Author's response to reviews

Title: Maternal lifestyle characteristics during pregnancy, and the risk of obesity in the offspring: a study of 5,125 children

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Author's response to reviews: see over
Dear Editor

We thank you and the reviewers for your thoughtful comments and critiques, which significantly improved our manuscript. We have responded to all comments and incorporated the major points into the revised manuscript.

Response to Reviewers’ comments

Reviewer #2

Major Compulsory Revisions

Comment 1.

1. In the regression analyses, the authors do not appear to have considered or adjusted for potential confounders of the associations between maternal characteristics and offspring overweight/obesity, e.g. how much of the association between GWG and childhood weight status could be explained by physical activity during pregnancy, birth weight, maternal weight status pre-pregnancy, or child lifestyle characteristics etc? Clarification of the hypothesised relationships between the explanatory variables, key covariates and outcomes would be helpful, and could also inform the development of multivariable models that take into account alternative explanations. It may also be interesting to conducted stratified analyses that explore whether there is any effect modification of the relationship between risk factors and childhood obesity, e.g. is the relationship between GWG and childhood overweight modified by maternal weight status at baseline?

Response to Comment 1.

Our model was build to test the hypothesis that the following maternal characteristics i.e.; Gestational Weight Gain (GWG), smoking during pregnancy, alcohol consumption during pregnancy and level of physical exercise of the mother could affect the obesity status of her offspring at the age of 8. We had already adjusted for the possible confounding effect of age. Following the reviewer’s recommendation we now expanded the number of confounders by adding in our analyses birth weight, maternal weight status pre-pregnancy and history of breastfeeding. No other lifestyle characteristics were recorded. Moreover we examined for possible effect modification of the relationship between maternal characteristics and childhood obesity for all the model’s confounders by adding interaction terms in the model, but no statistical significant effect was found. Therefore, we adapted Table 2 by adding the crude odds ratios, the multiple model with and without the adjustment
for the effect of the confounders. Additionally, changes were made in the corresponding statistical analysis section (Line 169-180).

Comment 2.

More detail is needed about how variables were selected and categorised for analyses: Physical activity: there is a long explanation of different types of physical activity, but no clear description of how questionnaire responses were categorised for analysis - e.g. how were categories of often, daily, sometimes per week defined? Were activities categorised according to frequency, intensity and/or duration? It may help to describe the questions used in the questionnaire, and to describe whether the questionnaire was validated in any way - it seems the potential for recall bias is extremely high given that women were asked about their physical activity more than 8 years previously.

Response to Comment 2.

A more detailed description of physical activity was added to the text based on the relevant questions (Line 147-151).

Recall bias related to exercise practices is also acknowledged as a limitation of the study. The following information was added to the article: An earlier survey by Villar et al. showed high correlation between measured and recalled variables, such as anthropometric measurements of the mother and the offspring, but low correlation to factors such as physical activity during pregnancy and blood pressure (Villar et al., 1988). Finally, a review of studies that employed physical activity questionnaires during pregnancy compared to ones that employed objective measurements (e.g. accelerometers) showed that the association between them was low to moderate (Evenson et al., 2012). Hence the results, as in the present investigation, should be interpreted with caution. (Line 306-312).

Comment 3.

a. More careful consideration of the choice of explanatory variables is needed. E.g. is it useful to treat gestational weight gain as a continuous exposure in kg? Given that virtually all women will gain weight during pregnancy, it does not seem useful from a policy perspective to know that each 1kg increase in weight during pregnancy is associated with increased odds of overweight/obesity in the children. A more useful/important question might be: what is the level of gestational weight gain above which there is an adverse effect on childhood weight status?
Response to Comment 3a.

We thank the reviewer for this comment. Indeed, the gestational weight gain above which there is an adverse effect on childhood weight status is of greater clinical value than to treat gestational weight gain as a continuous exposure in kg.

Additional analysis was undertaken which showed that offspring of women who exceed the IOM maternal weight gain recommendations were at an increased risk of obesity (OR: 1.45; 95%CI, 1.26, 1.67) compared with offspring of women with adequate GWG. This was added to the article in Lines (216-218)

Comment 3b

b. Line 196 refers to weight gain 'above the one recommended' - it's not clear what this means, given that methods do not describe this.

Response to Comment 3b.

This was removed.

