

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data
AUTHORS	zhang, ran; Lu, Yun; Shi, Liuyan; Zhang, SongLin; Chang, Feng

VERSION 1 - REVIEW

REVIEWER	Antonio Gimeno Miguel Instituto Aragonés de Ciencias de la Salud, Spain
REVIEW RETURNED	06-Jun-2018

GENERAL COMMENTS	This work addresses an important current health issue as it is multimorbidity. The results obtained on prevalence and patterns of multimorbidity in China could be of potential interest for the scientific community. However, the methodology and analyses conducted are not sufficiently explained and lack of robustness, the results are not presented properly, the discussion is not conducted in depth, and the writing in general and the English used are not suitable for publication.
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REVIEWER	Albert Roso-Llorach IDIAP Jordi Gol, Catalonia, Spain
REVIEW RETURNED	18-Jun-2018

GENERAL COMMENTS	<p>First of all, thanks to the editor for asking me to review this paper. I would also like to thank the authors for this well written paper. I have some questions and issues and a number of minor points that should be addressed in a revised version of the manuscript.</p> <p>Major issues:</p> <p>1. Methods The description of methods partly needs more detail.</p> <p>1.1 Please clarify inclusion/exclusion criteria of the population. A flowchart of CHARLS population would be helpful.</p> <p>2 Results: As mentioned above, the selection of the population needs more detail. The exclusion of incomplete data may cause a selection bias. Have the authors considered imputation methods or any alternative solution? A sensitivity analysis with the incomplete</p>
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	<p>cases should be helpful. This issue has to be explained in the strengths and limitations section.</p> <p>3. T-test and Chi-squared tests of Table 1 should be explained in the Statistical analysis section.</p> <p>4. Please don't discuss the results in the Results Section, for example: page 7 line 18 "which could be explained by the longer average life expectancy of women" should be included in the Discussion section.</p> <p>5. Please clarify the sentence and the following value, "Considering that the prevalence of these fourteen chronic diseases in the elderly population in China has reached 69.10%". Is it the prevalence of having at least one of the 14 diseases? The description is unclear.</p> <p>6. Table 2, Table and Table 4, 95% confidence interval of the RR and Proportion should be helpful.</p> <p>7. Table 5 presents high values of O/E ratios, can you include as a supplementary material the individual prevalence of each diseases and the dyad and tryad prevalence in order to clarify the obtained values.</p> <p>Minor points:</p> <ol style="list-style-type: none"> 1) Abstract (line 9) should be "Design: Cross-sectional study" 2) Abstract (line 44) should be "in the elderly population in China" 3) Statistical analysis page 5, line 52. "Adjusted prevalence" Adjusted by? Please clarify the adjusting variable. 4) Page 6 line 4. "VAN DEN's" should be replaced by Van den Bussche 5) Stata version?? 6) Please consider to include the frequency and percentage for categorical variables in Table 1. 7) It would be interesting to include age as categorical variable in Table 1. 8) Please clarify the Mean Values and the group (no MCC and MCC) in Figure 2. 9) Table 2, Title should be replaced by "Relative risks". 10) Page 10, line 36, "72 dyad combinations" Is it correct? You mentioned 76. 11) Page 14, line 11, "since only 15 chronic conditions were included in the survey" Is it correct?
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REVIEWER	Christian Brettschneider University Medical Center Hamburg-Eppendorf, Germany
REVIEW RETURNED	13-Aug-2018

GENERAL COMMENTS	<p>The manuscript „Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data” addresses the topic of multimordibity in the elderly, a frequent topic in research. A novel aspect of this manu-script is the focus on China. The authors used data from a large biennial survey of the Chinese elderly. 14 diseases or –better- groups of aggregated diseases were considered. At least two coexisting diseases defined multimordibity. The authors present mainly descriptive results on demographic characteristics, prevalence</p>
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rates of conditions, dyads and triads, relative risks and O/E ratios. The rationale for the study is convincing. The methods section, especially the description of the statistical analysis, is rather short and should be supplemented. The results section is comprehensive. However, it could benefit from some clarifications. In the discussion section the authors highlight their findings, put them in context to previous research and discuss limitations. The conclusions are in line with the findings. In summary, as this is one of the first attempts to put a focus on multimorbidity in China, the manuscript has its merits. However, there are some aspects and weaknesses in the manuscript the authors have to address and change to warrant a valuable and convincing addition to the literature.

