

Dear Editor and reviewers,

**Title:** Fourth-generation quinolones in the treatment of *Helicobacter pylori* infection: a meta-analysis

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**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 39203

**Manuscript Type: META-ANALYSIS**

Thank you for your letter and the reviewers' valuable comments concerning our manuscript. These comments are all helpful for us to reconsider the strengths and weaknesses of our manuscript. As well, these comments have improved the significance of our research. We have made careful revisions 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 updated according to the Guidelines and Requirements for Manuscript Revision and the Format for Manuscript Revision. Additionally, revisions have been made according to the suggestions of the reviewers:

Responses to the third peer-reviewer (Reviewer code: 03476682)

- (1) **Comment 1:** Methods please describe any efforts to address potential sources of bias.

**Answer:** The efforts to address potential sources of bias have been added to the section "Risk of bias" of "MATERIALS AND METHODS". Two independent reviewers assessed the risk of bias through six domain-based evaluations according to the Cochrane Handbook for Systematic Reviews of Interventions, including selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting) and other bias. Each indicator was scored by low risk of bias, unclear risk of bias and high risk of bias. Any disagreement was discussed and decided by a third reviewer.

- (2) **Comment 2:** Subgroup analyses: In the Europe subgroup, the pooled eradication rates of control group and experimental were 74.0% (347/469) and 89.1% (399/448) respectively by ITT analysis (OR=0.661; 95%CI: 0.447-0.977; P=0.000), and 78.5% (347/442) vs 91.3% (399/437) respectively by PP analysis (OR=0.361; 95%CI: 0.240-1.016; P=0.000). You concluded that, the use of the fourth-generation quinolones in Europe can significantly improve the eradication rate. I think is missing the concept, because, 95%CI: include 1 (0.240-1.016). Please revise the result.

**Answer:** We apologize for our negligence to mistype the wrong data "95%CI: 0.240-1.016". The 95%CI in the Europe subgroup was "0.240-0.544" by PP analysis. We are so sorry for this mistake. We really thank you for this comment which makes

our paper more exact.

- (3) **Comment 3:** Discussion     Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.

**Answer:** Any potential bias has been added in the discussion. We have analyzed potential bias that led to the unreliability of our conclusion. The problems with concealment of allocation and blinding caused the selection bias. The restrictions on the language of publication implied other bias. All included studies were performed in Europe and Asia led to the conclusion bias, and so on.

- (4) **Comment 4:** I have minor concerns regarding the English language used in this manuscript.

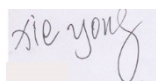
**Answer:** We are so sorry for the English language used in this manuscript. And then, we have referred a native-English speaker of Corporation of American Journal Experts to edit our manuscript.

- (5) **Comment 5:** Please at the end of discussion summarizing the work/describing conclusions and pointing out the future directions in the field.

**Answer:** Summary and future directions in the field have been added at the end of discussion. Therapies containing fourth-generation quinolones can achieve a higher eradication rate of *H. pylori* infection, but the eradication rate remains poor. So, we suggested such regimens as a rescue treatment based on antimicrobial susceptibility testing. We will draw more solid conclusions about the use of fourth-generation quinolones in the treatment of *H. pylori* infection and study more effective therapies for *H. pylori* infection if necessary.

Thank you very much again for your letter and all reviewers' comments and suggestions.

Sincerely yours,



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