Comment 3c

c. GWG - what were the average gestational ages at which the first and last maternal weights were assessed, and how were variations in gestational age at measurement taken into account?

Response to Comment 3c.

Following the reviewer’s suggestion, variations in gestational age were explored but no statistically significant influence was observed. Average gestational age was 27.84 years (Table 1). More detail information about gestational is now presented in lines 191-192 (Results section). The median maternal age at pregnancy was 28 years (1st, 3rd tertile 25, 30 years) and the age range was 15 to 48 years.

Comment 3d

d. Please clarify whether standard BMI cut-offs (25 kg/m2, 30 kg/m2) were used to assess weight categories in women at the end of pregnancy.

Response to Comment 3d.
Standard BMI cut-offs (25 kg/m², 30 kg/m²) were used to assess weight categories in women at the end of pregnancy. This was added to the text (Line 169).

Minor Essential Revisions

Comment 1.

1. The title refers to maternal lifestyle characteristics (physical activity, smoking habits and alcohol consumption) without mention of age or gestational weight gain.

Response to Comment 1.

A more general title was adopted due to word limit (Line 1-2).

Comment 2

2. Abstract - positive results are selectively reported - the effects of age and alcohol on childhood overweight/obesity should also be reported. A 95% CI should be given for the OR for GWG. The recommendations do not follow directly from the study findings given that a causal effect of maternal smoking and physical activity on offspring weight status cannot be established from these analyses.

Response to Comment 2.

All recommended additions to the abstract were done. (Line 31-35)

Comment 3

3. Introduction - the rationale for the choice of variables could be strengthened, giving a sense of why this analysis is needed.

Response to Comment 3

The rationale for the choice of the variable was added in Introduction (Line 78-80).

Comment 4.

4. More information on the response rates to the questionnaire is needed - it is reported that the 5,125 women in the sample are those of the 5,500 with complete data, but there must also have been women who could not be contacted or refused to participate in the study - these rates should be reported and the implications considered in the discussion.
Furthermore, the decision to include underweight babies and macrosomic babies in the dataset should be discussed.

Response to Comment 4.

We did not obtain full sets of data from 192 women (3.5%). The mothers that did not want to participate in the study were 183 (3.3%). These facts have been added to the text (Line 189-191).

The percentage of macrosomic and underweight babies was small and their inclusion in the study did not affect the statistical significance of the model (Line 220-222).

Comment 5.

5. Statistical analyses line 157 - would recommend using term 'mean' rather than average. Line 159 - clarify that BMI categories refer to those for children.

Response to Comment 5.

Mean was changed to average (Line166).

Clarification on offspring BMI categories was introduced (168).

Comment 6

6. Results - text refers to tertiles, but table 1 presents quartiles - authors should be consistent unless there is a good reason for presenting both. Could alternatively provide standard deviation as a measure of distribution.

Response to Comment 6.

We thank the reviewer for his/her fruitful comment. We provided the mean values and the standard deviations for the continuous variables in Table 1, after evaluating and validating the normality of the distribution of the corresponding variables by using histograms and P-P plots. Appropriate changes were made in the Statistical Analysis and Table 1 (Line 166-167 and Table 1).

Comment 7.

7. Given that it is the main outcome, the % of children that were overweight and obese at age 8 should be reported.
Response to Comment 7.

This was added to the text as well as Table 1 (Line 204-206).

Comment 8.

8. Discussion needs more critical review of the study limitations, e.g. data availability, response rates.

Response to Comment 8.

We consider the percentage of mothers (3.3%) that did not want to participate in the study as not affecting the validity of the results (Line 190-191).

Several studies in recent years have evaluated the reliability of recalled information relating to the perinatal period. Specifically, studies have been conducted involving recall intervals from 7 to 22 years and on the whole concluded that this information is reliable. This was added to the end of the discussion (Line 302-305).

Comment 9.

9. Some review of the English is recommended, e.g Introduction line 43 (‘act synergistically by burdening health of individuals’), line 49 (‘its risk’ - what risk does this refer to?), line 54 (‘the increasing trend’ - it’s not clear what trend this refers to)

Response to Comment 9.

Burdening was changed to affect (Line 46).

Risk was changed to health risks (Line 52).

Increasing trend was changed to increasing incidence of obesity (Line 57-58).

Comment 10.

10. ORs are given to 3 decimal places - 2 d.p. are sufficient.

Response to Comment 10.

Changes made.