Reviewer's report

**Title:** Smoking during Pregnancy and Risk of Abnormal Glucose Tolerance: A Prospective Cohort Study

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**Reviewer:** Magnus Fasting

**Reviewer's report:**

The authors have written a paper on the association between smoking in different stages of pregnancy and the occurrence of abnormal glucose tolerance (AGT) among a cohort of Hispanic mother-child pairs in Western Massachusetts. Their main conclusions were that light pre-pregnancy smoking and pregnancy awareness smoking cessation may be associated with increased occurrence of AGT. A secondary conclusion was that smoking during pregnancy was not associated with the development of AGT. The paper is in general well written, and the data supports the main conclusions drawn. However, I have some issues of concern.

**Major compulsory revisions:**

1. The authors cite several previous studies assessing the research question, as well as a recent review. These studies mainly conclude that there is no association between maternal smoking in pregnancy and AGT. They also argue that the study has merit because the population under study is Hispanic. What I miss is a clear research hypothesis stated in the introduction, and a discussion of the results according to this hypothesis. Would one believe that the association between maternal smoking and AGT would be different between other ethnicities and Hispanics? And in that case, why?

2. The authors state in the methods section that the final sample size is 1006. However, they operate with different numbers of subjects in all the tables. I would like to know how many of these they had exposure data, i.e. smoking status at different stages of pregnancy.

3. The authors elaborate on how the confounders for the statistical analyses were chosen in the methods section, and I have some comments to this section. First, there is clearly a typographical error, where the authors state: “To assess confounding we independently included each potential confounder in the model: those factors that changed the association between smoking and preterm birth by more than 10% were included...” Second, the authors do not state which variables that became confounders after this test, which they should. Third, the authors also state that some variables were chosen as confounders a priori without stating why, they should do that as well. The authors could do these changes, and it would be okay by me. However, I personally, have some problems using the 10%-cutoff method to arbitrarily choose confounders. In my
opinion, a better method, is to just choose confounders a priori, based on knowledge of the subject at hand.

4. The authors report in the beginning of the results section and in table 1 several associations between various covariates and abnormal glucose tolerance. I count 13 statistical tests, suggesting that: higher age, higher education, higher household income, higher prepregnancy BMI, family history of diabetes, personal history of GDM and current history of hypertension is associated with AGT. Some of these results, that higher education and higher household income is associated with AGT is surprising to me. However, the authors do not discuss these findings at all, and they do not focus on these associations as a research questions. I suggest removing these statistical tests from the table, and use table 1 as a purely descriptive table of the population. However, if the authors disagree, at least they should discuss these results in the discussion.

5. Table 2 is the main table of the study, and I have some questions about the number of mother-child pairs in this table. When I sum the non-smoker and smoker categories for pre-pregnancy, early pregnancy and mid-pregnancy smoking, I get 912, 847 and 697 subjects, respectively. Additionally from table 1, the number of mother-child pairs with information on age, prepregnancy BMI, parity, weight gain and education (variables in the multivariable model) is 1006, 986, 1003, 805 and 909, that is, 20% missing in one category. This brings me to the question: how many mother-child pairs were included in the statistical analyses in the different steps? Did the authors restrict the analyses to only those with complete information in the unadjusted analyses? Often, small changes in odds-ratios observed like this are simply due to subjects falling out of the statistical analyses because of missing variables. I would like the authors to clarify this.

6. Despite that the authors do not state this as a research object in the background section, the main conclusion of this paper is that maternal smoking cessation at pregnancy awareness may be associated with the development of AGT, possibly through increased pregnancy weight gain. The authors support this idea by the finding that those mothers who were light smokers before pregnancy had a possible elevated odds ratio for AGT compared to never-smoking mother. I find this conclusion a bit too speculative based on the data and literature presented in this study. I suggest that this finding is reduced to a secondary finding, and that the sequence of the discussion is changed accordingly.

7. In the literature referenced in this paper, only human epidemiological studies are presented. Does it exist any animal studies on this subjects, possibly shedding light on a putative biological basis of the associations presented?

Minor compulsory revisions

1. The authors state that the mean weeks of gestation at inclusion was 15 weeks. I would like them to also report some measure of the spread of this variable, e.g. standard deviation or min-max. The same is for the mid-pregnancy interview.
2. The authors wanted to examine the effect of quitting smoking with the onset of pregnancy in relation to the risk of AGT. They state that they studied 316 women who smoked at pregnancy awareness, of whom 45% quit at pregnancy awareness. However, in table 3, I miss the total number of subjects in the cont. smoking and the quit smoking categories. Is the 16 and 7 the number of subjects with AGT, or is it a typographical error and was it supposed to be the total number of subjects?

Minor discretionary revisions

1. The authors use, as many others also do, the wording “statistically significant association” several times in the papers. However, this wording is unnecessary and puts too much focus on the p-value. If there is an association between two variables, it is implied that this association is statistically significant. If it wasn’t, there would be no association. For example, in the first paragraph the authors write: “... however, this result was attenuated and no longer statistically significant after adjusting for weight gain...” A better way to word this, in my opinion, would be: “… however, this result was attenuated after adjusting for weight gain …”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.