

June 1, 2022

Re: Submission of a Revised manuscript to the World Journal of Clinical Cases

Dear Editors and Editorial Committee,

Thank you very much for giving us the opportunity to revise our invited review (Manuscript number: 76792)

We would be grateful for the consideration of our revised manuscript “Glucose substrate in the hydrogen breath test for gut microbiota determination: a recommended non-invasive test” (by Yuanlong Gu, Wei Shen, Zhipeng Li, Bo Zhou, Zijun Lin and Lianping He) for publication in the World Journal of Clinical Cases. The authors have read and complied with author guidelines, and they all have seen and approved this manuscript for publication. None of the authors had a conflict of interest to disclose concerning this manuscript.

We are grateful to the Editors for their precious contributions and comments. We have revised our manuscript accordingly for grammar, style, structure and we hope that you will now find it suitable for publication in the World Journal of Gastroenterology. In case of final acceptance, we agree to make this manuscript open-access.

The changes in the manuscript are identified in track change mode. Below you can find a point-by-point reply to the reviewers. We used red to denote revised or inserted text.

Thank you for your precious time.

We are looking forward to receiving your decision in due time.

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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

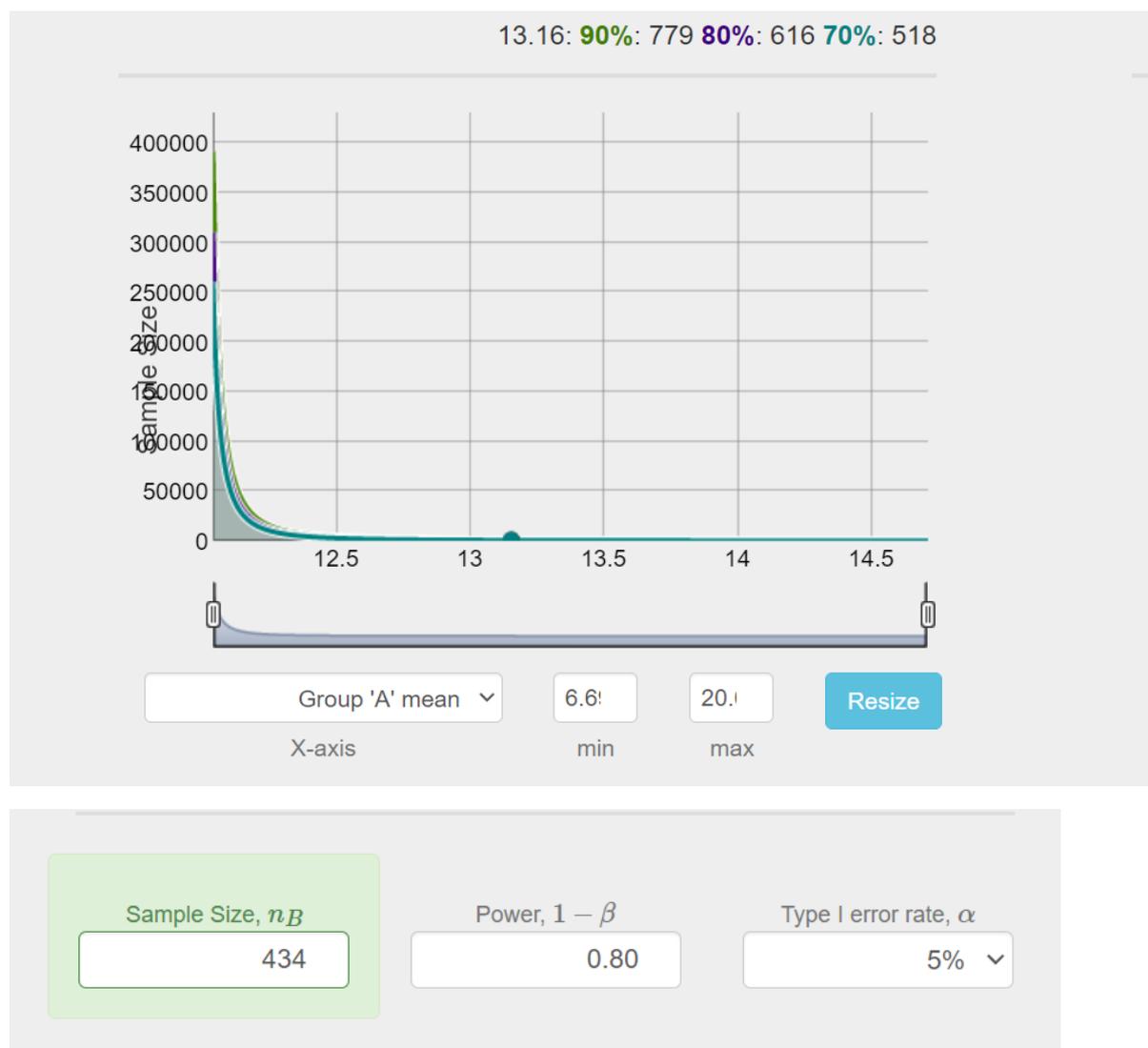
Specific Comments to Authors: In principal i agree with the suggestions provided in this letter to editor, but i have the following suggestions: 1. I agree that using glucose as a substrate is more sensitive than using lactulose as substrate in detecting SIBO, but it has been reported as well that different substrates can detect bacterial growth in different areas of the small intestine. Glucose is a sugar that is fermented in the upper (proximal) part of the small intestine; while lactulose is fermented in the lower (distal) part of the small intestine. therefore using a combination of both could be also recommended. 2. I agree that the sample size in the study should be higher, but i recommend the authors to include a justification (or an excuse) for using this samples size, for instance, " although a larger sample size is recommended in this study, but it is worth mentioning that recruiting a high number of cirrhosis patients is difficult".

