PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Urban-Rural Disparity in Prevalence of Multimorbidity in China: A Cross-sectional Nationally Representative Study
AUTHORS	Ma, Xiaochen; He, Yu; Xu, Jin

VERSION 1 – REVIEW

REVIEWER	Narges Khanjani Kerman University of Medical Sciences
REVIEW RETURNED	22-Mar-2020

GENERAL COMMENTS	The study is generally well written. 1- In the article summary, strengths and limitations, the first sentence should be corrected. "… is associated with higher prevalence of what ? in middle-aged and elderly Chinese." The last sentence should be corrected too. "… the prevalence of multimorbidity in the rural population." 2- In the Introduction, the authors should add some information about the population of China and its demographics. It would be interesting to know for example what percent of people live in villages in China? 3- In the Methods, the authors write "In the dataset, a survey weight variable was created using household and individual nonresponse adjustment." The meaning is vague. The authors should describe what they did better than this. 4- In the Methods, the authors write "13 chronic illnesses … were assessed based on self-reported diagnosis by a doctor. It is not clear to me what this means. Does it mean that they asked each individual if they have diabetes, hypertension, … , but they emphasized that has a doctor made this diagnosis ? In this case people who did not visit the doctors for regular checkups would have been missed, especially in diseases that may not have any symptoms such as hypertension. Do the people in rural China visit medical clinics for regular checkups ? 5- The authors use the word "relationship" frequently throughout the text. This word is usually used for connections between human beings. It is more appropriate to use the word "relation" instead. 6- The phrase "rural hukou" has been used in the text (page 8). The authors should better write the meaning of this phrase in parenthesis.

	7- In the Discussion, one point that the authors did not mention is the fact that women usually express their complications and diseases better, or take better care of their health by visiting doctors and finding out about their diseases. This might be one reason for the higher prevalence of multimorbidity among women. The authors can do a search and see if there is any evidence about this among Chinese women. 8- The main reason for the different results of this study compared to previous studies seems to be including depression. Therefore it seems that in rural China, depression is much more prevalent than urban China. Could the author add some information and references about this issue and the reason why rural Chinese people are more depressed ? 9- In the abstract the authors write "Above 70% of chronic patients above 45 years old have multimorbidity"; while in the conclusion the authors write "Above 70% of all ? chronic patients have multimorbidity." Which one is correct ? Good Luck.

REVIEWER	Samuel Wong School of Public Health and Primary Care
REVIEW RETURNED	24-Mar-2020

GENERAL COMMENTS	Article summary: strengths and limitations of this study: This is the first study showing that rurality is associated with higher prevalence of middle aged and elderly Chinese? This needs to be revised as some words are missing here. For introduction, I think the authors can describe research related to multimorbidity in middle and low income countries where research have been conducted. Although it is not as commonly studied, it is not as rare as well. E.g. https://link.springer.com/article/10.1186/1475-9276-12-64; https://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-12-60 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3190372/ The review, instead of focusing on systematic review, should search for any study on MM in China to have a more thorough search. It would be useful to describe more the specific problems of multimorbidity, including etiologies which may be different between that of rural and urban population in China, taking into studies conducted in other middle and low income countries (which can be used for comparison to rural China). Methods and Results: I think the authors can describe and explain how using a scale to define depressive disorders is justifiable as the rest of the diseases were all self-reported, which created a methodological problem in definition. More information is needed on the definition of urban vs. rural areas/counties as most readers may not understand details on household registration in China. Moreover, much more information on differences in healthcare systems between urban and rural areas, as well as availability of facilities and diagnostic testing is

	needed to truly understand the potential causes of MM pattern seen. From the results, it seems the rate of depressive disorders is a bit too high, comparing to results previously published in China likely due to an important methodological issue, this must be addressed. Discussion: Much more discussion is needed to discuss how these findings from studies overseas and in previous studies in China, especially on the prevalence of depression in previous surveys/studies. Currently, the discussion is too brief and not enough references have been used from either China or overseas countries. The authors mention digital health solutions in rural China, more discussion is needed as cost and availability of facilities may be an issue.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Narges Khanjani
Institution and Country: Kerman University of Medical Sciences Please state any competing interests or state 'None declared': None

Comment: Please leave your comments for the authors below The study is generally well written.
Response: Thank you for the comment.

