PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice
AUTHORS	Harrison, Christopher; Britt, Helena; Miller, Graeme; Henderson, Joan

VERSION 1 - REVIEW

REVIEWER	Andrew Bonney University of Wollongong Australia The academic unit I lead at the University of Wollongong has a planned joint research project with the authors. I will be a co-investigator (not the Chief Investigator) on this project.
REVIEW RETURNED	23-Feb-2014

GENERAL COMMENTS	This well-written manuscript would benefit from some minor clarifications. Abstract The body of the paper is logically set out according to the three primary research questions. The methods, results and discussion reflect this structure and the manuscript concludes with some interesting proposals introducing the concepts of complex multimorbidity and complex co-morbidity. The abstract reverses the order of the primary research questions and lacks the clarity of structure of the manuscript itself. The concepts ('complex' multimorbidity) are not included in the abstract. The abstract would benefit from being structured similarly to the manuscript and some mention of the novel conclusions. Methods This is a prospective cross-sectional study with the major analytical approach being the comparison of point prevalence estimates and their 95% CIs. For readers not familiar with the BEACH study, it would be beneficial to make brief discussion of the generalisability of the sample and any associated limitations. It would also be helpful to know whether the study was designed with a priori power to detect differences at specified levels. The key statistical procedure is the adjustment for the single stage clustering to the 95% CIs of the prevalence estimates. To assist the interested reader, it would be helpful to outline the procedure used and provide some indication of the resultant degree of adjustment e.g. by providing relevant or indicative intra-cluster correlation co-efficients (ICCs). Publication of relevant ICCs would also be very helpful for other researchers planning studies in primary care.

	The statement was made that “Using this large prospective study we examined the effect of three different dimensions of measuring multimorbidity while controlling for other confounding variables.” Given the analytical approach and lack of further elaboration on the controlling of other confounding factors, I was unsure of the intention of the authors from this statement, which could be either elaborated upon or omitted. Limitations Discussion of any (potential) limitations associated with the sample would be helpful.

REVIEWER	Jean Yves le Reste department of general practice faculté de médecine université de bretagne occidentale
REVIEW RETURNED	23-Feb-2014

GENERAL COMMENTS	A more neutral and coherent writing should be applied throughout the manuscript (for example "we" and "this study" are alternatively used). INTRODUCTION: The research question should be clearly defined at the end of introduction. METHOD: The level of the cluster effect should be clearly defined with the level of the intra class correlation coefficient chosen according to the following formula :(1+ [m - 1] x ρ) where m is the size of the average cluster and p the intra class correlation coefficient. DISCUSSION: Limitations should be more focused on bias (selection, information and confusion) and on the sample's characteristics. REFERENCES: 1 seems to be a book the city of the editor should be described, 3 the webpage should be described with the consultation date. very interesting and challenging article of great value for all researchers working in the field of multimorbidity. Should be published with some minor revision.

REVIEWER	Amaia Calderón-Larrañaga Aragon Health Sciences Institute (IACS), Spain
REVIEW RETURNED	11-Apr-2014

GENERAL COMMENTS	This paper addresses an important issue as is the impact of certain parameters in the prevalence estimates of multimorbidity obtained from electronic health records from primary care. The definition of disease entities, the number of disease entities required to define multimorbity, and the number of baseline chronic conditions are all essential aspects affecting, not only the prevalence of multimorbidity but also the patterns of diseases showing up in a given population, as recently stated by Prados-Torres et al (JCE, 2014). My main concern is related to a lack of support for the

	conceptualisation made by authors regarding the differentiation between simple and complex multimorbidity. As recently stated by Richardson and Doster (JCE, 2014), multimorbidity and comorbidity need to be studied from the perspective of their impact on the process of evidence-based decision making. The term “complex” has more to do with how a given patient interferes with clinical decision-making and care processes, than with the simple number of health problems (Grant, Ann Intern Med, 2011). Indeed, the current definition of multimorbidity based on simple counts of conditions has been criticised as being little helpful when addressing the health care needs of patients with multimorbidity (Goodman et al, Ann Fam Med, 2012). Thus, eventual classifications of types of multimorbity need to consider other dimensions of patients’ health, related to their care and outcomes, which was not the case of this study. The authors should discuss and reflect on these aspects in more depth.

VERSION 1 – AUTHOR RESPONSE

Response to reviewer 1

Abstract
The body of the paper is logically set out according to the three primary research questions. The methods, results and discussion reflect this structure and the manuscript concludes with some interesting proposals introducing the concepts of complex multimorbidity and complex co-morbidity. The abstract reverses the order of the primary research questions and lacks the clarity of structure of the manuscript itself. The concepts (‘complex’ multimorbidity) are not included in the abstract. The abstract would benefit from being structured similarly to the manuscript and some mention of the novel conclusions.

