PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comparison of count-based multimorbidity measures in predicting emergency admission and functional decline in older community-dwelling adults: a prospective cohort study
AUTHORS	Wallace, Emma; McDowell, Ronald; Bennett, Kathleen; Fahey, Tom; Smith, Susan

VERSION 1 - REVIEW

REVIEWER	Jonathan Hewitt Cardiff University, UK
REVIEW RETURNED	22-Jun-2016

GENERAL COMMENTS	Many thanks for asking me to review this article which considers a count based system to further define the concept of multimorbidity Overall this is a well written and constructed article. My comments are intended to improve the work even further. 1, Introduction. I appreciate this is listed in the methods section but it would be helpful to the non multimorbidity specialist if you could explain exactly what you mean by a 'count based' model in this section. 2. Methods. You have included a number of exclusion criteria. While I have objections to these being used. I think you need to include a line in the limitations section about these, as they do limit, albeit to as modest degree, the generalizability of your findings. Statistical analysis (applicable throughout the manuscript) I have no problem with any of the statistics used but formal expert comment is above my level of competency and I would ask the editors to consider formal statistical review Results: First para page 12. These are essentially your prevalence estimates for each of the counts that you are using and that you mention in the abstract. I think you need to emphasise this to the reader in this paragraph ie use the word prevalence. Discussion: Well written and well balanced (See point above re limitations) Minor point pg 18 line 21 remove/change traditional as it implies that it is very well established and useful.

REVIEWER	Iñaki Martin Lesende Bilbao-Basurto Integrated Healthcare Organization (IHO), Osakidetza – Basque Health Service, Bizkaia, Spain
REVIEW RETURNED	27-Jun-2016

GENERAL COMMENTS	I consider the article and the study very good and interesting, and well designed-structured. Only I have to make a few recommendations and suggestions.

The main recommendation is to include in the manuscript the estimation of the necessary sample, considering the study design and objectives. In case this estimation has not been carried out previously to the beginning of the study, at least the stadistical power with the sample managed should be indicated. This is very important because the limitation of the sample size is mentioned in several sections of the manuscript, but not objectively justified.

Other minor comments are:

-I recommend that keywords are included in the MESH index.

-First of all, I praise the statistical analysis employed; do you think a logistic regression analysis could offer complementary information considering all basal count-based variables together?. It's just a suggestion, as I consider the main analysis developed very good and adequate.

-In "article summary", I suggest briefly explain why "the prospective study design and calculation of the exposure using medication linked pharmacy claims data" are strengths of the study.

-correct in reference 12 "primary care".

Again, congratulations for the article!!

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Jonathan Hewitt
Institution and Country: Cardiff University, UK
Please state any competing interests or state 'None declared': None Declared
Please leave your comments for the authors below:
Many thanks for asking me to review this article which considers a count based system to further define the concept of multimorbidity Overall this is a well written and constructed article. My comments are intended to improve the work even further.
1, Introduction. I appreciate this is listed in the methods section but it would be helpful to the non multimorbidity specialist if you could explain exactly what you mean by a 'count based' model in this section.
Response
Thank you. I have added the following to clarify: Utilising a count-based approach, such as simple disease or medication counts, in measuring multimorbidity has several advantages in that it is reasonably simple to apply and replication is more straightforward, important for achieving consistent definitions of multimorbidity across research studies.
2. Methods. You have included a number of exclusion criteria. While I have objections to these being used. I think you need to include a line in the limitations section about these, as they do limit, albeit to as modest degree, the generalizability of your findings.
Response
We agree-thank you. I have added this as a limitation as follows;
As one of the outcome measurements depended on participants' filling in a postal questionnaire those with cognitive impairment at the level that would impact their ability to complete the outcome measure (defined as Mini Mental State Examination ≤20) were excluded from this study which may also impact on generalisability of the findings.
Statistical analysis (applicable throughout the manuscript) I have no problem with any of the statistics used but formal expert comment is above my level of competency and I would ask the editors to

consider formal statistical review

Results: First para page 12. These are essentially your prevalence estimates for each of the counts that you are using and that you mention in the abstract. I think you need to emphasise this to the reader in this paragraph ie use the word prevalence.

Response

Thank you. We have added the following: The prevalence of patients with multimorbidity as defined by each of the five multimorbidity measures is presented in Table 2.