Response:

Thank you for your patience in reading our article. We humbly accept your comments on us. After reading your comments in detail, we agree that our article does have the above problems.

1. Thank you for your patience in reading our article. We humbly accept your suggestions. Regarding your proposal to use the combination of glucose and lactulose as an indicator for the detection of SIBO, we think it is feasible, but our article aims to emphasize the advantages of glucose as a substrate, and there is no conflict with your point of view, thank you your suggestion.

2. Regarding the sample size, we have estimated the sample size, aiming to suggest that the sample size is insufficient. Therefore, we suggest that researchers expand the sample size when conditions permit to make the research report more scientific.



Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: " SIBO may be caused by cirrhosis, or it could be a mechanism of gastrointestinal diseases." should be changed to "The etiology of IBO apart from cirrhosis be considered" "We recommend that investigators investigate the gastrointestinal disease" should be change to " We recommend insvestigators exclude confounding gastroinstestinal diseases...."

Response:

Thank you for your suggestions for our article, and we accept your revisions to our

article. We have made the following changes to the article with reference to your suggestions.

" SIBO may be caused by cirrhosis, or it could be a mechanism of gastrointestinal diseases." changed to "Apart from liver cirrhosis, SIBO may also be caused by gastrointestinal diseases."

"We recommend that investigators investigate the gastrointestinal disease" change to " We recommend investigators exclude confounding gastrointestinal diseases...."

Science editor:

- 1.The authors should use a combination of glucose and lactulose as substrate in detecting SIBO.
2. The authors should include a justification for using the samples size.
3. The language still need to be corrected.

Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

Response:

Thank you for your suggestion to our article.

