Dear Editors,

Thank you very much for your letter and for the reviewers' comments on our manuscript [NO. 79136] entitled "Features of gastric cancer by anatomic subsite in northern China: a multi-center Health Science Report (HSR) database study." We appreciate the opportunity you have provided us to revise and resubmit our manuscript; all the comments were valuable and helpful in revising and improving our manuscript, and we consider them of great guiding significance to our research. We have read the comments carefully and made revisions accordingly, upon which we hope that the manuscript will meet your expectations. The revised portions of the manuscript are marked in red font. The manuscript was also edited for the English language by a native English speaker, and an English editing certificate has been provided (attached at the end of this letter and in the tracking system). Our responses to the reviewers' comments are provided below. Please accept our thanks in advance for your continuous help with our manuscript.

Response to Editors and Reviewers：

(1) Science editor:

The manuscript has been peer-reviewed, and it' s ready for the first decision. Language Quality: Grade B (Minor language polishing) Scientific Quality: Grade C (Good)

Response: Thank you very much for providing us with the chance to revise our manuscript. Please refer to the revised version of the manuscript (as submitted in the tracking system) and our responses to the editors and reviewers.

(2) Company editor-in-chief:

1. I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response: Thank you very much for your careful review of our manuscript and the opportunity you provided us for revision. We carefully read all comments from the editors and reviewers and revised our manuscript according to the suggestions. Please refer to our revised version of the manuscript.

2. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: Thank you very much for your kind suggestion. We have merged the figures with similar contents and uploaded the decomposable PowerPoint versions to the tracking system.

(3) Reviewer #1: Specific Comments to Authors:

1. 1 Title. YES 2 Abstract. OK 3 Key words. OK 5 Methods. YES. SUITABLE 8 Illustrations and tables. OK 9 Biostatistics. OK 10 Units. OK 11 References. SUITABLE 12 Quality of manuscript organization and presentation. WELL 13 Research methods and reporting. SUITABLE

Response: Thank you very much for your careful evaluation of our manuscript.

2. 4Background. Does the manuscript adequately describe the background, present status and significance of the study?

Response: Thank you very much for your review. In the Introduction, we described the increasing burdens of gastric cancer, the relationship between gastric cancer and its risk factors, including lifestyle and environment, the meaning and present status of identifying gastric cancer through anatomical subsite both in China and globally, and the purpose and significance of our study that, for the first time, identified the status of gastric cancer through anatomical subsite in northern China.

3. 6 Results. THERE SHOULD BE SOME RELATIONS ABOUT TUMOR SITE, OPERATIVE PROCEDURES AND SOCIOECONOMIC CONDITIONS. 7 Discussion. WELL AND CLEAR. BUT NEEDS SOME MORE INFORMATION ABOUT TREATMENT MODALITIES AND SOCIOECONOMOC CONDITIONS OF THE PATIENTS. I THINK THAT OPERATIVE PROCEDURES MAKE THE COMPLICATION RATES DIFFERENT?

Response: Thank you very much for your important suggestions. We do believe that the operative procedures and economic conditions are important in gastric cancer when comparing differences between anatomical subsites. However, we have to apologize for not being able to provide all this information due to the retrospective nature of this study and the limitations of the Health Science Report database. Unfortunately, detailed surgical and economical information about the patients is not currently available. We have addressed these limitations in the Discussion section. To partially describe the social-economic status, we added the insurance data of the patients to **Table 2**, next to the patient source (urban or rural), which may offer a reference. We are now conducting a prospective study in this field involving a detailed collection of patient information, including surgical and economical information, and we will further improve our content in the future based on your suggestion.

(**4) Reviewer #2: Specific Comments to Authors:**

1. This is a good article to introduce the composition ratio characteristics and changes to gastric cancer trends based on anatomical sites in patients in northern China. There are only a few minor issues to fix.

Response: Thank you very much for your kind comments on our manuscript. Please refer to the revised manuscript and the responses below.

