Reviewer’s report

Title: Application of the matched nested case-control design to the secondary analysis of trial data

Version: 0 Date: 06 Feb 2020

Reviewer: Claudia Pedroza

Reviewer's report:

Review of BMRM-D-19-00566

This manuscript presents an example of a matched nested case-control study used in a completed randomized clinical trial. This is a well-designed and well-written paper. The authors used appropriate methods for defining cases, risk sets, and sampling of controls. However, I have a few questions about the analyses conducted.

1. It is recommended that the analysis include the matching variables and any other potential confounders. Is there a reason why these were not included in the analyses?

2. The data used is from a multicenter RCT. However, the authors do not mention whether center was considered as a matching variable. This is important since it is known that centers differ in the care provided and hence would be important to account for it.

3. The authors could use a logistic model with random effects for matching ids and center (separate effects).

4. P 4-5: I don't understand how exposures 3 &amp; 4 are defined for controls. I think this needs to be explained better.

5. P6 lines 10-11, consider rephrasing "...who had not experienced NEC at that time point" with "...who had not experienced NEC at the failure time of the case"

6. P6 line 19, last sentence should clarify that infants could not be selected as controls if they had already been selected as controls for another case, since sampling was done without replacement.

7. P8 line 51, can you state how many of the matched controls were cases?

8. Looking at Table 1 and Fig 3, birthweight is larger in the control group, particularly if you look at the % infants &lt; 750g. I think this is another reason why you would want to include sex, GA, and BW as variables in the regression model.

9. Figure 4, please clarify in description what the ORs are adjusted for
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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