Reviewer’s report

Title: Latent class analysis of multimorbidity patterns and associated outcomes in Spanish older adults: A prospective cohort study

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Reviewer: Wencong Chen

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Title: Latent Class Analysis of Multimorbidity Patterns and Associated Outcomes in Older Adults: A Prospective Cohort Study

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Summary

This paper tries to determine the multimorbidity patterns of non-institutionalized older people, using Latent Class Analysis method. Furthermore, the multiple and logistic regression methods were applied to explore the association between these latent class variables and observed health outcomes, including health, functional activities, disability, quality of life, memory test.

Primary Concerns

This paper is well-written and precise. However, it suffer from the following issues.

1. Around 50% measurements of memory function, verbal test, and quality of life, ADLs, IADLs, and hospitalization were missing at follow-up in the linear regression model, which may introduce bias in the statistical analyses. People may argue that the sensitivity analysis support the results from imputation data sets. However, it is insufficient to draw the conclusion that the missing data is ignorant. It will inflate the type I error.

2. The author tried to fit the regression model at baseline and 3 years follow-up, without considering the time effect and the nature of missing data. Repeated measurements mixed model or generalized estimation equation approaches will be more appropriate detect the time effect in the association. Two time points will be included in the repeated measurements models: Baseline and 3 years follow-up. Again, sensitivity analysis is needed.

3. It would be better that some discussion was put on the Latent class separation. Make sure there no two latent classes have the same mapped response.
4. Number of hospitalization in the past 12 months is an objective health outcome, comparing with the hospital admission. Usually, the number of hospitalization follows Poisson distribution. Logistic regression is not appropriate.

Specific comments

Line 83, "subgroups" is not appropriate, change to "latent class variables"

Line 84, Delete "a" before "useful".

Line 96, "cluster" change to "clusters".

Line 97, "subgroups" is confused. Check with the reference make sure consistent with the definition.

Line 108, Specify the stratification factors.

Line 121, Move "also" to the end of 1886.

Line 123, Eleven chronic conditions, only 9 conditions were reported in the following line 125-126.

Line 130, Self-reported diagnosis. Although the authors have discussed the bias of self-reported diagnosis. It is better to provide more context and scope of self-reported outcome. E.g. WHOQOL-AGE. The participants whose score are low may die earlier than the healthy group. A Self-reported outcome table of listing will improve the clarification.

Line 153, Provide the validity of verbal memory test, if there is no validity report, reference is needed.

Line 168-170, Recommend to use hospitalization only, since the visit of health professional may not reflect the real condition of participants, while hospitalization is more objective measurements.

Line 173, Provide the reason that LCA was only perform at baseline, not 3 years follow-up. If performed at 3 years follow-up, it is possible that there is misclassification error.

Line 185, There is no chi-squared or Kruskal-Wallis test in the additional tables. If there do have any test statistics related to chi-squared and kruskal-Wallis test, it should be reported in the footnotes of additional tables or in the body.

Line 194, Specify the imputation method. It is multiple imputation.

Line 213, Both BIC and CAIC statistics are based on G2 statistics. Due to the missing data, adjusted G2 will be more appropriate than the original scale. Schafer (1997) provide a details of
adjusted G2 statistics. Make sure Stata package automatically perform the adjustment automatically.

Line 221, Break the sentence into two sections.

Line 238, Change "class" to "latent group".

Line 252, It is better to provide the number of participants in the table 3.

Line 266, "Predicted" change to "mapped".

Line 308, "subgroup" is not appropriate. Change "subgroup" to "latent group" or "latent class".

Line 332, Duplicated reference number

Line 340, Add "the" before "abnormalities" and change "in" to "of".

Line 344, Add "the" before inflammation.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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