Author’s response to reviews

Title: Factors associated with utilization of maternal serum screening for Down syndrome in mainland China: a cross-sectional study

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Author’s response to reviews:

Dear Dr. Claudia Hanson,

Thank you very much for taking time to review our manuscript and giving us the opportunity to revise the submitted paper (ID: BHSR-D-15-00072) entitled “Factors associated with utilization of maternal serum screening for Down syndrome in mainland China: A cross-sectional study”. We are also very grateful to the two reviewers, Dr. Neeltje Crombag and Dr. Linda Martin, for their thorough reading and constructive comments that significantly helped us to improve the manuscript.

The manuscript has been carefully revised in response to both reviewers’ comments and suggestions. Revised portions are marked in blue in the paper. The main corrections in the paper and the responses to the reviewers’ comments are as following:

Responses to the reviewers’ comments:
Reviewer #1:

1. First, in the background (page 5, second paragraph), I would suggest to expound/reformulate this written statement. In most of European countries, the aim of providing MSS is to enable prospective parents in making reproductive (informed and autonomous) choices. One could take into account general costs of healthcare and consequences of introduction of a screening program on the general health care expenses, but reduction of societal costs should not be the aim of these programs, and is even considered as unethical as being a goal in itself.

Response to comment: about the aim of providing MSS in China

We fully understood the concern by the reviewer, thus we rephrased the background part according to her suggestion. It is true that birth defects (BD) bring great burden not only to the family but also to society as a whole. The aim of providing MSS and other BD prevention strategies is not to decrease the number of BD patients so as to reduce the societal cost, but to enable prospective parents to identify and manage BD risk so as to make informed reproductive choice. BD prevention strategies are considered public health programs which make them equitable for the whole population.

2. Another concern I have, regards the Andersen model, first I would recommend to give some more background information on the model and how it can help in explaining health care utilization (p 7, second paragraph) and later use this information in the discussion as well. Besides I am a bit confused with the interpretation of Health Beliefs (page 10, first paragraph). As can be read from the paper "Revisiting the Behavioral Model and Access to Medical Care: Does it Matter?" by RM Andersen, health beliefs are attitudes, values and knowledge that people have about health and health services that might influence their subsequent perceptions of need and use of health services. Could you explain better how attendance at maternal classes explains the individual health beliefs of a person?

Response to comment: about adding more information on the Andersen model not only in the background part, but also in the discussion part.

We have added additional information on the Anderson model according to your comments. Please see revised background and discussion sections for these additional comments.

3. Besides I am a bit confused with the interpretation of Health Beliefs (page 10, first paragraph). As can be read from the paper "Revisiting the Behavioral Model and Access to Medical Care:
Does it Matter?" by RM Andersen, health beliefs are attitudes, values and knowledge that people have about health and health services that might influence their subsequent perceptions of need and use of health services. Could you explain better how attendance at maternal classes explains the individual health beliefs of a person?

Response to comment: about interpretation of health beliefs.

As you mentioned, health beliefs in the Andersen model refer to attitudes, values and knowledge that people have about health and health services that might influence their subsequent perceptions of need and use of health services. Previous international studies typically interpret health beliefs as attitudes toward BD and their health interventions, attitudes toward termination of pregnancy or abortion. Based on our understanding of MSS utilization in China, we think that whether or not participating in maternal preparation classes can be considered as a proxy for health belief. There are three justifications for this.

1) Whether or not participating in maternal preparation classes reflects one’s attitude toward health intervention. Those willing to take part in maternal preparation classes believed that knowledge and behavior change can help improve one’s health.

2) Whether or not participating in maternal preparation classes reflects one’s attitude towards their pregnancy. Those willing to take part in maternal preparation classes are much more likely to expect better delivery outcomes.

3) Whether or not participating in maternal preparation classes would influence ones’ decision on subsequent perceptions of MSS utilization, as maternal preparation classes were held before pregnancy.

4. Results Table 3, it took me some time to understand, finally I managed, but the use of abbreviations or codes in the table were a bit confusing.

Response to comment: about the abbreviations and codes in table 3.

We have corrected the abbreviations and codes in all the tables.

