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: Ingmar Schaefer

Reviewer's report:

This is an interesting and well written paper that tries to identify specific problem combinations that could be a relevant focus for RCTs or management guidelines for multimorbid patients. A strength of the approach is that not only prevalence but also clinical relevance of problems is assessed and that the authors go beyond the limitation of the ICD and also include social problems and problems from the medical history of the patients that could interfere with problem management in general practice. The authors also found a reasonable way for including relevant but low prevalent problems by using additional CIRS domains.

Major compulsory revisions:

1. The title “Multimorbidity: structure of chaos?” does not fit, because this is not a question the paper tries to answer. The authors should find a title that fits better with their analysis.

2. There are some interesting results – only: the discussion part is very thin. The authors state themselves that they are not the first who identified the combination “hypertension – osteoarthritis”. However, this is the only combination that is discussed regarding medical consequences. There should be lots of other combinations which have a rather high prevalence, are clinically relevant and should therefore be worth discussing.

3. The authors should also discuss the consequences of combinations with social problems they found for disease management by GPs, because this is one of the main strengths of this paper.

4. The disease associations from table 3 also need to be discussed regarding implications for general practice.

Minor essential revisions:

5. p.4 para 3 line 5: GPs “assessed whether or not a problem interfered with patients’ normal activity and/or whether continuous treatment was needed”. Was this an inclusion criterion for problems? If yes, this should be mentioned.

6. p.4 para 3 line 5: “social problems” and “relevant medical history” of the patients were also assessed. Please give a detailed operation definition of these issue, i.e. which facts were counted as social problems or relevant medical history.

7. p.8 para 3 line 1: “The main strength of this study is that the morbidity
estimates are derived from chart review rather than automated diagnostic codes”. In my experience data from GPs patient charts are automatically extracted and sent to health insurance companies to justify insurance claims. For this reason automated diagnostic codes are usually the same as data from chart reviews. If this should also be the case in your study, this sentence needs to be adjusted.

8. p.8 para 3 line 4: “Moreover, the way we constructed the problem list enabled us to include every condition instead of a limited list.” If a patient had two or more problems with a low prevalence that had to be coded in one CIRS domain how did you proceed? Were they counted as only one CIRS problem? If yes, you should discuss that.

9. p.9 para 1 line 4: “However, due to the high morbidity load and complexity of the patient population we do believe that this population was suitable to identify relevant combinations at practice level.” It should be noted as limitation of the study that – compared to the complexity of multimorbidity – a very low sample size was obtained. For this reason the study might have missed possibly relevant combinations.

10. As additional limitation it should be noted that only combinations of two problems are considered while elderly patients normally have a much larger number of problems.

There are also some typos that need to be corrected:

11. p.5 para 2 line 5: “constructed a list 23 problems” -> an “of” is missing
12. p.6 para 2 line 2: “in the study sample is f 73 years” -> the “f” should be deleted
13. p.6 para 3 line 1: “problem pairs who occur” -> “who” should be replaced by “which”

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.