Specifically this means:

- Introduction: There is a citation missing to support the sentence that MM among elderly imposes an enormous societal cost [...]
- Methods: The authors say that they report adjusted prevalences. The open question is: How did they adjust and for what did they adjust? In the Variables chapter, the authors mention three independent variables: age, gender and number of comorbidities. In case these are the variables the prevalences were adjusted for, I would like to ask the authors to consider further variables. As this is a survey, I am pretty sure that there are further sociodemographic and socioeconomic variables.
- Methods: The authors say that they calculated O/E ratios according to Van Den's analysis method. First, the name of the first author of this publication is van den Bussche. Second, in the publication cited by the authors [9], the method is not directly described. I recommend that the authors describe explicitly the method they used to calculate O/E ratios.
- Results: The authors say that they excluded participants with incomplete data. The number of excluded participants should be presented. This facilitates the assessment of representativity of the sample.
- Results: Are there 9 participants without information on their gender (5,705 + 5,993 = 11,698)?
- Results: The sample size is rather large. Therefore, from my point of view, the statistically significant difference in age should not be overemphasized. A difference of 0.5 years is not large enough to conclude that the MCC group was generally older.
- Results: Looking at figure 2, I do not conclude that all 14 conditions have a prevalence of more than 10% in the MCC group. Additionally, why do the authors compare the prevalences in the MCC group to the entire sample? MCC and NMCC constitute the entire sample. Therefore, MCC is partially compared to itself.
- Results: On page 8 the authors say that there were 76 dyads, on page 10 they state that there were 72 dyads.
- Results: In table 3 the presentation of prevalence values is not consistent. The first column shows the prevalence of all respondents. The second and third the fraction of male and female participants with the dyad. This is confusing.
- Discussion: The authors draw conclusions for the influence of age and gender on MM. However, the analysis does not permit to draw these conclusions. There might be differences between age groups and gender groups but the way the data were analysed is not sufficient to identify statistically significant differences.
- Discussion: The authors say that 15 conditions were assessed in the survey, but they considered only 14. Which condition was number 15 and what is the reason for not considering it?

	<p>- Discussion: The prevalences for the different conditions appear a little bit odd to me. RA is rather high, while hyper-tension is quite low. This might be a usual phenomenon in China, but for a European or American reader this is uncommon. The authors should discuss international differences in morbidity and MM to support international readers by the transfer and interpretation of the results.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

This work addresses an important current health issue as it is multimorbidity. The results obtained on prevalence and patterns of multimorbidity in China could be of potential interest for the scientific community. However, the methodology and analyses conducted are not sufficiently explained and lack of robustness, the results are not presented properly, the discussion is not conducted in depth, and the writing in general and the English used are not suitable for publication.

Response: Your comments were of great importance to us. We addressed your concerns about our manuscript to the best of our abilities. In the revised version, we explained the methods employed in the article in more detail. For example, we described explicitly the method we used to calculate the O/E ratios and added the T-test and Chi-squared tests of Table 1 to the statistical analysis section. In addition, we modified the tables and figures in the manuscript to present the results more properly. In the discussion section, we explained the possible reasons that the results were not what one would imagine. As to the writing, we improved the quality of English throughout the manuscript with the assistance of a native speaking professional. Thank you again for your constructive criticism and valuable feedback. We would appreciate it if you could give our revised manuscript a second chance.

Reviewer 2:

Major issues:

1. Methods

The description of methods partly needs more detail.

1.1 Please clarify the inclusion/exclusion criteria of the population. A flowchart of CHARLS population would be helpful.

Response: Thanks for your suggestions. We clarified the inclusion criteria of the population in the Methods section as 1) with complete data on gender, age and health status information on the 14 chronic conditions and 2) being aged 60 and over. Besides, we drew a flowchart to illustrate the inclusion criteria as you suggested.

2 Results: As mentioned above, the selection of the population needs more detail. The exclusion of incomplete data may cause a selection bias. Have the authors considered imputation methods or any alternative solution? A sensitivity analysis with the incomplete cases should be helpful. This issue has to be explained in the strengths and limitations section.

Response: We fully agreed that there may be a selection bias and we were really sorry that we did not come up with a solution due to limited time and lack of professional knowledge. However, we did mention this issue in the strengths and limitations section.

