

Dear editors and reviews,

Thank you for the positive comments and professional suggestions for further improvement of our manuscript “Chinese research into severe ulcerative colitis has increased in quantity and complexity”. We have revised the manuscript as required and highlighted the revisions in yellow. Our responses to reviewers’ comments are listed below.

Responses to reviewers’ comments

Reviewer #1(Reviewer’s code: 00503545):

Comment 1: In this study, the authors investigate the current state of research output from Chinese studies into severe ulcerative colitis (SUC) using a bibliometric analysis of publications and concluded that the output and complexity of research related to SUC in China increased significantly over the previous 15 years, however few of these studies focused on salvage therapy. This paper is well written and the results of the study are clinically interesting. However, the authors should address the following points. 1. It is interesting that the both colectomy rate and short-term mortality rate of SUC patients in Chinese hospitals were lower compared with those in Western countries. On the other hand, the severity of UC is judged by using the several criteria. In this context, the authors should show how the severity of UC was judged in these Chinese hospitals.

Response to comment 1: Thank you for your positive comments. In this study, we report a lower colectomy rate and short-term mortality in Chinese SUC patients compared with those in Western countries, which are consistent with that reported by population-based studies in China and in other Asian countries like Japan and Korea. In addition, milder disease course, lower colectomy rate and lower colorectal cancer rate in Asian UC patients were also reported by Siew C. Ng *et al.* The lower colectomy rate in Asian countries for may due to cultural differences, a higher threshold for surgery in Asia or a milder disease course for UC subjects (S.C. Ng. Epidemiology of inflammatory bowel disease: Focus on Asia. Best Practice & Research Clinical Gastroenterology 28 (2014): 363–372). However, our study is based on bibliometric analysis and literature review, further population-based studies are required to validate our results. According to your suggestion that we should show how the severity of UC was judged in these Chinese hospitals, we reviewed all of the 96 original articles included in this study again. Of the 96 original articles, 65 (67.8%) have reported the adopted diagnostic criteria for severe ulcerative colitis, which are diagnostic criteria in “Consensus on the Diagnosis and Management of Inflammatory Bowel Disease” that developed and revised by Chinese Society of Gastroenterology in 1978, 1993, 2000, 2007,

or 2012. In these consensuses, severe ulcerative colitis is diagnosed according to Truelove and Witts' criteria (six or more bloody stools per day plus at least one of the following: temperature >37.8°C; pulse rate >90 bpm; hemoglobin ≤75% of normal; ESR>30 mm/h). Above all, the severity of UC was judged according to Truelove and Witts' criteria in these Chinese hospitals, consistent with the criteria applied in Western countries.

批注 [w1]: These results were added to the seventh paragraph of the "Discussion".

Comment 2: The authors should check the sentence that "UC is associated with an increased risk of developing colorectal cancer, with t.(p16, lines 22-23)"

Response to comment 2: I'm sorry that we made a mistake in the sentence that "UC is associated with an increased risk of developing colorectal cancer, with t." We revised the sentence by deleting the unnecessary words: "developing" and " , with t."

Reviewer #1 (Reviewer's code: 02438879):

Comment: This is an interesting manuscript defining the status of Chinese ulcerative colitis research. The data is worth publishing. However, more search is advisable to incorporate the currently available literature's as the mode of treatment is continuously changing day by day.

Response to comment: Thank you for your comment. We agree that the mode of treatment is continuously changing day by day. For example, there's no article about biological agent therapy of SUC published in Chinese medical journals until 2013. In our study, we included Chinese SUC related literatures published in the years from 2001 to 2015 and investigated the state of research output in each 5-year period. Publications from 2016 were excluded since only partial data of this year was available when the database search was performed. To evaluate the current state of literature, we repeated the database search with published year limited to 2016 and 2017. We retrieved 33 publications, included 23 original articles, 6 case reports, 2 reviews, and 2 papers published in journals of nursing. In these 23 original articles, 21 focused on the management of SUC, included Traditional Chinese Medicine (17.4%), corticosteroid therapy (8.7%), immunosuppressive drugs (4.3%), biological agents (26.1%), and probiotics (17.4%). There is an increase in articles about biological agents. However, not all of the publications in 2016 and 2017 are available online. Further studies with prime focus as the change of treatment mode are required.

批注 [w2]: These results were added to the 7th paragraph of the "Discussion".

Editor

Comment 1: This statement must be mentioned in the text, and a certificate of statistical review signed by a biostatistician must be provided in PDF format.

Response to comment 1: We have added a biostatistics statement in the text and a certificate of statistical review is provided.

Comment 2: A short running title of less than 6 words should be provided.

Response to comment 2: A short running title "Chinese research into severe ulcerative colitis" is provided.

Comment 3: You should list the contribution of every author.

Response to comment 3: Cheng-Xin Luo and Zhong-Hui Wen contributed equally to this article. Cheng-Xin Luo and Zhong-Hui Wen designed the research, repeated the databases search, and drafted the manuscript. Yu Zhen, Zhu-Jun Wang, Jing-Xi Mu, and Min Zhu performed literature review, recorded and checked relevant information, and did statistical analyses; Qin Ouyang designed the study, and Hu Zhang designed and made critical revisions to the manuscript. All of the authors approved the version of the article to be published

Comment 4: Please provide the grant application form(s). If you can't provide it, please delete this part.

Comment 5: Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s). For manuscripts supported by various foundations (i.e., charitable, not-for-profit organizations), the authors should provide a copy of the full approved

Response to comment 4 and comment 5: The approved grant application forms are provided.

Comment 6: In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article.

Response to comment 6: An audio file for the core tip is submitted.

Comment 7: Please show reference like this.

Response to comment 7: All of the reference have been reedited and shown as requested.

In addition, we have written an "Article Highlights" according to the guidelines. The questions in the guidelines for *Research conclusions* and *Research perspectives* were answered one by one.

We have added the "Flowchart" of studies selection as "Figure 2" (cited in the second paragraph of Results), and the orders of other figures were adjusted.

The limitations of our study were discussed in last second paragraph of the "Discussion".

We sincerely hope our manuscript will be considered as eligible for publication in World Journal of Clinical Cases.

Best regards,

Correspondence to:

Hu Zhang, MD, PhD,
Department of Gastroenterology, West China Hospital, Sichuan University,
No. 37, Guo Xue Alley, Chengdu 610041, Sichuan Province, China.
zhanghu@scu.edu.cn
Telephone: 0086-28-85423387
Fax: 0086-28-85423387