Author’s response to reviews

Title: A Gestational Vulnerability Window for Smoking Exposure and the Increased Risk of Preterm Birth: How Timing and Intensity of Maternal Smoking Matter

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Reviewers Comments and Author Responses

REVIEWER # 1:

General:

The studies main strength is that it is based on a population register data, including a large sample. However, the major flow in the study is that the quality of exposure variable is questionable, and the quality of exposure and probable misclassification bias across the study sample is difficult to overcome. Rather than using a simple logistic regression model, the effect modifications and interactions should have been done with the available variables.

Thank you! We found your comments extremely helpful and have revised the text accordingly. We have added a paragraph on Quality of Self-reported Smoking Data (Methods section, lines 184-190) to better describe the quality of the exposure variable documented in prior research. In addition, we explain how our sensitivity analysis corrects the data for misreporting of smoking in the third trimester, the major source of error [Lines 216-218]. The main findings are not dependent upon precise third trimester reporting in any case. Results remain consistent with the few smaller studies in this field. We tested for effect modification and interaction by maternal race/ethnicity that is reflected in the Results section and the data support the final conclusions [Lines 275-278].

Introduction (Background):

Preterm birth estimates were given for 2014. Do you have newer estimates?
Thank you. We have provided more recent estimates of preterm birth rates in the text [Lines 64-66]

Methods

1. BMC Pregnancy and Child Birth is an international journal and the readership doesn't have an idea of the data source. It needs an explanation including the data, data quality, completeness etc. Though the references were given, the methods section is incomplete without those data.

We agree with the reviewer and thank you for catching these omissions. We have expanded on the US birth certificate data in more detail including information on the revised 2003 version [Lines 126-130].

2a. A previously reported level of underreporting and data quality needs to be discussed in Methods.

2a. We agree with the suggestion. We now discuss the underreporting and quality of smoking data in the Methods section, Quality of Self-reported Smoking Data, and provide supporting references [Lines 185-189]

2b. Also, references are needed for: “The estimates of smoking appear to have improved with the revised birth certificate”.


Results

1. All three-trimester smoking associated with lower OR was attributed to exposure measurement error. How come the same error could not have occurred in other estimates?

This is a valid and important question. Women may misreport their smoking status in the third trimester. Including women who gave birth preterm in the second trimester and reported smoking in the third trimester will make more women self-designated third trimester smokers and will result in underestimating (toward the null) the true risk. [Lines 263-266 and 311-316] Because no women gave live birth prior to the second trimester, smoking is less likely to be misreported in the first and second trimesters, and this underestimate did not occur in other trimesters.
2. Why “no smoking” was not considered a reference category?

This is a very relevant question. The focus of this study was on comparing timing and intensity of smoking among smokers from the beginning of pregnancy to determine when pregnant smokers should quit to minimize their preterm birth risk. Because many women lower their smoking intensity in the first trimester and quit thereafter, low intensity smoking in the first trimester only was considered the reference category. [Lines 208-211] (Explored previously in Reference # 41---England LJ, Grauman A, Qian C, Wilkins DG, Schisterman EF, Yu KF, Levine RJ. Misclassification of maternal smoking status and its effects on an epidemiologic study of pregnancy outcomes. Nicotine Tob Res 2007; 9:1005–1013)

REVIEWER # 2

Overall the paper addresses an important public health issue i.e. maternal smoking and preterm birth. The paper reads well. But, I made some suggestions to organize the paper, especially the method section.

Thank you.

Abstract

1. Lines 21-22: the aim of the study was not mentioned.

Thank you for noting this omission. We have now included the statement of study objectives in the Abstract Background section [Lines 21-24]

2. Line 25: is not clear why you used the word “uniquely”.

Thank you for this observation. We have deleted the word “uniquely” and rephrased the statement [Line 27].
3. Lines 25-26: it would be helpful to add how maternal smoking status was classified.

We agree, and following the reviewer’s suggestion, in the Methods, exposure variable subsection, we have explained in details how smoking exposure was classified in this study, [Lines 27-29]

4. Line 34: could you precise the reference category?

We are sorry for this oversight. We have now specified the reference category as “those who smoked only in the first trimester” [Line 31]

Background

1. Line 65: I suggest starting by presenting facts about preterm birth in the U.S. (why it is an important the public health issue?) and then mention why it important to address this issue.

Thank you for the suggestion. We have made the changes. [Lines 64-68]

2. Lines 68-69: could you provide more information about racial and ethnic disparities in the U.S.?

Thank you for mentioning this. We have now provided the percentage rates. [Lines 66-68] [Reference # 3]

Methods

Measurement

1. Lines 134-135: "self-reported…” this sentence is not clear.

We have edited the text to make it clear. [Lines 185-190]

2. Lines 135-141: I suggest moving this sentence to the discussion of the study strengths and limitations.
Thank you for this suggestion. We moved the sentence to the discussion of the strengths and limitations [Lines 337-338]

Statistical analysis

1. Lines 148-173: I suggest moving these sentences to the measurement section.
Thank you again for this suggestion. We made the change [Lines 148-152].

2. Did you conduct weighted analysis?
Our study analysis included the entire population, so weights were not needed [Lines 220-221].

Discussion

1. What are the implications of the study findings?
Thank you for reminding us that this is necessary. We have edited the text accordingly [Lines 281-283 and 343-351] We have completely revised the discussion section to clarify the results, how they link to underlying biologic processes, strengths and limitations, and implications for women, health providers, and researchers.