Author's response to reviews

Title: Patterns of multi-morbidity in working Australians

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Author's response to reviews: see over
Please find attached the revised manuscript for submission to the Population Health Metrics entitled “Patterns of multi-morbidity in working Australians”.

We obtained an extension on the due date of revisions on this paper, now due 08/02/2011 (via email correspondence with Jolayne Houtz dated 14/01/2011).

We are grateful to the reviewers for their time and detailed review of this manuscript. Their comments have helped to make the paper much more clear. The word count for this research report is 160 (Abstract) and 2,000 (main text, not including references, figures and tables). There are three tables and one figure.

This manuscript represents results of original work that have not been published or submitted elsewhere. This manuscript has not and will not be submitted for publication elsewhere until a decision is made regarding its acceptability for publication in the Population Health Metrics.

Each of the authors made a significant contribution to the conception and design, and/or data analysis and interpretation for the study. All authors have contributed to and reviewed the draft and final versions of this manuscript. No author has any affiliation or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the article.

Response to Editors Requests and Reviewers Comments

Editors Requests:
1. Revisions have been indicated using track changes.
2. Revisions conform to journal style for Population Health Metrics.
Reviewer 1: Martin Fortin

Reviewer’s report:
Thank you for inviting me to review this interesting paper. I think some more work is required but I’m confident that the authors will be able to provide the additional required information.

Major Compulsory revisions
1. Title is misleading because the paper is more about comparing two methods to identify non-random clusters of multi-morbidity and not to report on the results for the Australian working population.

All reviewers raised this issue; therefore we focused this paper on the exploratory factor analysis method to address the existing title of the paper: that is, reporting on patterns of multi-morbidity in working Australians.

2. Introduction should be improved. Third paragraph starting with: The study of patterns... should be completely re-written to clearly identify the rationale of doing this study, to justify the need of this study.

This paragraph has been changed to include the following sentences in appropriate places:
“The above methods do not use statistical approaches to identify the non-random cluster patterns of individual health conditions into groups of multi-morbid conditions. The objective of this study was to use software and statistical analysis methods that allow for the dichotomous nature of disease data, to identify non-randomly occurring clusters of multi-morbid health conditions. Identifying clusters of multi-morbidity is important due to rising health care costs associated with servicing an increasingly aging population with complex health care needs. Health service providers need to better understand the complexity of the health status of consumers to ensure more strategic and tailored health care is provided.”

Third sentence starting with "These methods...": it's not clear which methods the authors are referring to.

This has been changed to read as follows: “The above methods do not use statistical methods to identify the non-random cluster patterns of individual health conditions into groups of multi-morbid conditions.”

Be sure not to include elements that should go in the methods section like the sentence: "We chose to use exploratory..."

This sentence has been deleted.

3. Objective: I would suggest reformulating the two last sentences of the introduction like: The objective of this study was to identify non-randomly occurring clusters of multi-morbid health conditions by using two different methods...

The last two sentences have been deleted and replaced with the last two sentences written in response to item 2 above. The first sentence begins with: “The objective ...”
4. Methods: For the purpose of coherence, the authors should avoid giving results in the methods section. One could argue that those results (n, response rate...) belong to another study and should be presented in the methods section but the authors chose to give some of the results in the results section. I can't see any good raisons to present the results of the former study in two different sections.

The section titled study sample has been deleted except for the first two sentences. The last sentence of the methods section commencing: “Table 3 shows...” has been deleted from the methods.

5. The authors should also avoid mixing the sections. The results section is somewhat contaminated with elements of discussion particularly p.7 at the end of the results section.

The last paragraph of the results section commencing: “Comparison of methods” has been deleted”

6. The discussion should be strengthened and should include a discussion of the contribution of this study to the body of knowledge on multi-morbidity and its measure. The comparison with the Cumulative Illness Rating Scale is interesting but need some more thoughts and connections with the objective of the study.

