Author's response to reviews

Title: Knowledge, attitudes, and practices of parents in rural China on the use of antibiotics in children: a cross-sectional study

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Author's response to reviews: see over
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Dear Editors,

We thank the *BMC Infectious Diseases* for considering another review of our paper entitled “Knowledge, attitudes and practices of parents in rural China on the use of antibiotics in children: a cross-sectional study.” We have revised the manuscript in light of reviewers’ comments carefully with colored text (red). Below is a point-by-point explanation of our revisions with respect to each comment of reviewers.

**To reviewer 1**

**Methods**

1. Lines 113-114: The score was subsequently dichotomised using 8 as the cut-off, and the dichotomised variable used as the outcome for simple and multiple logistic regressions. This should be mentioned in this section rather than in Results section (lines 149-152)

   **Response**: Thank you for your suggestion. We have revised it in the updated version.

   Please see the section of methods.

2. Line 116: It was mentioned that "Continuous variables were reported with median and interquartile range." However, interquartile ranges were not reported in the manuscript. Perhaps, the authors would like to consider removing this?

   **Response**: Thank you. Revised.

3. Lines 153-154 - “Parents’ education status was the only factor significantly associated with the better awareness of antibiotic knowledge in multiple logistic regression analysis (Table 3).”

   - Think would be good to highlight the observation that there is a dose-response with increasing educational level.

   **Response**: Thank you. We have revised it in the updated version.

4. Interaction between parents and physicians (Line 168-187).

   These paragraphs provide important information that could guide interventions to improve antibiotic use. However, the data is not displayed. Can the authors present a table on the main findings please?

   **Response**: Thank you for your suggestion. Indeed it will be clearer to display the result in table, however, the questions about interaction between parents and physicians were dispersed in three different parts of our questionnaire. They had different categories and standards, such as from never to always, from strongly disagree to strongly agree, etc. So we have to present them separately.
5. Line 183 - "Most parents (82%, CI, 80%-85%) reported that..." what is the purpose of presenting the 95% CI in this statement?

Response: Thank you. We have revised it in the updated version.

6. Lines 203-209
- For the ORs presented here, think it's important to present the adj OR and 95% CI.
- And, to mention that these are factors independently associated with self-medication of children, after adjusting for potential confounding.

Response: Thank your suggestion. Actually, the ORs in text were adjusted ORs, the same with those indicated in Table 5. We revised the former sentence into" After adjusting for potential confounding factors using multiple logistic regression, self-dedication of children with antibiotics was significantly associated with......", so that readers would not confuse the adjusted ORs presented in text as crude ORs. We also added the 95% CI following ORs in the updated version.

To reviewer 2
1. The title referred to “rural China”. Please clarify on this since the study consisted of parents from rural villages and central towns.

Response: According to the China Statistical Yearbook published by National Bureau of Statistics of China, the administration under each province has three levels: regions at Prefecture level, regions at county level and regions at township Level. The county and township refer to rural areas and township is at the lowest administrative level which is usually composed by 10-20 villages and 1 town. The central towns in our study were the town under the administration of township. Compared to village, central towns are usually more populated with a bit better living and working conditions. But they are still in rural area.

2. Methods (Para 1): Please clarify the time period of the study.

Response: Thank you for your suggestion, and we have clarified it in the updated version. The study was carried out in March-May of 2012, with subjects’ recruitment from March 14-24 in country A and May 11-25 in county B. Subjects were recruited consecutively during the recruiting weeks.

3. Methods (Para 2): Regarding survey subject recruitment, please provide more details on how the survey participants were enrolled including total number of parents invited and the eventual response rate.

Response: it is a pity that we didn't record the number of parents who refused to participate in our survey. However there were very few parents (less than 5 parents in each county) who refused. The vaccination is under the national Expanded Program
on Immunization (EPI), and children should stay for about 20 minutes for adverse event observation following the inoculation. We did our investigation during their waiting time. All the parents were very friendly to us, and the few parents who could not join us were mainly because of being hurry or the baby making too many troubles. Anyway it was a mistake not recording those who refused. The students have learnt the lessons and this won't happen in future.

4. Statistics: Please provide more details on construction of the multiple logistic regression models and how the best model was chosen.

**Response:** Thank you. According to the advances in modern epidemiology, here we adopted Rothman’s sufficient causal model in our analysis, i.e., we constructed the model first. We started from defining all the independent variables; then, instead of using forward or backward stepwise models, we used the enter model, and got the adjusted ORs for all independent variables as reported.

5. Results (Para 4): Please clarify which the groups were being compared (30% vs. 11%).

**Response:** Thank you for your suggestion. We have clarified the two groups in the updated manuscript as follows. A sizeable minority (43%) believed that antibiotics could protect children from the common cold, and these parents were more likely to give their children preventative antibiotics than those who knew that antibiotics could not prevent the common cold (30 vs. 11%, \( \chi^2 = 62.852, P < .001 \)).