3. T-test and Chi-squared tests of Table 1 should be explained in the Statistical analysis section.

Response: Thanks a lot for your valuable advice. We explained the methods we used by adding the sentence "We applied the T2 and χ^2 tests to test the differences in age, gender and the mean number of chronic conditions across different subgroups." to the statistical analysis section.

4. Please don't discuss the results in the Results Section, for example page 7 line 18 "which could be explained by the longer average life expectancy of women" should be included in the Discussion section.

Response: We were sorry for such mistakes and we removed the sentences from the Results section as suggested by the reviewer.

5. Please clarify the sentence and the following value, "Considering that the prevalence of these fourteen chronic diseases in the elderly population in China has reached 69.10%". Is it the prevalence of having at least one of the 14 diseases? The description is unclear.

Response: We apologize for our earlier lack of clarity. The sentence "Considering that the prevalence of these fourteen chronic diseases in the elderly population in China has reached 69.10%" was deleted. However, we did rewrite a similar sentence in page 13 line 14 "The results of the study indicated that the prevalence of the 14 chronic diseases in the elderly reached 69.10% in China" according to your suggestion.

6. Table 2, Table 3 and Table 4, 95% confidence interval of the RR and Proportion should be helpful.

Response: We added the 95% confidence interval to Table 2 according to your recommendations. In order to present the results more clearly, we modified the other two tables.

7. Table 5 presents high values of O/E ratios, can you include as a supplementary material the individual prevalence of each disease and the dyad and triad prevalence in order to clarify the obtained values.

Response: We included the information on the prevalence of each disease and their dyads and triads in Annex 1.

Minor points:

1) Abstract (line 9) should be "Design: Cross-sectional study"

Response: We corrected the mistake accordingly.

2) Abstract (line 44) should be "in the elderly population in China"

Response: To be accurate, we added "in China" to the sentence.

3) Statistical analysis page 5, line 52. "Adjusted prevalence" Adjusted by? Please clarify the adjusting variable.

Response: The prevalence was not adjusted so that we replaced the word "adjusted" with "respective".

4) Page 6 line 4. "VAN DEN's" should be replaced by Van den Bussche

Response: We checked the article cited and corrected the name of the first author.

5) Stata version?

Response: We specified the Stata version (Stata software V.14.0 for Windows (Stata Corp)) in the revised manuscript.

6) Please consider to include the frequency and percentage for categorical variables in Table 1.

Response: The frequency and percentage for male and female participants were presented in Table 1.

7) It would be interesting to include age as categorical variable in Table 1.

Response: Thanks a lot for your advice. However, we intended to focus on gender in Table 1 due to limited time.

8) Please clarify the Mean Values and the group (no MCC and MCC) in Figure 2.

Response: In the revised manuscript, the green bars represented the non-MCC group while the MCC group was denoted by blue bars. The mean number of chronic diseases for the non-MCC group was 0.45 and that for the MCC group was 3.01.

9) Table 2, Title should be replaced by "Relative risks".

Response: We are very sorry for this typo.

10) Page 10, line 36, "72 dyad combinations" Is it correct? You mentioned 76.

Response: We made a grave mistake about the number and thank you for pointing it out. A total of 72 dyad combinations were detected.

11) Page 14, line 11, "since only 15 chronic conditions were included in the survey" Is it correct?

Response: We feel really sorry for our carelessness. There were 14 chronic conditions included.

Thank you again for your positive comments and valuable advice.

Reviewer 3:

1 Introduction: There is a citation missing to support the sentence that MM among elderly imposes an enormous societal cost [...]

Response: Thank you for pointing it out. We searched the literature on multimorbidity among the elderly in China and added a citation to support the sentence. (Lee J T, Hamid F, Pati S, et al. Impact of Noncommunicable Disease Multimorbidity on Healthcare Utilisation and Out-Of-Pocket Expenditures in Middle-Income Countries: Cross-Sectional Analysis. PLoS One 2015;10:103-110. doi: 10.1371/journal.pone.0127199.)

2 Methods: The authors say that they report adjusted prevalences. The open question is: How did they adjust and for what did they adjust? In the Variables chapter, the authors mention three independent variables: age, gender and number of comorbidities. In case these are the variables the prevalences were adjusted for, I would like to ask the authors to consider further variables. As this is a survey, I am pretty sure that there are further sociodemographic and socioeconomic variables.

