Reviewer’s report

Title: Representation of people with comorbidity and multimorbidity in clinical trials of novel drug therapies; an individual-level participant data analysis

Version: 0 Date: 21 Jun 2019

Reviewer: Adam Todd

Reviewer's report:

Thank you for the opportunity to review this paper. The work seeks to address an important question, and challenges the current thinking around the inclusion of multimorbidity in clinical trials, and how this is applicable to the general population. The work is well written, the research question is well articulated, and the paper would definitely be of interest to the readers of BMC Medicine. Many congratulations to the authors for producing such an important piece of work.

My main comment relates to the discussion: given the findings of the paper, where do we go next in terms of trial/guideline development? Is the approach of NICE (and other organisations) in developing a specific multimorbidity guideline (to be used alongside disease specific guidelines) the correct one? The current narrative (of practice, not the paper) is that more trials need to be developed that include older people, multimorbidity, polypharmacy etc. These are obviously very challenging, and expensive things to undertake - do the authors feel as though this is the correct approach? I feel as though more could be made of the findings, given the problems we have of applying disease specific clinical practice guidelines to people in a general population. The conclusion (co-morbidity is less common in trials than in community populations, but it is still common in trials) could be also strengthened. Also, given that long-term conditions tend to cluster (i.e. it is more likely for people with chronic pain to also have mood disorders, or people with diabetes will also have hypertension etc.), could the authors make some comment in the discussion about this.

A minor comment would be to try and avoid the term "multimorbid" - a better term would be people/patients with multimorbidity.

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.

Unable to assess
Are the conclusions drawn adequately supported by the data shown?
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Yes

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