Comment: 1- In the article summary, strengths and limitations, the first sentence should be corrected. "… is associated with higher prevalence of what ? in middle-aged and elderly Chinese." The last sentence should be corrected too. "… the prevalence of multimorbidity in the rural population."
Response: Thank you for pointing out the errors. We have accepted the suggestions, corrected the mistake on Page 3, and also checked the rest of the text multiple times to clear up potential errors.

Comment: 2- In the Introduction, the authors should add some information about the population of China and its demographics. It would be interesting to know for example what percent of people live in villages in China?
Response: Thank you for this comment. We have accepted it and strengthened the introduction. We added materials regarding population distribution and demography in China on Page 4 from Line16 onwards. We gave the proportion the age structure of urban, rural and overall Chinese and of rural populations.

Comment: 3- In the Methods, the authors write "In the dataset, a survey weight variable was created using household and individual nonresponse adjustment." The meaning is vague. The authors should describe what they did better than this.
Response: Thank you for the comment. We have now revised the sentence as "To address potential non-response bias, we weighed the samples using a survey weight variable provided by CHARLS, which gave sampled units (households and individuals) weights inversely proportional to their probability of having been selected and responded." on Lines 25-27, Page 4.

Comment: 4- In the Methods, the authors write "13 chronic illnesses … were assessed based on self-reported diagnosis by a doctor. It is not clear to me what this means. Does it mean that they asked each individual if they have diabetes, hypertension, … , but they emphasized that has a doctor made this diagnosis ? In this case people who did not visit the doctors for regular checkups would have

been missed, especially in diseases that may not have any symptoms such as hypertension. Do the people in rural China visit medical clinics for regular checkups ?

Response: Thanks for this comment. The reviewer understood correctly that 13 chronic illnesses were self-reported diagnoses by doctors. In China, access to basic health services is considered good in general, though the quality varied. In the recent decade, the Chinese government has implemented the Essential Public Health Scheme to particularly address identification and management of non-communicable diseases like hypertension and diabetes. Regular physical checkups for elderly population (above 65 years old) is universally provided. Universal coverage of social health insurance schemes also allows patients much greater access to health service facilities. On average, Chinese visit health facilities 5.6 times per year in 2015. These being said, previous studies have reported gaps in hypertension diagnosis and the compromised validity of self-reported diagnosis of diabetes. We have added materials regarding these points in the Methods section (from Line 39 Page 5 to Line 3 Page 6), and also strengthened the relevant text in the Discussion section (Line 33 Page12).

Comment: 5- The authors use the word "relationship" frequently throughout the text. This word is usually used for connections between human beings. It is more appropriate to use the word "relation" instead.
Response: Thank you for the comment. We followed the comment and used the word of "relation" instead throughout the manuscript.

Comment: 6- The phrase "rural hukou" has been used in the text (page 8). The authors should better write the meaning of this phrase in parenthesis.
Response: Thank you for pointing this out. Taking into consideration this comment, we have revised the expression. We are now using urbanity/rurality, rural/urban residence (the original term used in the survey to reflect the nature of neighborhood where respondents lived) instead. We have also included a brief explanation about the implication of the urban and rural residence in our methods section to ensure consistency of terms used Lines 16-24 Page 6, so that the meaning is easy for international audience to understand.

