

AUTHOR RESPONSE TO COMMENTS

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Title: Family history and disease outcomes in patients with Crohn's disease: A comparison between China and the United States

This manuscript was first submitted to World Journal of Gastroenterology (WJG) on 06/06/2016, and was accepted to be published on World Journal of Gastrointestinal Pharmacology and Therapeutics (WJGPT) on 07/22/2016.

We thank the editors and reviewers for their thoughtful comments on our manuscript. We appreciate the opportunity to revise and resubmit the manuscript.

Below find the reviewer's comments with responses. All changes in the manuscript are highlighted in yellow.

Sincerely,

Peiqi Wang, on behalf of the authors

REVIEWERS' COMMENTS

Reviewer #1:

In the presented study the differences in family history and clinical outcomes among individuals residing in China and the US were investigated with a survey-based cross-sectional study. It was found that the prevalence of family history of IBD was significantly lower in China. Crohn's disease is caused by a combination of environmental, immune and bacterial factors in genetically susceptible individuals, and about half of the overall risk is related to genetics in western countries. Although the study is well designed and conducted, it can be more valuable if the questions below are answered.

We thank the reviewer for his/her interest.

1-Although age at diagnosis of CD is similar in two groups, there is no information about actual ages of the patients.

We had included the age at diagnosis and duration of disease at time of the survey (= age at survey completion – age at diagnosis). As suggested by the Reviewer, we now include all 3 elements (age at diagnosis, age at survey completion, duration of disease at time of survey). We have added the mean and range of participants' actual age at the time of survey completion as the second row of Table 1. We also added this comparison to the first paragraph of results.

2-Duration of disease at time of survey is lower in Chinese patients. It is known that more patients need surgical intervention as the disease duration prolongs. Half of CD patients will require surgery for the disease at some point over a ten-year period. So, it would be valuable to know what is the percentage of patients who had surgery during the first 10 years after diagnosis of CD in the US? Is it possible to say that Chinese patients needs surgery in younger ages compared to American patients?

Among the participants whose duration of disease is at least 10 years and who gave information about the date of their surgery (USA=46; China=2), the percentage of participants who have undergone surgery for IBD within 10 years of diagnosis was 100% in China and 74% in the United States. Because there were only 2 individuals from China with at least 10 years of disease duration, we did not add this information to the manuscript.

3-It would be very valuable information that if it could be possible to know if there is difference between Chinese Americans and Americans of other ethnic origin.

We absolutely agree that it would be meaningful to compare Americans of Chinese descent with Americans of other races, which could potentially lead to findings about the importance of the role that genetic background and environment each plays in the development of the disease. However, in our current sample, there were NO Americans of Chinese origin, which made it temporarily impossible to conduct this comparison.

Reviewer #2:

It seems quite interesting to present such epidemiological difference between patients but the study needs to be more balanced.

We thank the reviewer for his/her interest. The current study was conducted utilizing a subset of data we collected for an ongoing, international, multicenter epidemiological research project,

named Migrant IBD Microbiome Analysis Study (MIMAS). MIMAS, starting from 2014, has been recruiting cases with Crohn's disease or ulcerative colitis, as well as their friend or family member controls, to participate in a comprehensive survey of risk factors and outcomes associated with IBD.

Given that we had been recruiting for only less than two years, and the fact that in China, IBD emerged much later and has low incidence rate, we did not have the luxury to include as many CD participants from China as the United States, despite our best intentions. However, the statistical methods we used should be able to address the imbalance between sizes of study population in two countries, by taking into consideration the increased variance and widening the confidence interval, which led to more conservative inferences.

As the recruitment goes on, we are making enormous progress in increasing sample size, and we are also planning to launch the second round of questionnaire and bio specimen sample collection, which will hopefully lead to many more interesting findings.