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Dear Editor,



**Title:** Standard triple therapy for *Helicobacter pylori* infection in China: A meta-analysis

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Thank you for the reviewers' comments concerning our manuscript. These comments are all valuable and have helped us to revise and improve our manuscript. Additionally, these comments have improved the significance of our research. We have made careful modifications to the original manuscript based on these comments and suggestions. All of the changes made to the manuscript are highlighted. In addition, we have consulted native English speakers for revisions before resubmitting. We hope the new manuscript will meet your journal's standard for publication. The manuscript has been improved according to the suggestions of reviewers:

1 The format has been updated.

2 Revisions have been made according to the suggestions of the reviewers.

Responses to the first peer-reviewer (Reviewer code: 02460199)

(1) Comment 1: In the section "Search Strategy" in methods, it was mentioned databases that were not found at abstract and results, such as Science Citation Index and CNKI. Were these databases really used? If yes, why weren't they included in the results?

Answer: We apologize for our negligence of the Science Citation Index database, which we mentioned in the section "Search Strategy" of the methods. We searched the Science Citation Index database and found that the studies that met our inclusion criteria had already been selected from PubMed, Embase and the Cochrane Central Register of Controlled Trials. Thus, we did not show the results of this database, and it should not affect our meta-analysis. We apologize for our failure to delete this database from the text. CNKI was used for the search and it has been included in the results. We are sorry for this negligence. We really thank you for this comment which makes our paper more exact.

(2) Comment 2: In the section "Statistical Analysis", it is not reported the statistical method used, in this case, the Mantel Haenszel. And it is not reported which value for  $p$  was considered statistical significant ( $p < 0.05$ )?

Answer: The Mantel-Haenszel statistical method has been added to the section "Statistical Analysis". We have indicated that  $P$ -value less than 0.05 were considered statistically significant.

(3) Comment 3: In the section "Data Analysis" it is mention that it was evaluated the methodological quality of the studies by jadad score, however, these results are not showed. The issue quality is only covered in the section strengths and limitations.

Answer: The Jadad score has been added in table 1.

(4) Comment 4: In the comparison standard triple therapy versus dual therapy is found a  $I^2$  value equal to 63%. Sensibility analysis were carried out for this comparison? If yes, why these results were not showed?

Answer: In the comparison of standard triple therapy versus dual therapy, the results of the Sensibility analysis has been added. We apologize for omitting these results in the original submission.

(5) Comment 5: In the comparison standard triple therapy versus sequential therapy is not informed the  $I^2$  value found for the adverse events meta-analysis.

Answer:  $I^2$  value has been added in the adverse events meta-analysis of the comparison of

standard triple therapy versus sequential therapy.

(6) Comment 6: In the graphics showed, it was not reported the  $I^2$  value obtained in neither meta-analysis.

Answer: The graphics were exported by CMA 2.0, which did not show the  $I^2$  value. Thus, we have added the  $I^2$  value through Photoshop.

(7) Comment 7: Despite of it was reported the sensibility analysis that were carried out, it was not reported the  $I^2$  values obtained after these analyses were performed.

Answer: We have added table 2, which includes all the RRs and  $I^2$  value.

(8) Comment 8: Due the great number of results, you should put them in a table, removing a good part of the text and making easier the comprehension by the reader.

Answer: We have put the results in table 2 to improve comprehension by the reader.

(9) Comment 9: In the section "Strengths and Limitations" it is reported that was performed meta-regression analysis, but these results were not showed.

Answer: It is our negligence that we reported meta-regression analysis was performed in the section "Strengths and Limitations". The exact word was "sensitivity analyses". It was our mistake to mistype the wrong word "meta-regression analysis" which confused you. We have changed "meta-regression analysis" into "sensitivity analyses". We decided not to perform meta-regression analysis because we have performed many sub-analyses and sensitivity analyses to assess the heterogeneity.

Thank you very much for your comments and suggestions.

Responses to the second peer-reviewer (Reviewer code: 00618257 )

(1) Comment 1: Abstract: - Background: o Please write the meaning of the achronym "PPI" o "clarithromycin" is mistyped

Answer: The meaning of the "PPI" has been written as "Proton pump inhibitors" when it first appeared in the paper. The clarithromycin has been corrected in the background which we removed from the abstract into comments according to the format of structured abstract given in the writing requirements of meta-analysis. We are very sorry for our incorrect writing.

(2) Comment 2: Aim: Delete "thereby providing a glimpse of the changing eradication rates of this standard regimen in China"

Answer: "Thereby providing a glimpse of the changing eradication rates of this standard regimen in China" has been deleted in the aim. The aim is limited to no more than 20 words, so we revised it as follows: "To assess the efficacy and safety of standard triple therapy compared with other pre-existing and new therapies in China."

(3) Comment 3: Methods: o Please write the meaning of the achronym "VIP"

Answer: "VIP" is not an acronym. It is a Chinese database, the full name of which is also VIP.

(4) Comment 4: Results: There is controversy if IC95% that include the RR = 1 should be considered "marginally superior"

Answer: We agree with your suggestion that it is controversial whether the 95% CI that includes the RR = 1 should be considered "marginally superior". Therefore, we revised our description to "The meta-analysis also suggested that standard triple therapy is slightly more effective than dual therapy [RR=1.14; 95% confidence interval (CI), 0.99-1.31]. Nevertheless, the differences were not statistically significant."

(5) Comment 5: Text Body: - Methods: o The specific search algorithm used for each database should be provided.

Answer: The specific search algorithm used for each database has been provided: PubMed - ((Amoxicillin) AND Clarithromycin) AND triple)) AND "Helicobacter pylori"[Mesh], Filters: Randomized Controlled Trial; Embase-(*helicobacter pylori*/exp and 'amoxicillin'/exp and 'clarithromycin'/exp and triple and 'human'/de and 'randomized controlled trial'/de); the Cochrane Central Register of Controlled Trials-(Amoxicillin AND Clarithromycin AND triple AND *Helicobacter pylori*); the VIP database, CNKI database and CBM database-(searching with the

following keywords: "helicobacter pylori", "amoxicillin", "clarithromycin" and "triple")

(6) Comment 6: Exclusion criteria should be provided.

Answer: The exclusion criteria have been provided: 1) articles and/or abstracts not reporting tests used to diagnose infection and/or to follow-up infection were not included; 2) articles and/or abstracts not conducted on the Chinese mainland; and 3) articles with inappropriate treatments in the control group or standard triple group, such as using traditional Chinese medicine or probiotics.

Thank you very much for your comments and suggestions.

3 The abstract has been revised.

4 The major suggestions and comments have been added and considered.

6 Table 2, which includes all the results, has been added.

7 The pooled RR of the meta-analysis of the comparison "standard triple therapy versus sequential therapy" has been changed from 0.87 (95% CI, 0.831-0.911) into 0.863 (95% CI, 0.824-0.904) when we found the data of one study included was mistyped. This change does not affect the original conclusions and discussions for there are no significant differences between these two RRs.

8 The figures have been reformatted.

9 The references and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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