

Reply for reviewers

We are grateful for the reviewer's critical comments and useful suggestions that have helped us to improve our paper considerably (Manuscript ID:58328). As indicated in the following responses, we have incorporated all these comments into the revised version of our paper. The changes are shown in red text in the manuscript.

Reviewer #1

The manuscript provides the data of a national study on the correlation between meteorological factors and healthcare utilization related to GERD. Several considerations were taken into the account during review process. Novelty: the study is original and novel; no other studies (at least with such a sample size and number of studied parameters) was published. Adequacy: The methods used for data collection, and especially statistical analysis, are relevant for the study purpose, allow to make the conclusions provided by the authors. The study provides new data that have scientific and practical importance. The study has several limitations, however most of them are addressed by the authors in the discussion. I have only a few minor comments. Though meteorological factors are well-described, there is some uncertainty on the type of GERD-related medical care sources utilizations.

Comment 1: Normally in health care, "utilization" is the consumption of services or supplies, such as the number of office visits a person makes per year with a health care provider, the number of prescription drugs taken, or the number of days a person is hospitalized etc (McGraw-Hill Concise Dictionary of Modern Medicine. (2002)). This information is important and requires clarification as causality in case of GERD may depend on different factors - either dependant on the disease itself (like symptom exacerbation) or behaviour

models, not directly related with the disease itself. Probably type of utilization, like physician office visit or new prescriptions of PPI should be analysed separately in the further studies.

Response: Thank you for your sharp comment. As pointed out, the first visit date of the outpatient clinic, the duration for observation, the first date for PPI, duration and dose of medication, duration of hospitalization, and compliance for medication are necessary to evaluate GERD-related medical utilization. In addition, the first date of PPI administration could be affected by several other conditions of the patient; interest in health, how busy, or sensitivity. Additionally, it could vary depending on the preferences of the physician. In order to derive accurate results, all these items and their correlations should be considered and analyzed.

This study is a big data study through NHIS data, and there are limitations in the information that could be identified. The visit to the outpatient clinic and the date of administration could be known, while detailed information about the patient's personal situation, symptoms, compliance for medication, preferences, and physician's preferences, etc., is not available. In order to minimize the bias, the authors defined the first date of PPI administration, the most clearly known item, as medical utilization.

It is expected that more accurate results can be derived as data collection and analysis methods such as artificial intelligence development in the future.

We added this to the discussion.

Comment 2: It is not quite clear, whether the code for "fundoplication" served a stop-criterion for further analysis of a patient's use of medical care resources related to GERD?

Response: In Korea, fundoplication is on the rise in recent years, while it had been scarce during the study period. In fact, out of a total of 2,007,190 patients, only 116 cases of fundoplication were performed during the period, and all of these cases were eliminated in the process of selecting the urban area and random sampling. Therefore, it is thought that fundoplication did not affect the results.

Comment 3: The date of GERD-related medical utilization was defined as the first date of PPI administration, however GERD is a chronic condition that requires long-term treatment with PPIs especially in case of erosive esophagitis. Thus, it is not clear whether the start of PPI treatment really a good time point for this purpose.

Response: Thank you for your kind advice. The authors agree with the reviewer's opinion. GERD is a chronic condition. Symptoms often appear slowly, and PPI may be administered for diagnosis. Therefore, there is a limitation in specifying only the first administration of PPI as a time point. However, as mentioned above, there is no information on patients' symptoms, duration, medication compliance, etc. in this study's data. Therefore, the authors were based on the distinguishable date of the first administration of PPI. In future research, if the above information is accurately investigated and analyzed, more accurate results would be obtained.

We added this to the discussion.

Comment 4: A number of medical procedures was used to support the diagnosis of GERD. Still, some of them are not routinely used to support the diagnosis (like esophageal manometry), the others are usually performed in certain situations (like esophageal pH monitoring). Please, explain inclusion of these procedures in the analysis (for example in the

discussion).

Response: As the reviewer pointed out, several methods are used to diagnose GERD. There is a way to see the change in symptoms by administering PPI based on symptoms, esophagogastroduodenoscopy, pH monitoring. Manometry and esophagogram can be performed for differential diagnosis. In this study, patients who underwent more than one esophagogastroduodenoscopy, esophagogram, manometry, and pH monitoring were defined as an occurrence to improve the accuracy of diagnosis, excluding empirical PPI administration or PPI administration for the treatment of other diseases.

Comment 5: As only data of urban population was used for the analysis, it may be necessary to reflect this in the title.

Response: We revised the title according to your advice.

Comment 6: Moreover, health care resource utilization may depend on some other factors, like type of health care system, insurance coverage of the procedures/visits/treatment, specialists availability etc. It is clear, that in a single country, these factors may not be taken into the account as the situation is more or less homogeneous in different cities. However, this also may need to be addressed in the discussion (for example in context of further research).

Response: In particular, the national medical environment, insurance system, and medical accessibility significant influence medical care utilization for GERD, a non-life-threatening chronic disease. In Korea, the national medical insurance system covers GERD for all

populations, and medical accessibility is high, especially in urban areas. Therefore, these items are thought to have worked similarly to the entire study group, and the resulting bias is not likely to be substantial.

We added this to the discussion.

Comment 7: Despite mentioned above, the data, provided by the authors may serve as a basis for further research and may be helpful for practice.

The reviewed manuscript requires language polishing (see, for example, page 8, lines 3-4; page 12, line 1).

Response: Thank you for your comments. The language was revised.

Issues raised from Science editor

Comment 1: I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: We attached related PDF file

Comment 2: I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and

Response: We uploaded figures in Powerpoint version.

Comment 3: I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text

Response: Thank you. We added article highlight section at end of the main text in red color.