2. The authors concluded that the patients in northern China are unique and significantly different from those in other regions, and the authors need to provide further evidence.

Response: Thank you for your important suggestion. Differences in anatomical subsite ratios between different regions (both within China and globally) are shown in **Table 1**, which is believed to be one of the major unique features of our study. The constituent ratio of gastric cardia

cancer in northern China was higher than the average level in China (18−27%) and Europe (26−31%) and lower than that in North America and West Asia (both >40%). Compared to previous reports in China, the constituent ratio of gastric cardia cancer in this study was slightly higher than that in the Gansu Province (northwest China) and lower than that in southwest China but showed high inner similarity compared with those in other global regions. These comparisons were also described in the Discussion section (labeled in red font). Moreover, we compared the general information (including age, gender, anatomical subsite proportion, etc.) between our results regarding gastric cancer patients in northern China and the reported data of other regions (southwest and northwest) in China; please refer to **Supplementary Table 5**, which summarizes the similarities and differences. However, limitations still exist in this study. For example, detailed information, including lifestyle, was not included in the database and should be further examined in the future to better identify the unique features of patients in northern China. We have addressed this point in the limitations section of the revised manuscript.

3. Results of the multivariate analysis were not tested. It is recommended that the authors use data from an external independent cohort of patients or other additional methods to verify the accuracy of the results.

Response: Thank you very much for your important suggestion. We apologize, but validation through an external independent cohort of patients could not be achieved owing to our data limitations. However, we are now conducting a prospective study on this topic, with the collection of more detailed patient information, including surgical procedures, examination results, and economical information, and we will refer to the results of this study as suggested in the future. Please accept our thanks again for this valuable advice.

4. The discussion section could be compressed, the author added too much introductory content to the discussion.

Response: Thank you very much for your great suggestion. We have removed the unnecessary introductory content from the Discussion section of the revised manuscript. Additionally, we addressed several limitations in this section to enable the careful interpretation of the presented findings.

(5) Reviewer #3: Specific Comments to Authors:

1. The authors investigated the features of gastric cancer by anatomic location in northern China. This is an interesting and valuable article. I, the reviewer, would like you to consider the following modifications.

Response: Thank you very much for your careful evaluation of our manuscript. Please refer to the revised manuscript and the responses below.

2. The division of cardia, body, and antrum is an anatomical classification and is mainly diagnosed by post-mortem examination or barium meal study. However, because the shape of the stomach exhibits a three-dimensional structure and differs slightly from patient to patient, this classification is somewhat ambiguous and difficult to diagnose accurately. In particular, cardia must be handled with care, as the range of cardia varies depending on the investigator. In general, when gastric

cancer is registered in databases, the occupied lesion is classified into upper, middle, and lower, which simply divides the stomach into three equal parts. In this article, it is better to use upper, middle, and lower divisions instead of cardia, body, and antrum classifications.

Response: Thank you very much for your valuable suggestion. We do agree that the "upper, middle, and lower" classifications are suitable for the analysis of gastric cancer; however, owing to the retrospective nature of this study, we identified the anatomical subsite through the ICD-10 codes, which were identified in "cardia, body, and antrum," as was previously suggested (Zhou et.al, *Cancer Lett* 2008; Liu et.al, *Ann Surg* 2016). The detailed classification of anatomical subsites into three equal parts may not be available and accurate owing to this limitation of the database that lacks more detailed information. We have added this limitation to the Discussion section. We are now conducting a prospective study in this field, and we aim to identify the anatomical subsites in three equal parts as suggested. Please receive our thanks again for your important suggestion.

3. Although calculating the cost of gastric cancer treatment is important, the calculation of the cost of surgical treatment varies considerably depending on the country, insurance system, and surgeon, so it is better to use this only as a reference. You should delete the last line of Table 2.

Response: Thank you very much for your kind suggestion. We have removed the last line of **Table 2** and briefly described it in the Results section (and moved the information to the newly added **Supplementary Table 2**). In addition, to better describe the social-economic status, we added the insurance data of the patients to **Table 2**.