Comment: 7- In the Discussion, one point that the authors did not mention is the fact that women usually express their complications and diseases better, or take better care of their health by visiting doctors and finding out about their diseases. This might be one reason for the higher prevalence of multimorbidity among women. The authors can do a search and see if there is any evidence about this among Chinese women.
Response: Thank you for this comment. We have accepted your suggestions. On Page 11 (Lines 6-10), we have added references about potential explanations behind women's greater likelihood of having multimorbidity. We have not identified specific evidence about Chinese women though.

Comment: 8- The main reason for the different results of this study compared to previous studies seems to be including depression. Therefore it seems that in rural China, depression is much more prevalent than urban China. Could the author add some information and references about this issue and the reason why rural Chinese people are more depressed ?
Response: Thank you for the comment. We agree and have revised the paper based on your comment. We have rewritten part of the introduction, highlighting the fact that depression is more prevalent in rural China than in urban China (Line 42, Page 4--Line 3, Page 5). We have also provided references showing that in rural areas, the low socio-economic status, poorer childhood health, poor social services and poorer access to quality health services and the nature of rural residence and lifestyle likely contributed to the higher prevalence of depression and the higher coexistence of chronic physical conditions and depression than in urban areas. These are added to the text between Lines 1-6 Page 12.

Taking into consideration this comment, we have also revised the background section of our abstract (Line 3-6, Page 2).

Comment: 9- In the abstract the authors write “Above 70% of chronic patients above 45 years old have multimorbidity”; while in the conclusion the authors write “Above 70% of all ? chronic patients have multimorbidity.” Which one is correct?
Good Luck.
Response: Thank you for this comment. All of the study participants were 45-years-old or older, so the former statement was correct. We agreed that the statement in conclusion was not clear and might lead to confusion. We have now revised the relevant text in the conclusion as “aged 45 years or above” (Line 12 Page 13.)

Reviewer: 2
Reviewer Name: Samuel Wong
Institution and Country: School of Public Health and Primary Care Please state any competing interests or state ‘None declared’: Nil

Comment: This is the first study showing that rurality is associated with higher prevalence of middle aged and elderly Chinese? This needs to be revised as some words are missing here.
Response: Thank you for pointing out this error. We have revised it as “higher prevalence of multimorbidity in middle aged and elderly Chinese”. We have also strengthened the remaining text by checking multiple times to identify and correct other potential language errors.

Comment: For introduction, I think the authors can describe research related to multimorbidity in middle and low income countries where research have been conducted. Although it is not as commonly studied, it is not as rare as well. E.g. https://link.springer.com/article/10.1186/1475-9276-12-64; https://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-12-60
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3190372/
Response: Thank you for this comment. We find these suggested references helpful and have cited these papers and revised the text Line 16-24 Page 4. This included a systematic review on prevalence of multimorbidity in South Asia (Line 18 Page 4) besides other references on multimorbidity from elsewhere (Line 24 Page 4).

Comment: The review, instead of focusing on systematic review, should search for any study on MM in China to have a more thorough search.
Response: Thank you for this comment. Taking into consideration the comment of the reviewer, we have now strengthened the relevant text, highlighting that what we did was a systematic search on the terms related to China, prevalence and multimorbidity and included both systematic reviews and papers about national prevalence of multimorbidity in China. We also updated our search and identified several recent publication on multimorbidity and related topics in China and have now included them in the Introduction section (Line 34-38, Page 4, and so on) and the Discussion section (Line26-38 Page12).

Comment: It would be useful to describe more the specific problems of multimorbidity, including etiologies which may be different between that of rural and urban population in China, taking into studies conducted in other middle and low income countries (which can be used for comparison to rural China).
Response:
We have added materials showing that hypertension in rural areas were more likely to led to depression. We also provided evidence for the relatively poorer capacity of mental health services. We have also compared the findings from a systematic review about prevalence of multimorbidity in South Asian countries (Lines 19-24 Page 11). To facilitate comparison with findings from this review,

we have revised table 3 to further compare the prevalent chronic conditions in urban and rural China (Line 12 Page 10).

