Author’s response to reviews

Title: Adherence to drug therapy for hypertensive disorders of pregnancy: a cross-sectional survey

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Version: 2 Date: 17 Dec 2019

Author’s response to reviews:

Dear editor,

Thank you very much for your letter and advice before further process for our manuscript (AOPH-D-19-00276R1). We have carefully revised the paper according to your comments. We uploaded the revision manuscript. We hope that the revision is acceptable, and we are looking forward to hearing from you soon.

Sincerely,

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Response to the editors' comments

[METHODS]

1) You have used several definitions of adherence plus underuse/overuse; What is the main endpoint? What are the secondary? Please detail.

Thank you for your valuable advice. Adherence rate is the main endpoint in our study, and underuse and overuse rates are the secondary. We detail this in “Indicators of adherece measurement” in the method.

2) You have used adherence as a continuous variable but in the multivariate analysis you have translated into dichotomous. Why, and what has been the threshold used?

We are very sorry to confuse you for our poor writing. Adherence in our study is a binary variable that is whether adherence or not, so in the multivariate analysis we used binary regression analysis. We thought the expression “Average adherence rate for drug therapy” in the “Indicators of adherence measurement” in the method may confused you, so we revised it into “Overall adherence rate for drug therapy”.

3) You have categorized evidence according to its level; however, you have used it as dichotomous in the multivariate regression. Why you have decided and what are the categories

We are very sorry to confuse you. Although we have categorized evidence according to its level, we found none of six items was moderate evidence according to Chinese guideline. So the evidence levels of these items were either high or low, and we used it as dichotomous in the multivariate regression. We add some explanation in the “Recommendation evidence measurement” in the method.

4) In addition, you have to explain why are you just running multivariate analysis for one of the endpoints.

Thank you for your valuable advice. First, we thought adherence rate are the primary indicators. Second, each item (Q1, Q2, Q3, Q4, Q5 or Q6) could be evaluated with whether adherence, but whether underuse or overuse could only be applicable to drug dosage which was the details of item 2.4 or 6 (Q2, Q4, Q6). In the multivariate analysis, analytical unit was each item for every women excluding the details of item (Q2-1, Q2-2, Q4-1, ect.). Therefore, we just running multivariate analysis for one of the endpoints. We add some explanation in the “Statistical analysis” in the method.

5) Please provide insight on how you assess the goodness of fit of your model (e.g., area under the ROC curve)

Thank you for your valuable advice. We use Pearson Chi-Squared goodness-of-fit test (P value=0.974) to assess the goodness of fit of our model. We add this information in the table 3 and “Statistical analysis” in the method.
[LIMITATIONS]

1) Discuss on the threshold that you have used (not clarified in the methods) and provide sensitivity analysis using other thresholds

We are very sorry to confuse you. According to the response for recommendation 2 and 3 [METHODS] above, adherence in our study is a binary variable that is whether adherence or not. Besides, evidence level is also a binary variable because none of six items was moderate evidence according to Chinese guideline. Therefore, we did not use threshold in our study.

2) Adherence to guidelines is professional-specific but the professional has not been included as an independent variable. If the variation across professional were high, would that have changed something in the model results?

Thank you for your valuable advice.

If the variation across professional were high, it may change something in the model results. For example, physician factors, such as unfamiliarity of the guidelines [1], lack of guideline awareness [2], and difficult to change routines and habits [3], may cause low adherence. However, data of professional characteristics were not available, so we have list it as a research limitation. We add this limitation in the discussion section.

References

3) There very likely be latent variables that would explain the lack of adherence and are not collected. An poor goodness of fit of the model would point out on that way then giving room for those unmeasured factors.

Thank you for your valuable advice.

There very likely some variables, such as physician factors (unfamiliarity of the guidelines, lack of guideline awareness, and difficult to change routines and habits), that would explain the lack of adherence and are not collected. We add this limitation in the discussion section.
4) Evidence has been treated as dichotomous factor when actually is not (strong to low evidence). Explain whether this decision might entail a limitation and whether the results would have changed.

We are very sorry to confuse you.

The same as your recommendation 3[METHODS]. Although we have categorized evidence according to its level, we found none of six items was moderate evidence according to Chinese guideline. So the evidence levels of these items were either high or low, and we used it as dichotomous in the multivariate regression. We have add some explanation in the “Recommendation evidence measurement” in the method.

5) Is there any possibility of bias when a practice has been classified as adherent? For example, when observers collect the information, is there any chance to missclassification?

When faced with uncertainty with classifying a practice as adherent, we will consult with clinical specialist, or discuss with our authors. We thought the chance to missclassification is little.

6) You have mentioned one limitation but you have not discuss on the potential of altering your findings. What do you expect less adherence in more severe/complicated patients? The other way round? Discuss

Thank you for your valuable advice.

In the former version of our manuscript, we thought “the guideline adherence for drug therapy may have been underestimated by complicated clinical conditions”. Because we thought women with complicated clinical conditions may be applicable for different clinical guideline, physician may adhere to other guidelines but not COGA guideline in some condition. However, we only pay attention to COGA guideline in our study, and other clinical guideline is not the research range of our study. Therefore, we thought this limitation is not appropriate, and delete this limitation.

7) You last comment about generalizing your results. Following your argument other hospitals with the same toll of severe cases, will not find the same results. Am I correct? However, you meaningful unit of analysis are doctors (you are looking at clinical adherence), so the reason why your results might not be transferable to other settings is very likely in the doctors’ side - different doctors working in different contexts.

Thank you for your valuable advice.

The expression of our comment about generalizing our results was not clear. So we revise the expression according to your advice. In the discussion section, the expression of this limitation revised into “Adherence to guidelines is professional-specific and different physician working in different contexts, so our results might not be transferable to other settings”.

8) The sample size might not be sufficient for the multivariate analysis. Please, estimate statistical power and discuss

Thank you for your valuable advice.
We thought the sample size may be sufficient for the multivariate analysis. Because in the logistic regression, analytical unit was each item (Q1, Q2, Q3, Q4, Q5 or Q6) for every woman, and overall items for 306 women was 647 (Standard error was clustered at the patient level). Therefore, the sample size for the multivariate analysis in our study is 647 (adherence and not adherence are 312 and 335, respectively), and the overall adherence rate is 48.22%. The amount of independent variables is 10. According to the rule of thumb that logistic models should be used with a minimum of 10 events per predictor variable[1], we estimate that the minimum sample size should be 208 ((10*10)(48.22%)). We add some explanation in the discussion section.

References