Response: We apologize for our lack of clarity. The prevalence was not adjusted so that we replaced the word "adjusted" with "respective".

3 Methods: The authors say that they calculated O/E ratios according to Van Den's analysis method. First, the name of the first author of this publication is van den Bussche. Second, in the publication cited by the authors [9], the method is not directly described. I recommend that the authors describe explicitly the method they used to calculate O/E ratios.

Response: We feel sorry for our carelessness. First, we checked the article cited and corrected the name of the first author. Second, as suggested by the reviewer, we explained the method we used to calculate the O/E ratios in the Statistical analysis section. (Next, the expected number of patients with a chronic disease were calculated, and the observed-to-expected (O/E) ratios were determined by dividing the number of patients in those groups by the expected number of patients.)

4 Results: The authors say that they excluded participants with incomplete data. The number of excluded participants should be presented. This facilitates the assessment of representativity of the sample.

Response: As suggested by the reviewer, we added the number of those with incomplete data (1002) and aged below 60 (9259).

5 Results: Are there 9 participants without information on their gender (5,705 + 5,993 = 11,698)?

Response: We made a mistake about the number of female participants and corrected it as 6002.

6 Results: The sample size is rather large. Therefore, from my point of view, the statistically significant difference in age should not be overemphasized. A difference of 0.5 years is not large enough to conclude that the MCC group was generally older.

Response: We agree that the difference in age between the MCC group and the non-MCC group was not large enough to conclude that the MCC group was generally older. So we simply stated the fact that "Samples in the MCC group were 0.66 years older than those belonged to the non-MCC group." instead of drawing conclusions.

7 Results: Looking at figure 2, I do not conclude that all 14 conditions have a prevalence of more than 10% in the MCC group. Additionally, why do the authors compare the prevalences in the MCC group to the entire sample? MCC and NMCC constitute the entire sample. Therefore, MCC is partially compared to itself.

Response: Thank you for pointing it out. It was true that not all the 14 morbidities had a prevalence of more than 10% in the MCC group. Therefore we deleted the sentence which stated otherwise. Besides, according to your feedback, we modified this figure to compare the prevalence in the MCC group and the non-MCC group to avoid repetition.

8 Results: On page 8 the authors say that there were 76 dyads, on page 10 they state that there were 72 dyads.

Response: We made a grave mistake about the number and thank you for pointing it out. A total of 72 dyad combinations were detected.

9 Results: In table 3 the presentation of prevalence values are not consistent. The first column shows the prevalence of all respondents. The second and third the fraction of male and female participants with the dyad. This is confusing.

Response: Thank you for your valuable feedback. We noticed the confusion the original table might create. So we replaced the proportions in the second and third columns with the prevalence of different dyads in male and female participants.

10 Discussion: The authors draw conclusions for the influence of age and gender on MM. However, the analysis does not permit to draw these conclusions. There might be differences between age groups and gender groups but the way the data were analyzed is not sufficient to identify statistically significant differences.

Response: We agree with you that our analysis did not present enough evidence to confirm the impact of age and gender on multimorbidity, therefore we removed the conclusions from the Discussion section.

11 Discussion: The authors say that 15 conditions were assessed in the survey, but they considered only 14. Which condition was number 15 and what is the reason for not considering it?

Response: We feel really sorry for our carelessness. There were 14 chronic conditions included in the survey.

12 Discussion: The prevalences for the different conditions appear a little bit odd to me. RA is rather high, while hypertension is quite low. This might be a usual phenomenon in China, but for a European or American reader this is uncommon. The authors should discuss international differences in morbidity and MM to support international readers by the transfer and interpretation of the results.

Response: As suggested by the reviewer, we explained the possible reasons that the prevalence of arthritis or rheumatism was particularly high.

Thank you again for your time and valuable feedback.