Comment: Methods and Results:
I think the authors can describe and explain how using a scale to define depressive disorders is justifiable as the rest of the diseases were all self-reported, which created a methodological problem in definition.
Response: Thank you for this comment. Indeed, we used self-reported physician diagnosis for 13 chronic conditions, and a scale of CES-D 10 to measure depressive symptoms. The main reason we included depression was that it is a key condition in mainstream international multimorbidity measures as we argued in Lines 41-42, Page4. We also believed including depression is important from a gender perspective, as women were more likely to develop depression than men. Accepting the importance of depression, we used what was available to us to capture the prevalence of multimorbidity. The 13 conditions were only measured using self-reported diagnosis, while depression was only available through the CES-D 10 scale. As the reviewer correctly pointed out, this indeed led to the coexistence of apparently different approaches to measure depression as compared to conditions in our multimorbidity measure. We have now added a substantial discussion on the methodological considerations and implications in relation to CES-D 10 (Line 39 Page 12-Line 5 Page 13).

Comment: More information is needed on the definition of urban vs. rural areas/counties as most readers may not understand details on household registration in China. Moreover, much more information on differences in healthcare systems between urban and rural areas, as well as availability of facilities and diagnostic testing is needed to truly understand the potential causes of MM pattern seen.
Response: Thanks for the comment. We have now revised the text regarding urban and rural residence which was the original term used in the corresponding question asked in CHARLS. We have also provided more information on how urban or rural residence was defined and different in the Chinese context. (Lines 15-24 Page6)
We appreciate the reviewers' interests in causes of the multimorbidity pattern. Following the reviewer's suggestion, we have included substantially more information related to the causes of multimorbidity pattern seen (Lines 20 Page 10—Line 6 Page 12). We have added information regarding the weaknesses of health services and care coverage in rural areas in comparison with urban areas (Line 2 Page 5 in Methods and Line 34 Page 12 in Discussion). Particularly, the lack of mental health might have particularly affected rural population.

Comment: From the results, it seems the rate of depressive disorders is a bit too high, comparing to results previously published in China likely due to an important methodological issue, this must be addressed.
Response:
Thanks for the comment. We agree this is an important methodological point that needs to be put in light of previous studies about depression. Following the reviewers' comment, we have now included several key references regarding prevalence of depressive disorders (Line 25 Page 10-Line 5 Page 11). There had indeed been a large range of reported prevalence. CES-D as one of the screening tools for depression used most widely internationally and has been well established in China. We acknowledged that, while the sensitivity of CES-D has been found to be high, there had been some concern with the compromised specificity of CES-D that may led to over-inclusion of somatic symptoms. We noted this potential limitation in our discussion. We have also provided evidence on depressive symptoms showing that current estimated prevalence of depression varied substantially, largely because of the various tools used. Considering the importance of this methodological issue, we suggest future research may be done using alternative measurement instruments for comparison and sensitivity analysis.

Comment: Discussion:
Much more discussion is needed to discuss how these findings from studies overseas and in previous studies in China, especially on the prevalence of depression in previous surveys/studies. Currently, the discussion is too brief and not enough references have been used from either China or overseas countries.
Response: Thank you for this comment. We accepted your suggestion and have now essentially rewritten the Discussion section and included several paragraphs and several new references about both multimorbidity and depression (Line 22 Page 10--Line 5 Page 13).

Comment: The authors mention digital health solutions in rural China, more discussion is needed as cost and availability of facilities may be an issue.
Response: Thanks for this comment. We accept your suggestion and have now added a review on the potential of digital health solutions in improving care for people with multimorbidity. We also stressed that the digital health efforts should be thought through, taking consideration the cost of services and mobilization of care providers , as well as be informed by the urban-rural gap in multimorbidity prevalence. Meanwhile, we also emphasize that public finance seems necessary to allow resources online to flow towards the remote rural areas (Lines 23-29, Page 12).