

Dear Fang-Fang Ji,

We sincerely thank the reviewers for their thorough review and valuable comments on our manuscript entitled “**Treating chronic hepatitis B virus: Chinese physicians’ awareness of the 2010 guidelines**”. Below, please find our responses to each comment. Changes that were made in the document in an effort to address the comments are shown in track changes.

Comment	Response	Changes made in manuscript
Reviewer 00011164		
A. The article is about the levels of awareness of the physician to the 2010 guidelines, but nothing is said about the usage of these guidelines in other countries	We thank you for pointing out this shortcoming in the Introduction of our manuscript. We have updated the manuscript with general information about physician adherence to clinical practice guidelines. Currently, there is limited published data on the rate of adherence to these specific guidelines in various countries across the globe. Nonetheless, we have added some data regarding physician adherence to HBV treatment guidelines for patients with HBV/HIV co-infection	We have added the following text in the Introduction part of the manuscript:  It is known that the implementation of treatment guidelines in clinical practice can improve the outcome of patients, but despite wide promulgation, many guidelines are not readily accepted by physicians or incorporated in clinical management strategies <sup>[11]</sup> . There is some evidence of poor adherence to HBV treatment guidelines among healthcare providers in the United States who treat HBV/HIV co-infected patients <sup>[12]</sup> , but in general, real-world clinical practice with CHB guidelines is not well understood. In China, the prevalence of HBV is high <sup>[13,14]</sup> and physician adherence to CHB treatment guidelines could potentially have an important impact on the long-term outcome of a large proportion of the CHB population.
B. Non-specific facts in the introduction should be deleted	We thank you for your advice. We have deleted non-specific information and considerably shortened the Introduction of our manuscript.	
C. The discussion part can be reduced	We thank you for your advice and considerably shortened the Discussion	
Reviewer 00504271		
1. The manuscript should be revised for non-Chinese audiences	We thank you for your advice. We have now included information in the manuscript to explain the China-specific information, such as the hospital grading and city tier classification.	We have added the following text to page 8, paragraph 1 (Methods section)  In China, the Ministry of Health grades hospitals according to a three-grade system, which assesses a hospital’s ability to provide medical care and medical education, and to conduct medical research. In general, grade III hospitals are considered the highest level in China. These hospitals are able to provide high quality, specialized care in well-equipped facilities. Considering

		<p>the availability of medical education and specialized care at grade III hospitals, in general, physicians at these hospitals are thought to at the forefront of clinical medicine.</p> <p>and page 10, paragraph 1 (Results section)</p> <p>(In China, cities are ranked into tiers (tier I through IV) according to size and economic development, with tier I cities generally the largest economical hubs.)</p>
2. Are there any differences between physicians working in grade I, II or III hospitals	Considering that grade III hospitals have specialized facilities and medical education, specialist physicians are more concentrated in these hospitals. We have updated our manuscript to provide clarity on this.	<p>See page 8, paragraph 1 (Methods section), also cited below:</p> <p>These hospitals are able to provide high quality, specialized care in well-equipped facilities. Considering the availability of medical education and specialized care at grade III hospitals, in general, physicians at these hospitals are thought to at the forefront of clinical medicine.</p>
3. The gender difference is mentioned, but it is not clear if it is important	We have noticed the gender difference in our survey respondents. However, we believe this is merely a random effect. We have therefore not analyzed or discussed this further in the manuscript	No changes made
4. Interpretation of Fig. 4 is difficult to understand	We have updated the figure legend so as to better describe the information in Figure 4.	<p>Please see Fig 4 Legend and citation below:</p> <p><b>Figure 4 Physician familiarity with various indications for antiviral medication</b></p> <p>Physician familiarity with the different indications for antiviral medication as described in the Chinese chronic hepatitis B (CHB) guidelines<sup>12</sup> is depicted here. The various indications are listed on the left. Physicians were asked, ‘Does antiviral medication apply to the following cases?’ and the proportion of physicians who would consider antivirals, no antivirals, and follow-up for each indication, is depicted in each horizontal bar.</p>
5. The 3 <sup>rd</sup> paragraph on p. 10 is confusing and the discussion on the same topic (p. 13) is also confusing	We have reworded these sections so as to more clearly describe our findings.	<p>Please see updated text below:</p> <p>Most physicians used antiviral medications consistent with guideline recommendations. However, in patients older than 40 years, who were HBV DNA-positive (but with <math>&lt;1 \times 10^4</math> copies/mL), and with alanine</p>

		aminotransferase (ALT) levels above the upper limit of normal (ULN), 196 (39%) of the surveyed physicians did not consider antiviral medication necessary (Figure 4). The guideline recommends that in these patients, the presence of liver fibrosis (as judged by the physician), should be an indication for antiviral therapy.
6. The authors speculate as to why adherence to guidelines was the lowest in Northwest China. The reasons should be statistically analyzed	Northwest respondents were mainly concentrated in lower level facilities. Also, the Northwest territories have a poor compliance to guidelines. Whether there is a causal relationship between these 2 factors is not clear. Unfortunately, it would not be possible for us to re-do our statistical analysis at this stage.	We have updated the text related to Northwest respondents in the discussion section:  In Northwest China, the percentage of physicians who adhered to the guideline was noticeably lower than in other regions.
7. The title should be “Treating chronic hepatitis B virus in China. Chinese physicians’ awareness of the 2010 guidelines’	Thank you for your suggestion. Considering the formatting requirements of the journal, we are limited to the word count (12 words) and therefore did not make any changes to the title	
Editor		
1. Any manuscript describing a study (basic research and clinical research) that used biostatistics must include a statement in the Materials and Methods section affirming that the statistical review of the study was performed by a biomedical statistician.	Thank you for your guidance. We have added a data statement in the Materials and Methods Section under the subheading: Data analyses	The following text was added to the last paragraph of the Methods Section” The statistical methods of this study were reviewed by Qing-Qing Dai of SmithStreet. No statistical tests were performed. The data are presented as percentages and described.