5. The discussion could benefit from more connection between results and what is written in the discussion section; this is in particular evident on page 16 (end of first paragraph should connect with first paragraph p 19), and page 16 second paragraph which might need some rewriting and it is unclear to me which point is being made here.
Response to comment: about the improvement of discussion section.

Response: We have re-written the discussion section.

6. Page 18, first paragraph, would the combination of older women that make less use of MSS and less use of routinize prenatal check ups, provide a conclusion? e.g. access to care for older women is less (is there any information on where women of older age were more likely to live, educational status or receive their prenatal care?). But I agree I can not see these connections arising from the provided data.

Response to comment: about the explanation on the combined results of older women that make less use of MSS and less use of routine prenatal checkups.

Response: As you indicated, the reason that advanced age women making less use of both MSS and routine prenatal checkups was puzzling. According to your suggestion, we performed chi-square test to find potential factors among these relationships, but failed to find any related factors. In our view, a possible reason was the difference between primipara and multipara. We are sorry that we have not covered the factors in our questionnaire, so that we can’t provide a clear explanation. It was just a limitation of the study (see Discussion section).

7. Overall, the manuscript would benefit form some careful proof reading, especially with regards to grammar (and sentences are sometime very long and hard to read and understand), preferably by a native speaker.

Response to comment: about the writing.

We have modified the manuscript, especially the grammar. We have also edited the paper.

Reviewer #2:

1. Please change the abstract after addressing the remarks below.

Response to comment: about revising the abstract.

We have changed the abstract according to the revised manuscript.
2. The introduction could be more concise. Some tips:

Please start to describe the aim of the Chinese prenatal anomaly screening, more to the point MSS for Down Syndrome (and trisomy 13 and 18?), and the prenatal anomaly screening program (is the NIPT offered to pregnant women yet?). Compare this aim and program with the aims and programs of other countries, including those who have other aims and goals.

Response to comment: about the aim of MSS delivery in China.
We have re-written the background section according to your suggestion.

3. Then describe the number of children born with DS and the uptake of MSS for DS in China from 1990 on. Compare figures to other countries. How many parents choose to terminate the pregnancy after they found out their unborn child had DS? What are the factors influencing the uptake as far as you know? Review of the literature about factors influencing MSS uptake.

Response to comment: about the figures of DS intervention in China and the associated factors of MSS uptake.
We are sorry that there is no national or regional report or public information about the figures of Down syndrome babies delivered or related termination in China. Therefore, we can’t make comparison between China and other countries on this. The factors associated with MSS uptake were reviewed in the background section.

4. Paragraph about the aim of this study, including the usefulness of the results in the light of the aim of the prenatal screening program and your hypothesis. How does this study add to relevant knowledge given the introduction of NIPT?

Response to comment: about the aim of the present research.
We have re-written the aim according to your suggestion. Actually, NIPT has recently been approved by MOH in 2015 in China, although it had been studied, piloted and performed during past several years. In our view, results from this study can provide reference for NIPT utilization, especially the provider and contextual factors.
5. Describe the study context; e.g. The one child policy of China is not mentioned in the introduction. Why not? It seems an important part of the study-context.

Response to comment: about the One Child Policy of China and other meaningful context.

We have added the contextual information of the study, which includes the national Regulation on Administration of techniques for Prenatal Diagnosis in 2003, the requirement of equitable access to public health service from the new round of health system reforms in 2009 and MSS delivery situation before and after 2003. In our view, there is not much relationship between the One Child Policy and MSS utilization. According to the One Child Policy, if a serious BD infant (eg. DS) was delivered, the family can have another healthy child.

6. p. 5 line 41: "The needs of special care for DS patients usually bring tremendous financial and psychological burden not only to the family, but also to the society. The lifetime economic burden of each new DS case estimates to be US$55,000 in 2003 in China from a societal perspective [5]." What is the point here? Please clarify in the study context of the aim of the prenatal anomaly screening program and reconsider this part of the text.

Response to comment: about the study context and the aim of screening.