The discussion has been changed considerably, particularly in response to the second reviewer’s comments. As a result, the first two paragraphs of the discussion have been deleted including the paragraph referred to above.

In addition to these changes (described in response to comments by reviewer 2), the following sentence has been added to the first paragraph of a new section of the Discussion titled “Strengths and Limitations of the Study”

“This study adds to the only other available study [21] to use statistical methods on a group of individual health conditions to explore non-random clustering of multi-morbidity. With an increasingly aging population and evidence that co-morbidity and multi-morbidity increase with age [3-5], combined with rising health care costs associated with new procedures and treatments, a better understanding of how health conditions cluster together will enable better care management of individuals with chronic and complex diseases.”

7. The last paragraph of the discussion is about psychological distress. The authors should suggest potential reasons to explain their findings.

Two of the three reviewers raised concerns about this paragraph. We have decided to delete this paragraph as it is not the focus of this paper. We feel that further research is needed to adequately explain the relationship between psychological distress and patterns of multi-morbidity.
8. The clinical content of the discussion could be improved.

The following paragraphs have been added to the Discussion which are of a clinical nature:

“Interpretation of findings:

Some conditions appear in more than one factor. Exploratory factor analysis allows for this which is appropriate for the objectives of this study. Previous studies that use statistical methods to explore relationships of multi-morbid conditions or clusters of organ systems have also found this. [6, 20, 21] Of the 23 conditions available for analysis in our study, we found chronic pain to be in three of the six clusters, diabetes, high blood pressure and high cholesterol to be in the same two of the six clusters; and arthritis and irritable bowel to each be in two different clusters.

We found that health conditions do not cluster neatly into organ or body system as has been assumed in the methods underpinning the Cumulative Illness Rating Scale [22] A study by Britt et al. [20] demonstrates this. They used the CIRS and explored patterns of multi-morbidity and found that groups of individuals fitted into between two and eight combinations of CIRS domains. [20]

Only one other study was found that explored patterns of multi-morbidity among individual health conditions. [21] A study by Cornell et al. of more than 1.3 million primary care patients cared for by the Veterans Health Care System with two or more co-morbidities categorised 45 health conditions. [21] Similarities exist between our fifth cluster and Cornell’s ‘Metabolic cluster’, the cluster that had the highest degree of association in their study. They reported that 83% of their sample fell into this cluster, three of which are represented in our fifth factor (hypertension, high cholesterol and diabetes). Differences between the study by Cornell et al. and this study include statistical method (cluster analysis relies on prevalence so conditions will low prevalence will be under-represented), sample size and composition (Cornell’s sample was much larger and all study participants had two or more health conditions whereas our sample were well enough and young enough to attend work), and the number of health conditions were greater in the Cornell study. These differences may account for discrepancies in the cluster composition between the two studies.”

9. A section on limitations is required and should include a discussion about the extremely low response rate and its potential impact.

The following discussion of limitations has been added:

“There are some limitations to our study that need to be considered. This is an opportunistic sample of willing employees from 58 large organisations. The response rate was low (22%). A comparison of respondents and non-respondents was not possible so the implications of the poor response rate are not known. For example,
only those at work during the data collection period responded. People on extended sick leave or out of the workforce are not represented. The sample also has over-representation of females. The self-reported nature of health conditions, and the number and type of health conditions available need to also to be considered. For example there is an absence of some high cost conditions such as kidney disease. Therefore extrapolation of these findings to the general population should be done with caution; however, the findings are relevant to those sectors and groups where the demographic profile is similar."

10. The conclusion should be directly in line with the objective which is not exactly the case at this time.

The conclusion has been re-written as follows:

“This study identified clinically meaningful clusters of multi-morbid health conditions that do not fall neatly into organ or body systems. Some conditions appear in more than one cluster. Few studies are available that use statistical methods to explore patterns of multi-morbidity in a group of individual health conditions. A large population based sample with reliable diagnosis data at an individual level is required.”

