Author’s response to reviews

Title: Diabetes, insulin use and Helicobacter pylori eradication: a retrospective cohort study

Authors:

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Author’s response to reviews:

Dear Editor,

The manuscript has been revised taking into account all the comments from the referees. The structure and references have been revised according to the styles of the journal. The title has been modified to include the “study design” as required by the Journal.

Please kindly note that the major revised parts are highlighted in red color in the revised manuscript for your convenience of re-reviewing.

The followings are the point-by-point responses to the comments of the referees.

Referee 1
Reviewer: Kazunari Murakami

1. In the manuscript, a phrase of “the risk of HP eradication” appears frequently. “Risk” may be often used as an epidemiological term, but the word “incidence” may be better. It should be changed.
Response: Done accordingly.

2. Page 9, line 16, please explain the mean of “a higher activity of HP infection in the diabetic patients”
Response: The last few sentences in this paragraph have been revised to give a clearer explanation of the meaning (Page 10, second paragraph of Discussion).

3. Page 10, line 11, Authors mention that HP eradication dose not related on the reduction of intestinal metaplasia (IM). But there are a lot of papers which mention improvement of IM after HP eradication. Authors should refer them for discussion.
Response: Thank you for your comments. This paragraph has been rewritten and some recently published references have been cited (Page 11, third paragraph).

Referee 2
Reviewer: David Whiteman

1. Is the question posed by the author well defined? No, the author has not explicitly stated their research question as a clearly testable hypothesis; rather, the question is implied in the title and in the Introduction to the study. This is a MINOR ESSENTIAL REVISION
Response: The title of the manuscript has been modified to fit the requirement of the Journal to refer to the study design. Furthermore, the last paragraph of the Introduction has been revised to clearly state the testable hypothesis of the study (Page 4, last paragraph).

2. Are the methods appropriate and well described? No. I am not clear that I understand how exposure and outcome were defined. It is not stated explicitly whether the intent of the analysis was to constrain H pylori eradication to occur only AFTER diabetes was diagnosed, or whether it could occur at any time within the study interval. The former would imply that diabetes preceded H pylori treatment, and might therefore imply some temporal order. This has major implications for interpreting the analysis. Most readers would be expecting a retrospective cohort design, in which the cohort has been defined by date of assembly, and that the diagnosis of diabetes must precede the date of eradication of H pylori. Is this what happened? It appears not, and that there is simply an attempt to assess a cross-sectional association. This is a MAJOR ESSENTIAL REVISION
Response: In the previous version, though not explicitly described, we did consider the temporal order of exposure before outcome. An additional paragraph has been added in the revised manuscript to clarify the correctness of the temporal order (Page 7, first paragraph of “Statistical analyses”).

3. Are the data sound? The data were obtained from the national health insurance records of Taiwan. They are likely to be reasonably complete, and are not likely to be biased with respect to diabetes status or records of H pylori eradication. However, I suspect that there is considerable under-diagnosis and under-treatment of H pylori in this population. Some comment from the investigators is required. This is a MINOR ESSENTIAL REVISION
Response: The possibility of under-diagnosis and under-treatment of HP infection in the population is considered as a limitation of the study and is mentioned in the revised version (Page 12, last paragraph).