We have re-written this part of text. Actually, another reviewer also raised this point. It was true that birth defects (BD) bring great burden not only to the family but also to the society in China. The aim of providing MSS and other BD prevention strategies is not to decrease the number of BD patients so as to reduce the societal cost, but to enable prospective parents to identify and manage BD risk so as to make informed reproductive choice. BD prevention strategies are public health programs that the government develops to make equitable access to the whole population.

7. p. 6 line 44: "Both MSS and follow-up diagnostic procedures are voluntary and based on informed consent by pregnant women in China." What is the reference? And, since this is the case, why is your introduction focusing on the prevention of children born with DS? So again, I don't understand the Chinese prenatal anomaly screening context. Please clarify.

Response to comment: about the informed consent of service utilization.

We have added the information about national Regulation in the background section. The context of prenatal screening was clarified in the background section.
8. It might be interesting to use the following literature:


Response to comment: recommended literature for reference.

Three studies were read and cited in the present manuscript.

9. Overall I think that you have to re-run the results for those participating health care institutions who provided MSS service during pregnancy, and those who were not able to provide it. See also publication of Gitsels et al 2014 in which such an approach was used.

Response to comment: about including whether or not providing MSS as an associated factor in analysis.

We have considered including whether or not providing MSS as an associated factor to analyze. But there were two difficulties as discussed below:

1) It was not possible to obtain a correct answer about whether or not a health care institution was able to provide MSS through the questionnaire format.

2) Although the national Regulation issued in 2003 regulated that health care institutions providing prenatal diagnostic service (including MSS) should get certification from the provincial government, the implementation was not strict enough to cover MSS in some area. We cannot divide the health care institution into two parts based on their service certification, as there were some health care institutions that provided MSS without certification.

Theoretically, the health care institutions can be divided into four categories based on their function of MSS delivery as: diagnostic centers (providing MSS and further diagnostic tests), screening centers (providing MSS), blood taking centers (providing blood taking service and transferring the blood sample to another center for testing), and other centers (only providing
either MSS related health education, recommendation, referral or not). But it was very hard to obtain the exactly right information by providers’ self-report.

Besides, the pregnant women are provided freedom of choice on where to utilize their prenatal care. If there was no MSS delivery in the target health care institution, pregnant women could go to another health care institution for MSS utilization by herself (even across region) or through local referral system or service network (if there was).

Therefore, we didn’t include whether the target health care institution providing MSS or not as an associated factor. But we have also performed multilevel analysis and taken the effect of providers into consideration as what Gitsels et al did.

10. P. 8 line 56: "A total of 8110 puerperas from these institutions were accrued after their consent to participate in this study." This part belongs to the Result section.

Response to comment: about arrangement of survey information.

We have re-arranged the text you referred.

11. Define the word puerperas in the context of your study.

Response to comment: about the definition of puerperas.

In our study, all the respondents were puerperas, and they were interviewed within 7 days after their delivery. This point was added into the methods section.

12. Re-write the 'Design, setting and participants' part of the Methods concise and chronologically (Design, setting and participants) without giving double information and reporting results.

Response to comment: about the writing of 'Design, setting and participants' part.

We have re-written the 'Design, setting and participants' part of the Methods section according to your suggestion.

13. p. 10 line 2: Please show the final structured, interviewer guided questionnaire in an Appendix.

Response to comment: about sharing the questionnaire in appendix.
The questionnaire was designed in Chinese. If it is needed, we can help translate the useful part of the questionnaire into English and add it to the appendix.

14. It remains unclear when and how participants were interviewed or given the questionnaire. So please re-write the section so that any other researcher can reproduce the study.

Response to comment: about the data collection process.

The participants were interviewed by the local maternal and child health technicians face to face in the target health care institution before discharge. And related information has been added in the methods section.

15. How many local surveyors were 'used'?

Response to comment: about the number of local surveyors.

Generally, there were one or two surveyors used in a certain sampled health care institution. And in some health care institutions with large delivery numbers (and also large sample numbers, eg. more than 200), we used 2-3 surveyors.

16. How was Knowledge about DS measured?

Response to comment: about the measurement of DS knowledge.