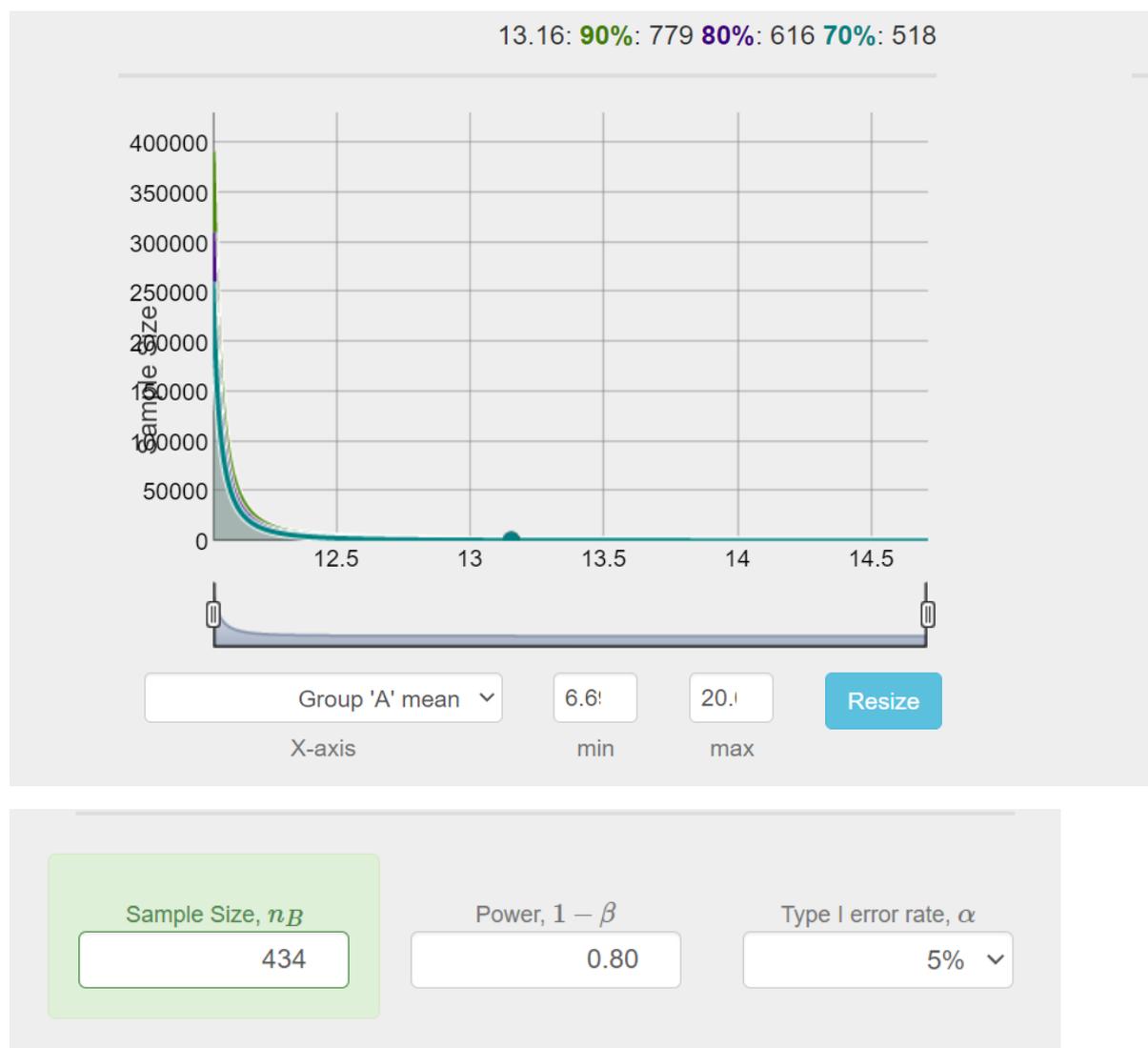
1. Thank you for your patience in reading our article. We humbly accept your suggestions. Regarding your proposal to use the combination of glucose and lactulose as an indicator for the detection of SIBO, we think it is feasible, but our article aims to emphasize the advantages of glucose as a substrate, and there is no conflict with your point of view, thank you your suggestion.

2.According to the study by Yao, we estimated the sample size of SIBO patients with liver cirrhosis (power and sample size calculation), and concluded that a sample value of about 400 cases is reasonable.

3. We have made the following corrections to the language.

" SIBO may be caused by cirrhosis, or it could be a mechanism of gastrointestinal diseases." changed to "Apart from liver cirrhosis, SIBO may also be caused by gastrointestinal diseases."

"We recommend that investigators investigate the gastrointestinal disease" change to " We recommend investigators exclude confounding gastrointestinal diseases...."