VERSION 2 – REVIEW

REVIEWER	Albert Roso-Llorach IDIAP Jordi Gol, Catalonia, Spain
REVIEW RETURNED	06-Nov-2018

GENERAL COMMENTS	<p>The authors satisfactorily addressed part of my comments raised in the first revision. But I still have some questions and issues that should be addressed in a new revised version of the manuscript.</p> <p>1) Thanks for considering my suggestion of including the presence of selection bias in the strengths and limitations section. I know the authors mentioned that limited time and lack of professional knowledge did not allow them to find a solution to solve this issue. But, as I mentioned in the first revision, a simple sensitivity analysis comparing the characteristics of the complete cases vs the incomplete cases can be carry out to add information in this issue. The authors can include the results as a supplementary material. The sensitivity analysis can significantly improve the scientific quality and transparency of the manuscript.</p> <p>2) My apologies but I still cannot understand the meaning of "The results of the study indicated that the prevalence of the 14 chronic diseases in the elderly reached 69.10% in China". Is it the prevalence of having at least one of the 14 diseases? The description still unclear.</p>
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	3) Please don't discuss the results in the Results Section, for example: The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%), which is in accordance with trends reported in other available literature. [15, 16]
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VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 2:

Thank you very much for your conscientiousness and valuable advice on our manuscript entitled "Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data". We are sorry for our failure to address all the problems to your satisfaction in the first revision. Based on your comments and suggestions, we have made further modifications to the manuscript. Below you will find our point-by-point responses to your comments/ questions. Our reply is in red, whereas your comments are in black.

1. Thanks for considering my suggestion of including the presence of selection bias in the strengths and limitations section. I know the authors mentioned that limited time and lack of professional knowledge did not allow them to find a solution to solve this issue. But, as I mentioned in the first revision, a simple sensitivity analysis comparing the characteristics of the complete cases vs the incomplete cases can be carry out to add information in this issue. The authors can include the results as a supplementary material. The sensitivity analysis can significantly improve the scientific quality and transparency of the manuscript.

Response: Thanks a lot for your helpful suggestions. We add a sensitivity analysis comparing the characteristics of the complete cases and the incomplete cases in Annex 1.

2. My apologies but I still cannot understand the meaning of "The results of the study indicated that the prevalence of the 14 chronic diseases in the elderly reached 69.10% in China". Is it the prevalence of having at least one of the 14 diseases? The description still unclear.

Response: We apologize for our earlier lack of clarity. In order to be clear, we replaced this sentence with a new one. (The results of the study indicated that 69.1% of the elderly population in China had at least one of the 14 diseases and that 43.6% of them suffered from multimorbidity.)

3. Please don't discuss the results in the Results Section, for example: The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%), which is in accordance with trends reported in other available literature.

Response: We were sorry for such mistakes and removed "which is in accordance with trends reported in other available literature." We also double-checked the whole Results Section and deleted similar sentences.

Thank you again for your time and valuable feedback.

VERSION 3 - REVIEW

REVIEWER	Albert Roso-Llorach IDIAP Jordi Gol, Catalonia, Spain
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REVIEW RETURNED	17-Mar-2019
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GENERAL COMMENTS	<p>The authors satisfactorily addressed part of my comments raised in the second revision. But I still have some questions and issues that should be addressed in a new revised version of the manuscript.</p> <p>1) Thanks for considering my suggestion of performing a sensitivity analysis comparing complete cases vs incomplete cases. From my point of view, the presentation and discussion of the sensitivity analysis should be improved by:</p> <p>a) I appreciate the inclusion of selection bias in the strength and limitations Box. But I miss some discussion in the limitations paragraph in discussion section. A sentence citing the results of Annex 1 Table should be included.</p> <p>b) The sentence "Given the exclusion of participants with incomplete data or aged under 60" is misleading. I suggest excluding " or aged under 60" because is an exclusion criterion and the aim of the sensitivity analysis is to compare people with missing data vs people without missing data. Therefore, the authors need to explain more clearly how the 876 participants with incomplete data shown in Annex 1 Table were obtained. I assumed that this number correspond to the number of participants over 60 years with incomplete data. But it is not straightforward from the added sentence in methods section and the numbers in Figure 1 (1002 participants with missing data overall).</p> <p>c) I suggest changing "complete samples" and "incomplete samples" by "complete cases" and "incomplete cases" in Annex 1 Table.</p> <p>d) Statistical tests used in Annex 1 Table are not reported. I suggest including them in a footnote.</p>
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VERSION 3 – AUTHOR RESPONSE

Response to Reviewer 2:

Thank you very much for your conscientiousness and valuable advice on our manuscript entitled "Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data". We are sorry for our failure to address all the problems to your satisfaction in the first revision. Based on your comments and suggestions, we have made further modifications to the manuscript. Below you will find our point-by-point responses to your comments/ questions. Our reply is in red, whereas your comments are in black.

