the small power found, a warning against a final no-difference conclusion has been added in the discussion and conclusion sections, along with a call for larger and more powered studies.

Additional changes:

# The title has been slightly modified in accordance with reviewer’s comments (the first three words “No difference in” have been erased).

# The main outcomes taken into account have been clearly specified in the methods’ section.

# A typo in CI for sepsis in singletons (table 3) has been corrected.

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