Reviewer's report

Title: Multimorbidity: Structure or Chaos? A practice-based observation of combinations of diseases in patients aged 65 or older in primary care.

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Reviewer: Hanna Kaduszkiewicz

Reviewer's report:

Major compulsory revisions:

This manuscript reports the results of a comparably small study on combinations of diseases in patients aged 65 or older in primary care. Against the background of the many possible combinations of diseases in multimorbidity (see van den Bussche et al., 2013) the analysis of only 543 patients in two family practices in Belgium is a limitation.

The authors argue that using insurance claims data – which offer the advantage of huge data sets - may lead to an over- or underestimation of diseases, because “these studies do not necessarily identify the combinations that are relevant at the patient-provider level”. Therefore they try to identify diseases that influence clinical management at the patient level and based on these diseases they try to find specific combinations of problems that could be a relevant focus for RCTs and/or management guidelines.

However, on the way to this goal the authors performed steps that are not clear.

1) Did they apply the CIRS-CI or the CIRS? In the methods section they introduce the CIRS-CI, but in the following they state, that multimorbidity was defined as the involvement of 2 or more body systems (CIRS > 1). What does this mean exactly? Were patients included who had illnesses in at least 2 body systems according to CIRS and at least a severity score of 3 in both of the systems? Please clarify.

2) Then, the research team constructed a list of 23 problems based on their clinical experience and reason. This selection process is not traceable and the problems are only partially comparable to problem/disease lists in other publications. Please describe in more detail.

3) Coming back to the authors’ statement at the beginning of the introduction: Given that these 23 problems are in fact “diseases that influence clinical management at the patient level”: to what extent do these problems differ from the problems routinely documented in the GP files? A comparison of these routine diagnosis data with these 23 problems would be of great help to substantiate the arguments in favour of this study.

4) In this context a discussion of the results of the study of van den Bussche et al. in the Journal of Clinical Epidemiology 66 (2013) 209e217 is missing. In this study claims data and data from GP interviews were compared with each other.
Interestingly the prevalence of most diseases was lower in claims data than in GP interviews.

5) Comparing the prevalences in this study with the study of van den Bussche et al. is limited. However, a few diseases allow comparison and here we see, that the prevalences are very much lower in the Belgium study than in the German:
   - Hypertension: 48% in Belgium, 78 in Germany
   - COPD: 14 vs. 24%
   - Diabetes: 14 vs. 38%
   - Ischemic heart disease: 14 vs. 31%
   - Lipid disorder: 14 vs. 59% etc.

In order to discuss these huge differences we need the results from the analysis that is described in comment 3.

6) The authors conclude that “performing trials or developing guidelines for people with specific combinations will ever be useful at the level of clinical practice.” I doubt that this strong conclusion can be drawn from this small study that partially used subjective measures of disease relevance.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.