1.Thanks for considering my suggestion of performing a sensitivity analysis comparing complete cases vs incomplete cases. From my point of view, the presentation and discussion of the sensitivity analysis should be improved by:

a) I appreciate the inclusion of selection bias in the strength and limitations Box. But I miss some discussion in the limitations paragraph in discussion section. A sentence citing the results of Annex 1 Table should be included.

Response: Thanks a lot for your helpful suggestions. We add a presentation of the sensitivity analysis in limitation paragraph in discussion section.

b) The sentence "Given the exclusion of participants with incomplete data or aged under 60" is misleading. I suggest excluding " or aged under 60" because is an exclusion criterion and the aim of the sensitivity analysis is to compare people with missing data vs people without missing data. Therefore, the authors need to explain more clearly how the 876 participants with incomplete data shown in Annex 1 Table were obtained. I assumed that this number correspond to the number of participants over 60 years with incomplete data. But it is not straightforward from the added sentence in methods section and the numbers in Figure 1 (1002 participants with missing data overall).

Response: We apologize for our earlier lack of clarity. In order to be clear, we replaced this sentence with a new one. (Given the exclusion of participants with incomplete data, a sensitivity analysis was conducted to compare the characteristics of the complete cases aged 60 years and above and the counterpart in the incomplete cases, which is presented in Annex 1.)

c) I suggest changing "complete samples" and "incomplete samples" by "complete cases" and "incomplete cases" in Annex 1 Table.

Response: Thanks a lot for your helpful suggestions. We replace "complete samples" and "incomplete samples" with "complete cases" and "incomplete cases" in Annex 1 Table.

d) Statistical tests used in Annex 1 Table are not reported. I suggest including them in a footnote.

Response: Thanks a lot for your helpful suggestions. We explain the methods of the statistical tests used in Annex 1 Table in the footnote.

Thank you again for your time and valuable feedback.

VERSION 4 - REVIEW

REVIEWER	Albert Roso-Llorach IDIAP Jordi Gol, Catalonia, Spain
REVIEW RETURNED	14-May-2019

GENERAL COMMENTS	<p>The authors satisfactorily addressed most of my comments of the 2nd revision. But I still have minor points that should be addressed.</p> <p>1) I completely disagree with the last point of the strengths and limitations box. The authors cannot conclude that there's no selection bias. Although p-values were not significant at $\alpha=0.05$ that does not imply that there is no selection bias. I suggest the authors to change that sentence to something more like:</p> <p>"This study only included older patients aged 60 years and above with complete data. Although exclusion of incomplete data may cause a selection bias, significant differences between included and excluded cases were not observed"</p> <p>The part of "Further research would be needed in other populations" can be removed as this idea is already mentioned in the conclusion section of the abstract.</p> <p>In addition, as I mentioned in the 2nd revision, I miss the discussion of the sensitivity analysis results in the discussion section (not in the strengths and limitations box).</p>
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VERSION 4 – AUTHOR RESPONSE

Response to Reviewer 2:

Thank you very much for your valuable advice on our manuscript entitled "Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data". We really agree with your point of view and have learned a lot in your comments. Based on your comments and suggestions, we have made further modifications to the manuscript. Below you will find our point-by-point responses to your comments/ questions. Our reply is in red, whereas your comments are in black.

1. I completely disagree with the last point of the strengths and limitations box. The authors cannot conclude that there's no selection bias. Although p-values were not significant at $\alpha=0.05$ that does not imply that there is no selection bias. I suggest the authors to change that sentence to something more like:

"This study only included older patients aged 60 years and above with complete data. Although exclusion of incomplete data may cause a selection bias, significant differences between included and excluded cases were not observed"

Response: Thanks a lot for your helpful suggestions. We strongly agree with your suggestions and have made changes based on your comments.

2. In addition, as I mentioned in the 2nd revision, I miss the discussion of the sensitivity analysis results in the discussion section.

Response: We apologize for the lack of discussion on the results of the sensitivity analysis in the discussion section. We have made additions in this revision.

Thank you again for your timely and valuable feedback.

VERSION 5 - REVIEW

REVIEWER	Albert Roso-Llorach IDIAP Jordi Gol, Catalonia, Spain
REVIEW RETURNED	30-May-2019
GENERAL COMMENTS	The authors satisfactorily addressed my comments of the 3rd revision.