We have restructured the abstract and have added an additional line which mentions the concept of “complex multimorbidity”

This is a prospective cross-sectional study with the major analytical approach being the comparison of point prevalence estimates and their 95% CIs. For readers not familiar with the BEACH study, it would be beneficial to make brief discussion of the generalisability of the sample and any associated limitations.

We have added the following sentence in the methods to show that the BEACH study (and this sub-study in particular) is representative of patients at GP encounters across Australia.
“This sample was previously shown to be representative of the age-sex distribution of patients at all GP encounters claimed (as items of service) through Medicare in 2008–09(18).”

We also added this paragraph in the limitations to remind readers that patients at GP encounters are not representative of the population.

“While our study was representative of patients at GP encounters, it should be remembered that patients are not representative of population. Patients at GP encounters are generally older and therefore more likely to have a chronic condition(18).”

It would also be helpful to know whether the study was designed with a priori power to detect differences at specified levels. The key statistical procedure is the adjustment for the single stage clustering to the 95% CIs of the prevalence estimates. To assist the interested reader, it would be helpful to outline the procedure used and provide some indication of the resultant degree of

adjustment e.g. by providing relevant or indicative intra-cluster correlation co-efficients (ICCs). Publication of relevant ICCs would also be very helpful for other researchers planning studies in primary care.

We did not perform a priori power calculation as the sample size of SAND substudies is built into the structure of the larger BEACH study. We did perform an ICC calculation and have added this line to the start of the results

“The intra-cluster correlation coefficient was 0.121 for patients with at least one chronic condition.”

“Using this large prospective study we examined the effect of three different dimensions of measuring multimorbidity while controlling for other confounding variables.”

Given the analytical approach and lack of further elaboration on the controlling of other confounding factors, I was unsure of the intention of the authors from this statement, which could be either elaborated upon or omitted.

The study design itself controlled for other confounding factors. We used the same data and only changed the value of the three variables under study. We have added an additional line underneath so that it now reads.

“Using this large prospective study we examined the effect of three different dimensions of measuring multimorbidity while controlling for other confounding variables. This is achieved through the structure of the study, by only changing one of the three variables at a time.”

Response to reviewer 2

INTRODUCTION: The research question should be clearly defined at the end of introduction.

It now reads
“Our study examines how multimorbidity prevalence estimates are effected by: the number of chronic conditions studied; how a disease entity is defined; and the minimum number of disease entities required to define multimorbidity.”

METHOD: The level of the cluster effect should be clearly defined with the level of the intra class correlation coefficient chosen according to the following formula :(1+ [m - 1] x ρ) where m is the size of the average cluster and p the intra class correlation coefficient.

As stated above, we calculated the ICC and have presented the result

DISCUSSION: Limitations should be more focused on bias (selection, information and confusion) and on the sample's characteristics.

As mentioned above we added the following statement about the study’s representativeness
“This sample was previously shown to be representative of the age-sex distribution of patients at all GP encounters claimed (as items of service) through Medicare in 2008–09(18).”

We also added this paragraph in the limitations to remind readers that patients at GP encounters are not representative of the population.

“While our study was representative of patients at GP encounters, it should be remembered that patients are not representative of population. Patients at GP encounters are generally older and

therefore more likely to have a chronic condition(18)."

REFERENCES: 1 seems to be a book the city of the editor should be described, 3 the webpage should be described with the consultation date.

We have corrected both references

Response to reviewer 3

We very much agree with reviewers three's comments on the subject of multimorbidity. Multimorbidity is more than simply patients with multiple chronic conditions. Patients with multimorbidity have been shown to: require more complex care; be more likely to be using multiple medications thus increasing their chance of an adverse event through medication interactions; have higher health care resource use; have lower quality of life; and have greater overall severity of illness. We acknowledge that multimorbidity is a complex concept.
However, the studies that have shown the above results have all used different definitions of multimorbidity, using different criteria. The point of our current paper was to first examine the effect of these different definitions on identifying patients with multimorbidity. The second was to recommend a new definition of multimorbidity that may indeed be better at identifying high need patients with multimorbidity.

The final sentence of our paper states
"However, further research is needed to assess whether 'complex multimorbidity' is indeed better than alternative measures of multimorbidity (such as counting individual chronic conditions, measures of severity etc.) in identifying patients with greater health care resource use, complexity of care, lower quality of life and overall severity of illness."

In our next paper we will be examining whether "complex multimorbidity" is actually a better predictor of many of the above adverse outcomes. We agree with the comments made by reviewer three, however their recommendation for this paper is the subject of our next paper, currently in progress.

VERSION 2 – REVIEW

REVIEWER	Jean Yves le Reste département de médecine générale université de bretagne occidentale Brest France
REVIEW RETURNED	01-Jun-2014

GENERAL COMMENTS	all comments were taken into account

REVIEWER	Amaia Calderón-Larrañaga Aragón Health Sciences Institute, Spain
REVIEW RETURNED	16-Jun-2014

GENERAL COMMENTS	The authors have adequately responded to the comments raised by the reviewers.