Company editor-in-chief:

I recommend the manuscript to be published in the World Journal of Clinical Cases. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

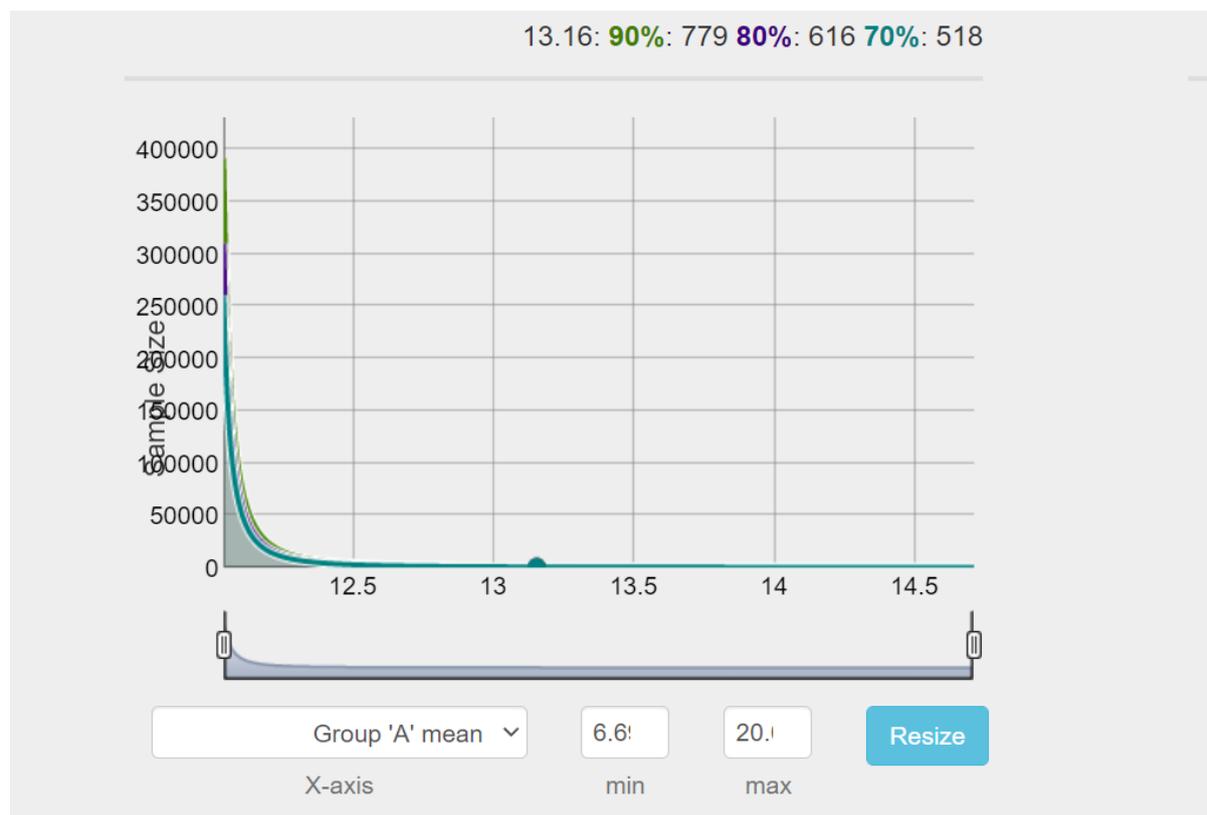
Response:

Thanks for your suggestion, we've polished the language of the article and delved into the science of the article. And referring to your suggestion, the keywords of the article are perfected according to RCA. The detailed modification is as follows.

" SIBO may be caused by cirrhosis, or it could be a mechanism of gastrointestinal diseases." changed to "Apart from liver cirrhosis, SIBO may also be caused by gastrointestinal diseases."

"We recommend that investigators investigate the gastrointestinal disease" change to " We recommend investigators exclude confounding gastrointestinal diseases...."

We evaluated the sample size and the evaluation results are as follows.



Sample Size, n_B	Power, $1 - \beta$	Type I error rate, α
<input type="text" value="434"/>	<input type="text" value="0.80"/>	<input type="text" value="5%"/>