The measurement of DS knowledge was one of the most important outcome variables in our study. Therefore we paid great attention to it. In the questionnaire, the following questions can be found:

1) Have you heard of DS?  A. Yes   B. No

2) What do you know about its risk factors? (Multiple Choice)

   A. Genetic factors   B. Environment factors
   C. Advanced maternal age   D. Not know

Only if the respondents chosen A in the first question and chosen A+B+C in the second question were defined as respondents with enough knowledge of DS.
17. Please clarify the next procedure: "Subsequently, multivariate analysis was conducted using a hierarchical logistic regression model including the characteristics of individuals at level 1, the characteristics of health care institutions at level 2 and the characteristics of cities as level 3." Make clear why you choose to make the models the way you did (it seems that you force your results to be in line with the Anderson model).

Response to comment: about the multilevel analysis.

The reviewer has two concerns. First, the reason to use multilevel analysis. It was presented in the manuscript as “given the hierarchical structure of the dataset, i.e. individuals nested within health care institutions, health care institutions nested within cities”, we used multilevel logistic regression to find the associated factors, and these factors were grouped into three levels as “individual”, “health care institution” and “city”.

Second, the reason to run another three regressions besides model one. The reason that we performed the latter three regression models was not to force our results to be in line with the Anderson model, but to find the key vulnerable population and the key intermediate factors of MSS delivery based on the Anderson model.

18. Please provide background information on participating institutions (see remark above)

Response to comment: about adding the health care institutions’ information.

We have added the information about the health care institutions where we found the respondents. Although we did not have the exact information on whether or not they were able to provide MSS or they provided MSS, we collected the information about its level, type and location.

19. Re-write the section based on new results.

Response to comment: about re-writing the result section.

We have added the information according to your comments.

20. Please start this section with the aim of the study. Your second paragraph is the key answer to your research question and can be stated as such after the aim.

Response to comment: about re-arranging the discussion section.

We have re-written the discussion section according to your suggestion.
21. More detail can be given with: "All the five kinds of factors from Andersen's behavioral model" e.g. Just mention these factors again.

Response to comment: about providing more detail about Andersen model in discussion section.
We have added more detailed information about the Andersen model in discussion section.

22. p. 15 line 54: Please notice also that the test-uptake in the Netherlands is lower compared to the test-uptake of MSS in your study. And the introduction of MSS was not so much earlier compared to China.

Response to comment: about uptake rate of MSS service in Netherlands.
We had read the recommended papers and in our view, the lower uptake rate in Netherlands could be partly due to the fact that it was not routinely provided compared to those in other developed countries. In China, MSS has already been one of the routine services in prenatal care in many health care institutions. Therefore there were also gaps between China and Netherlands in this figure.

23. p. 17 line 27: "If the above two results were combined, one possible explanation could be that part of pregnant women missed the service not because of the expenditure for utilization but they were not provided the option or suggestion to utilize." Or is it possible that they simply did not want to opt for screening? Please look for alternative explanations.

Response to comment: about the alternative explanations of the result.
We agree with you that is was possible that the respondents simply did not want to opt for screening. And we have added other alternative explanations in the manuscript according to your suggestion. But we still think that, the most likely explanation was that they were not provided the option. And if they were definitely provided, the discussion about the reason that they declined service utilization would be meaningful.


Response to comment: about the guiding information of the recommended paper.
The recommended paper was read and cited in our manuscript.

25. p. 19 line 19: some of the discussion here should be mentioned earlier as it is very relevant for understanding the study context. Knowing this, what were your hypothesis?

Response to comment: about the context information in the discussion section.

We have added the meaningful contextual information to the background section to make the context and hypothesis of our study much more understandable.

26. p. 13 line 46: Furthermore, it was intriguing to notice that .....as low risk ones, women "

Please formulate more neutral, since this is the Result section.

Response to comment: about the writing in the result section.

We have re-written the sentence according to your suggestion.

27. Please add a paragraph on the relevance of these results internationally also given the context of NIPT being more and more available.

Response to comment: about the internationally comparison about the result and future forward.

We have added a new paragraph on the internationally result comparison and provide future prospection about MSS delivery.

In conclusion, we have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your further consideration.

We would like to express our great appreciation to you and the reviewers for valuable comments on our manuscript. We look forward to hearing from you.

Thank you and best regards.

Yours sincerely,

Chuanlin Li and Yingyao Chen