Reviewer’s report

Title: Characteristics, service use and mortality of clusters of multimorbid patients in England: a population-based study

Version: 0 Date: 08 Jan 2020

Reviewer: Tatendashe Bernadette Dondo

Reviewer's report:

The study identified multimorbidity patient clusters across four age strata (18-44, 45-64, 65-84 and 85+ years) and investigated the impact of the derived clusters on mortality and service use. Latent class analysis was applied to derive the multimorbidity clusters and generalised liner models were fitted to assess the association of the multimorbidity clusters and outcomes. The authors identified 20 clusters across the four age strata, i.e. five class solution for patients aged 18-44 years, five class solution for patients aged 45-64 years, six class solution for patients aged 65-84 years and four class solution for patients aged 85+ years. For patients aged 18-64, highest mortality rates were noted in the cluster that comprised psychoactive substance and alcohol misuse, for patients aged 65-84, the cluster that comprised coronary heart disease, depression and pain, and for patients aged 85+, the cluster that comprised coronary heart disease, heart failure and atrial fibrillation. Highest service use was noted in the clusters that comprised depression, anxiety and pain (aged 18-64).

This work fills gaps in knowledge in highlighting multimorbidity profiles of patients that have implications for health services. The aims of the study are clear, the introduction provided the rationale for doing the study and appropriate methods were applied for the research aims. However, I have some comments and suggestions. See below;

Major

* How did the authors choose their reference cluster for the impact on outcomes analyses of the clusters? The ideal reference would be the cluster free of multimorbidity or with minimal multimorbidity compared with the other clusters. A sensitivity analysis including the patients without any multimobidity for each age strata as the reference would be interesting when assessing the impact on outcomes of the derived multimobidity clusters.

* Can you add estimates (IRR 95% CIs and ORs 95% CIs, as given in the supplementary tables) to the results section when you discuss the impact of the multimorbidity clusters on outcomes? Stating the P value only will not suffice as P values are a measure of statistical significance hence you need to report estimates too to show the size of the effects. Maybe create a results table for the main text summarising the estimates of the clusters for each age strata across all considered outcomes.

* Why did the authors use logistic regression models for 2-year and 5-year mortality and not time to event models?

* Can you reference supplementary figures 5-8 for definition of the optimal class solutions derived for each age strata considered for the study in the results section. Also add the latent class prevalences.

* Minimal detail is given on predictors of the derived clusters in the main text. However, there are tables in the supplementary summarising the results. Can you add to the methods section how these predictors were determined

* Why was age included as a potential predictor yet the clusters was were derived stratified by age?

* The discussion needs a bit more detail. There is little critical appraisal of previous research and comparisons to findings in this study.
Can the authors give more insight in the discussion on the finding that in the oldest age group the hypertension centred cluster was associated with the best survival and lowest health service use among multimorbid patients?

Minor

The results in the abstract are not supported by any stats estimates. Maybe add the mortality rates of the clusters? Maybe add the conditional item probabilities of the morbidities identified as key in derived clusters? Maybe add the rates of service use across the identified clusters?

Are the 38 conditions considered for this study exhaustive of the morbidities potentially inherent for the population under consideration?

Did the definition of morbidities adopted capture severity? Ignoring this aspect could bias the findings on impact on outcomes. If not add this to the limitations of the study section of the manuscript

Add detail on the study being observational as such we cannot infer causality to the limitations section of the manuscript not the results (lines 27-29, page 8).

**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

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

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