

Responses to Reviewers' comments

To Reviewer #1

Comments: This is an interesting study and only problem is in retrospective nature. It has original findings and proof for enhancement of other GI disorders while reducing the *H. pylori* gastritis. The quality of manuscript is acceptable and would be important to interested community. However, *H. pylori* diagnostic methods were not included. Also, better to compare 2 triple therapies in related to cure as well as development of other GI disorders.

Response: Thank you for your valuable comments and suggestions. In this study, we could only use information recorded in health insurance claims, and *Helicobacter pylori* diagnostic methods and results were not recorded. We defined target patients as those who received *H. pylori* eradication therapy based on prescriptions of medications approved for primary *H. pylori* eradication therapy in the *Patients* subsection of the MATERIALS AND METHODS (page 8, lines 22–28). We understand that the two triple therapies you suggested are PPI-based therapy and P-CAB-based therapy, and we agree it is better to compare these therapies in relation to the cure as well as the development of other gastrointestinal disorders. However, we cannot perform additional analyses because we had to delete the raw data and interim analysis data after the authorized research period, as described in the Data sharing statement. Moreover, information regarding the resolution of *H. pylori* infection was not included in the database. We have highlighted the lack of information on the results of eradication therapy in the database in the *Limits of the study* subsection of the DISCUSSION (page 18, lines 10–11).

To Reviewer #2

Comments: Mizukami et al. presented a retrospective cohort study on the analysis of the effect of eradication therapy of *Helicobacter pylori* on the development of diseases of the digestive system, allergic diseases and metabolic syndrome. The design of the study is well organized. The title, abstract and keywords correspond to the text of the article.

Materials and methods are described in detail and clearly. The authors carried out a huge and important work on a large population material: more than 5 million people were included in the study. Correct methods of statistical processing of the obtained data were used. The authors refer appropriately to the most recent and up-to-date references. In recent years, review publications have appeared discussing both the positive and negative role of *Helicobacter pylori* eradication on the development of diseases of the digestive system, allergic diseases, metabolic syndrome, etc. (<https://www.wjgnet.com/1007-9327/full/v27/i7/545>; DOI: 10.3748/wjg.v28.i7.766). The work presented by the Mizukami et al. is an original study performed on a huge clinical material, which confirms not only the positive, well-known, effect of eradication on the course and development of gastritis, gastric ulcer and duodenal ulcer, but also convincingly shows the negative role of eradication of *Helicobacter pylori* on the development of Barrett's esophagus, inflammatory bowel diseases, allergic diseases and metabolic syndrome. This is a huge merit of the authors. The data obtained by the authors are important for understanding the role of *Helicobacter pylori* for humans. The ambiguity of this bacterium for the macroorganism and the need for a more balanced approach to the implementation of eradication therapy are shown.

Responses: Thank you for your favorable comments and helpful insights. As you suggested, both the positive and negative effects of *Helicobacter pylori* eradication have been discussed. Our study examined the effects of *H. pylori* eradication and found both beneficial and unwanted effects, particularly an increase in the occurrence of allergic diseases. This is an original, novel finding that requires further validation in other populations. We believe that the information provided in this study could stimulate further research on the advantages and disadvantages of the eradication therapy. When considering the large-scale implementation of this eradication therapy, such information bears crucial importance.

To Reviewer #3

Comments: It is an interesting manuscript. but What are the original findings of this manuscript? What are the new hypotheses that this study proposed? What are the new findings of this study? What are the new concepts that this study proposes?

Response: Thank you for your review and valuable comments. While *Helicobacter pylori* eradication therapy has been verified to prevent some diseases, potentially unfavorable effects have also been identified. Therefore, we considered that a comprehensive study on both the positive and negative effects was necessary to evaluate the value of *H. pylori* eradication. To our knowledge, this is the first comprehensive study to examine the effects of *H. pylori* eradication therapy using a large-scale database in Japan. The results revealed not only beneficial effects on gastritis and gastric and peptic ulcers but also unfavorable effects in terms of the development of other concerning diseases. In particular, the estimated number needed to harm (NNH) for 3 years before and after eradication was 12.3 for allergic diseases; this is an original finding that has not been reported in the past. We have highlighted this finding in the first paragraph of the DISCUSSION (page 14, lines 9–12). We have also described this point in the ARTICLE HIGHLIGHTS, which were required in the revised manuscript.

With regard to language, the manuscript was checked by a specialist editor from a professional English language editing company before the original submission, and it has been checked again after revisions based on the comments of the reviewers.