Author’s response to reviews

Title: Syphilis-attributable adverse pregnancy outcomes in China: a retrospective cohort analysis of 1187 pregnant women with different syphilis treatment

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Author’s response to reviews:

Dear Dr. Devoto and Dr. Bristow,

Thank you for providing us with an opportunity to submit a revised manuscript. We appreciate your consideration and the reviewer’s insightful comments. We have discussed each of these comments and addressed them point by point below. We have highlighted the corrections in red in the revised manuscript for your review.

Thank you again for considering our manuscript.
Reviewers: 

Claire C. Bristow, PhD MPH MSc (Reviewer 1): Review of: Syphilis-attributable adverse pregnancy outcomes in China: a retrospective cohort analysis of 1187 pregnant women with different syphilis treatment 

This paper describes an analysis of programmatic data from China. In Guangzhou 1391 pregnant women tested positive for syphilis during pregnancy during the time period of data analysis. This was sufficient sample size to look at specific adverse outcomes of pregnancy and how timing of syphilis treatment and RPR titer can impact adverse pregnancy outcomes. This paper describes important results and should be published after minor revisions are made.

Response to the Reviewer #1: 

Abstract 

Comment 1.1 – “The described purpose of the study doesn't capture all of the aims of your analysis. You also showed how time of treatment and titer impacted adverse pregnancy outcomes and your conclusion doesn't speak to the purpose you state.”

Response 1.1 Thanks for your comment. We have revised the purpose in both the abstract and the introduction. The conclusion of the manuscript has also been revised accordingly.

“The purpose of this study was to compare the frequency of adverse pregnancy outcomes among syphilis-seropositive women who received different treatment regimens at different times in Guangzhou, China.” (Abstract section, line 22, page 2) 

Conclusion: “Our study reveals adverse outcomes were similar between syphilis-seropositive pregnant women who received one or two courses of penicillin treatment and treatment before 28 weeks gestation can avert a large burden of adverse outcomes. The results of our study have practical implications for the prevention and treatment syphilis-attributable adverse pregnancy outcomes. Strategies are warranted to promote higher-quality, more comprehensive prenatal healthcare services.” (Conclusion section, line 276, page 16) 

Background 

Comment 1.2 – “Line 55 (reference 9): Did those 15,884 cases test positive during delivery or at any point during pregnancy?”

Response 1.2 We have further clarified this in the manuscript part (reference 9). “For example, in 2013, the Chinese national surveillance reported 15,884 cases of syphilis among maternities, 55.6% (8,829) of these cases tested positive during pregnancy and 43.8% (6,968) tested positive at labor.” (Background section, line 53-56, page 3)
Comment 1.3—“Line 61: "…accurately captures data describing linking adverse.." I think there is an error in this sentence and it doesn't really read correctly as written. Please correct.”

Response 1.3 Thanks for your comment. We have revised the sentence as “China has a comprehensive longitudinal maternal health system that accurately captures data describing adverse outcomes and treatment.” (Background section, line 61, page 3)

Comment 1.4—“Line 61: It would be clearer if worded: "The city of Guangzhou has all medical...." -Line 62-63: "…compared to other cities." Are you saying that other cities don't have this? Please clarify.”

Response 1.4 Thanks for your comment. Other cities do have this system, so we have removed “compared to other cities” from this sentence “The city of Guangzhou has all medical institutions covered by the IPMTCT system and enhanced monitoring”. (Background section, line 63, page 4)

Comment 1.5—“The described purpose of the study doesn't capture all of the aims of your analysis. You also showed how time of treatment and titer impacted adverse pregnancy outcomes.”

Response 1.5 Thanks for your comment. We have revised the purpose of this paper as “The purpose of this study was to compare the frequency of adverse pregnancy outcomes among syphilis-seropositive women who received different treatment regimens at different times in Guangzhou, China.” (Background section, line 70, page 4)

Methods

Comment 1.6—“Line 75: You put a comma instead of a period.”

Response 1.6 Thanks for your meticulousness. We have replaced the comma with a period. (Methods section, line 78, page 4)

Comment 1.7—“Line 77: 1391 women were diagnosed with syphilis during this time period - were they diagnosed during pregnancy or at delivery or both?”

Response 1.7 All syphilis-seropositive pregnant women included had their syphilis diagnosed during pregnancy or at delivery, of which 200 were diagnosed at delivery. We have included this in the Results section as “402 (33.9%) participants were diagnosed with syphilis at or after 28 weeks gestation, of which 200 (16.8%) were diagnosed at delivery.” (Results section, line 176, page 9)

Comment 1.8—“Line 98 and line 106: I don't understand the need for 2 courses of treatment. Does the second course begin immediately following the first course? Why is this called two courses and not just one course that includes weekly benzathine penicillin for 6 weeks?”

Response 1.8 The definition of two separate courses of benzathine penicillin treatment meets the
following two criteria: 1) in each treatment, benzathine penicillin is given to the patient on a weekly basis for three consecutive weeks, and 2) there is an interval of more than one week between these two separate courses.

We have revised the definition of two courses in this manuscript as “completed two full treatment courses during pregnancy, with an interval of more than one week between each other.” (Methods section, line 108, page 6)

Comment 1.9-“Line 123: Please reword for clarity to "We chose not to include congenital infection in this…” because some people include all adverse outcomes of syphilis in pregnancy to be "congenital syphilis".”

Response 1.9 Thanks for your comment. We have revised the sentence as “We chose not to include congenital infection in this…” as suggested. (Methods section, line 125, page 7)

Results

Comment 1.10-“Line 166: why was <1:16 the cutoff rather than 1:8? ”

Response 1.10 Thanks for your comment. We have described <1:16 the cutoff as “≤1:8 ” as suggested.

Comment 1.11-“Were you able to look at differences in the proportion of adverse pregnancy outcomes between the different treatments (also adjusting for covariates such as time of treatment). ”

Response 1.11 We did not perform the analyses across different treatments due to the small sample sizes, of the 18 participants with Non-penicillin treatment, 6 received erythromycin, 2 received ceftriaxone, and 10 received other antibiotics.

Comment 1.12-“Are you able to compare the rates of adverse pregnancy outcomes of the syphilis infected with syphilis non-infected? ”

Response 1.12 Technically, it is feasible to conduct such a comparison. But analyses involving syphilis non-infected women are beyond the scope of our study, and we will have to obtain the permission from the Ethics Committee of the Guangzhou Women and Children’s Medical Center to get the access of additional data.

Comment 1.13-“Figure 2 could use some further clarification in the axis titles - specifically include information on what the adjusted RR shows and state what the comparison group was. "Adjusted RR of…””

Response 1.13 Thanks for your comment. We have presented the axis titles as “Adjusted RR (95%CI) of Composite Adverse Outcome” and “Non-treponemal Serum Test Titer”.