Reviewer’s report

Title: Relationship Between Multimorbidity, Demographic Factors and Mortality: Findings from the UK Biobank Cohort

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Reviewer: Mette Nørgaard

Reviewer's report:

The present study uses a well-characterized cohort, The UK Biobank Cohort, to assess an important issue, i.e. premature mortality in middle-aged people. In its current form, however, the novelty of the study is not clear.

The exposure is number of self-reported chronic diseases and the outcomes are all-cause mortality, cancer-specific mortality and cardiovascular mortality within 7 years of follow-up. It is demonstrated that a person's 7-year mortality is higher if that person has a chronic disease compared with no chronic disease and that 7-year mortality increases with the number of chronic diseases present. Which seems to be basic knowledge. That this is the fact across socioeconomic status groups is not really surprising either. It is also shown that the absolute mortality increases with age while the relative does not. But since the relative mortality depends on the risk of the outcome in the reference category - this is a well-known phenomenon as well. So what is the novelty? and what may the clinical consequences of these findings be? I do not think the findings have any major clinical impact - at least not in the current form.

The study does not at all address type of underlying chronic disease, which seems to be a major weakness. It is expected that 7-year mortality will vary by underlying type of chronic disease. Since an underlying cancer is needed in order to die of cancer, it would be relevant to know the prevalence of cancer in each comorbidity group at study entry. Also, it has been demonstrated in several previous publications that comorbidity is a predictor of mortality among patients with cancer. Can differences in prevalence of cancer between LCT groups at baseline perhaps explain most of the difference in 7-year cancer-specific death?

Similarly for cardiovascular death, it would be relevant to know the proportion of patients with cardiovascular diagnoses at baseline and to stratify the analyses according to presence of cardiovascular disease. Since, as also stated by the authors, it is well-known that presence of comorbidity is a predictor of death among patients with cardiovascular disease.

What is the validity of self-reported long-term conditions in the UK biobank cohort? - why is this information considered more valid than recorded ICD-10 diagnoses? Please discuss.
Premature death is mentioned in the title and in the background section. However, the authors do not at all address it in the result section or in the discussion. Since it is part of the title, please at least define the term in the method section and add a discussion of the results in relation to premature death in the discussion section.

On page 11 lines 229-232. The mortality rates are presented a bit backwards as if this was a case control study. In a cohort design, it is most logically to state the risk of the outcome according to exposure groups i.e. in the no LTC group 2408 (1.3%) died within end of follow-up, in the 1 LTC it was 4147 (2,5%). Instead of stating how large a proportion of the deaths were in the different LTC groups.

It does not seem clinically relevant to look at statistical interaction. Instead, it would be interesting to present data for biological interactions. I.e are some combinations of types of chronic disease related to a particularly high (or low) 7-year mortality. Or are high physical activity particularly beneficial in some types of chronic diseases measured on 7-year mortality? Particularly, since there are nice data on lifestyle factors in this cohort.

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

No

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

Yes

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