Discussion: Well written and well balanced (See point above re limitations) Minor point pg 18 line 21 remove/change traditional as it implies that it is very well established and useful.

Response

We have changed this as follows: Using the cut-point of ≥2 to define multimorbidity for the RxRisk-V measure.

Reviewer: 2

Reviewer Name: Iñaki Martin Lesende

Institution and Country: Bilbao-Basurto Integrated Healthcare Organization (IHO), Osakidetza – Basque Health Service, Bizkaia, Spain Competing Interests: The reviewer declares that he has no competing interests

I consider the article and the study very good and interesting, and well designed-structured. Only I have to make a few recommendations and suggestions.

The main recommendation is to include in the manuscript the estimation of the necessary sample, considering the study design and objectives. In case this estimation has not been carried out previously to the beginning of the study, at least the statistical power with the sample managed should be indicated. This is very important because the limitation of the sample size is mentioned in several sections of the manuscript, but not objectively justified.

Response

Thank you. This study was a secondary analysis of prospectively collected data designed to examine the association between potentially inappropriate prescribing and a primary outcome of adverse drug events. The sample size calculation for this question is as follows; 'Sample size was calculated at baseline for the study aim of determining an association between PIP and the primary outcome of patient self-report ADEs. In 2007, a study using the Irish HSE-PCRS database reported that approximately 36% of those aged >70 years received at least one PIP as per the STOPP criteria. Based on published literature, an ADE rate of 10% was assumed for those not prescribed any PIP and 20% for those prescribed any PIP.(119, 225, 226) Applying a two-sided significance level of 5% and power of 90% a sample size of 800 participants was required. (N=160-exposed to PIP group, n=640-unexposed to PIP group, total n=800). For a power of 80%, a smaller sample size of 656 participants was required (n=131 exposed group and n=525 unexposed group).

We conducted a post hoc power calculation for the question relating to multimorbidity measures and emergency admission. In this example we use the Charlson index (0: no Charlson conditions, 1: 1 or more Charlson conditions) as the exposure of interest and the emergency admission rate as the outcome of interest as follows.

340 participants had no Charlson conditions as baseline: of these 69 (20.29%) had at least one emergency admission at follow-up.

522 participants had at least 1 Charlson condition at baseline: of these 177 (33.91%) had at least one emergency admission at follow-up.

There is 99% power to detect a significant difference at the 5% significance level between the proportions of emergency admissions in these two groups if such a difference exists.

We also ran similar calculations using the other measures (disease counts, Barnett disease counts, RxRisk) and the power of the sample for the same question was >99% for all. Therefore we can say we were adequately powered to answer the questions of interest in this study. With this in mind I have clarified that this was a secondary analysis and that the sample was powered for a different question but have removed the limitation regarding sample size on the basis of the post-hoc power calculations.

This study was a secondary analysis of prospectively collected data examining the association between potentially inappropriate prescribing and adverse health outcomes in older people. Other minor comments are:

-I recommend that keywords are included in the MESH index.

Response

Thank you I have added the MeSH terms for emergency admission which is hospitalisation and functional decline which is frail elderly. I have added comorbidity as a MeSH term.

-First of all, I praise the statistical analysis employed; do you think a logistic regression analysis could offer complementary information considering all basal count-based variables together?. It's just a suggestion, as I consider the main analysis developed very good and adequate.

Response

Thank you for this interesting point. We were primarily interested in the diagnostic test accuracy of each of the multimorbidity measures rather than estimation of effects. With this in mind we used discrimination and ROC curves in the analysis. We could have ran logistic regression analyses for each multimorbidity measure adjusting for relevant confounders and then attempted to compare them based on effect size but this was somewhat outside the remit of what we wanted to examine in this study.

-In "article summary", I suggest briefly explain why "the prospective study design and calculation of the exposure using medication linked pharmacy claims data" are strengths of the study.

Response

Thank you. We have added the following to clarify: Some previous studies have been limited by study design (cross-sectional) and data available (e.g. self-report).

-correct in reference 12 "primary care".

Response

Thank you-this error has been corrected.

Again, congratulations for the article!!

VERSION 2 – REVIEW

REVIEWER	Jonathan Hewitt Cardiff University, Wales
REVIEW RETURNED	07-Jul-2016

GENERAL COMMENTS	I am satisfied that my minor comments have been revised.