6. Table 2: The column on “answer” can be very confusing for the readers. The table should be constructed as numbers and percentage of respondents who agree with the questions i.e. all answers as “Yes” as was presented in Table 4.

**Response:** Thanks. The 14 questions in Table 2 aimed to examine the parents' knowledge on antibiotic use. Through Table 2, we wanted to list the correct answer of each question as well as the number and proportion of parents who answered them correctly. In order to make it clearer, we have made revision on the two columns accordingly.

7. Table 3 and 5: Please provide confidence interval for “College or above”

**Response:** Thank you. In table 3 and table 5, the "College or above" is the reference group (dummy variable) in the analysis of education, so there are no confidence interval for it.

8. Discussion: Please comment on the generalizability of the study results. Would there be any possibility of selection bias.
Response: Thank you for your suggestion. There were selection biases in this field study indeed. For example, we did the study in vaccination clinics. According to the EPI in China, young children (0-3yr) might visit the clinics more frequently. Thus, part of parents we recruited might be less experienced in terms of children’s condition and treatment. We have addressed this in the section of methodology considerations.

Another limitation is the study was carried out in only 2 of the more than 2500 counties in China. We won’t say it would be a good representative to all rural China. But the counties are in the low-middle economic level of China, and the general development and health indicators of these counties suggested that the problems we found in this study should be also observable in other similar rural areas. In this manuscript, we don’t think it is appropriate to say the results could be generalized to all China, although we do think that findings from this study have its impacts on understanding the problem in rural areas and are helpful for developing effective interventions.

9. Discussion: Please address the concern that since this was a self-administered questionnaire, how could the investigators be certain that respondents were able to fully understand the questionnaire content? Would there be a possibility that respondents had mistaken other medications for antibiotics.

Response: Thank for your suggestion. The quality of survey was the key concern to us. Below is what we had done for quality assurance.

All the data collectors are graduate students specialized in epidemiology with experiences on field investigations in School of Public Health, Fudan University. Before the initiation of the survey, the data collectors received specific training with unified guidelines for the questionnaires.

As to the concerns that respondents may mistake other medications for antibiotics, we also took some ways to reduce the happening. Before the initiation of the study, we had monitored the antibiotic sales in the biggest pharmacy of each county for several months. We selected several antibiotics with top sales, such as amoxicillin, cephradine, norfloxacin, etc., as the examples to present to parents what are antibiotics referred in this investigation, and we also presented what are not antibiotics which were most frequently used in local.

We have also carried out a pilot study for improving the clarity of each question. Thus, we believe although there might be information bias, the probability that respondents mistake other medications for antibiotics should be very low.

10. Discussion: Please provide some insights on how results in this study compares to other studies conducted in China.
Response: Yes. It is essential to compare with other studies conducted in China on the same issue, and we have searched the related publications. Most of the studies on antibiotic resistance in China are based on the molecular mechanism and there are limited publications concerning Chinese parents' KAP on antibiotic use, especially in rural China. Among those papers we found and referred in our manuscript, the research questions are varied. Some paid attention to the perceptions of citizens in urban areas[1]; some kept their eyes on the relationship between patients and physicians[2]; also there is one paper discussing similar questions from a different perspective[3]. Considering the wide coverage of topics, we referred 6 papers about China together with international ones in different paragraphs and sections. It is a bit difficult to round up the comparison in one paragraph considering the logic and continuity of each paragraph and the whole article.

11. Discussion (Limitations): Please discuss on the external validity of current study.

Response: Thank you. We believe the problem of inappropriate use of antibiotics on children is universal, especially among poor population in less developed countries. Thus, we hope the impacts of our study findings could be shared internationally.

In terms of external validity, as mentioned above, this study was small and the limitation in generalizability is inevitable. But it should be relevant to population in the similar setting. The study subjects we defined were parents of children who receive routine immunization in the designated vaccination clinics. In this way, we hope to improve the representativeness of subjects. We have also calculated the sample sized based on pilot study which gave the study itself a relatively good study power.

But the study counties we choose was located in central China, in a resource-limited area compared with those provinces in East Coast. Consequently, the KAP on health and healthcare among people living in developed areas might be somehow better than our respondents.

12. Discussion (Limitations): Please address how the investigators can be certain that respondents understood the questionnaires and knew that they were referring to antibiotics.

Response: Thank you. Please see the response to No. 9 above.

On behalf of my co-authors, I thank the reviewers and editors for their insightful comments and suggestions. We feel the incorporation of this feedback has greatly improved this revised manuscript.

The language in our manuscript has been edited thoroughly by a native-English speaker with scientific expertise in related field from Edanz. Please find the Certificate of English Editing for our manuscript attached in the additional file.
Sincerely,
Biao Xu

Reference