11. One possible way to strengthen the discussion would be to put compare the result with a publish study by Cornell JE. MULTIMORBIDITY CLUSTERS: CLUSTERING BINARY DATA FROM MULTIMORBIDITY CLUSTERS: CLUSTERING BINARY DATA FROM A LARGE ADMINISTRATIVE MEDICAL DATABASE. Applied Multivariate Research, Volume 12, No. 3, 2007, 163-182.

This study has been used for comparison with our findings. See point 8 above.

Minor essential revision:
12. The authors should review the verb tenses used in this paper. The use of the present and the simple past is not always appropriate particularly in the sub-section of the methods presenting the Statistical analysis.

This revised paper has been proof-read with particular emphasis on verb tense and changes made where needed.

13. The authors should number the tables in the same order that they appear in the text. Table 2 is referred to for the first time after the table 3.

The reference made to Table 3 before Table 2 has been removed from the methods section, and all table numbering in text checked for logical order.

14. Results: The author should avoid repeating in the text information already present in the tables unless they want to bring attention to an important result.(ex. description of characteristics of the sample).

The discussion of the demographics characteristics of the study sample has been reduced in length.
15. The sentence starting with: Figure 1 is a dendrogram... reads funny. The authors should consider reformulation.

This paragraph has been removed due to the decision to make the paper more focused on exploratory factor analysis (see response to comment 1 above).

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interest

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Reviewer 2: Helena Britt

Reviewer’s report:
This paper aims to identify patterns of non-randomly occurring clusters of multi-morbid health conditions using a new statistical approach: using two approaches, hierarchical clustering Algorithm and Exploratory Factor Analysis methods. Both methods are said to have 'findings similar to those found in the Cumulative Illness Rating Scale based around body system groupings.

Minor essential revisions
1. Abstract:
1.1 Background: Not all previous methods have relied on counting the ‘number of health conditions (e.g. ref 23 groups to CIRS), ‘often in relation to an index condition’ (not indexed)…. You need to add in brackets after this statement (comorbidity).

These revisions have been made as follows:
“Previously used methods relied on counting the number of health conditions, often in relation to an index condition (co-morbidity), or grouping conditions based on body or organ system.”

1.2 Results: please see comments on your results in reference to the body of the paper.

The results in the Abstract results have been changed and this now reads as follows:
“Some conditions appear in more than one factor. Health conditions do not cluster neatly into organ or body system.”

2. Introduction.
2.1 You need to move reference 23 to a position after ref 5, and use this reference in para 2 line 2; in para 2 last line (this line uses results from ref 23 data but it is not referenced here); para 3 line 2; par 3 line 5.

These edits have been made to the first and second paragraphs of the introduction.

3. Methods
3.1 Sample- response rate of valid responses used in this paper is 21.5%. This is the response rate you should quote here, not the 24.7%. 
This section has been removed from the methods section in response to reviewer 1 point 4. The following sentence has been added to the discussion of limitations of the study. “The response rate was low (22%). A comparison of respondents and non-respondents was not possible so the implications of the poor response rate are not known. For example, ...” (see response to reviewer 1, point 9 for more details of the limitation section).

3.2 The inclusion of fatigue in the list of 26 selected conditions is interesting usually multimorbidity is limited to chronic conditions, and ‘fatigue’ (without further detail) can be either acute or chronic, but is largely non-chronic. Perhaps this should be discussed in the discussion.

A discussion of fatigue has been added to the end of the Strengths and Limitations of the Study section of the Discussion as follows:

“Fatigue, which may be either chronic or acute, was included in the model. As fatigue is mostly acute one may question whether it should be included. However, the results demonstrate that fatigue is included in two of the multi-morbidity groupings highlighting its importance for inclusion in multi-morbidity analyses.”

3.3 Page 4 last sentence: Do you mean all responses were exclude if this was the case for any one condition, or was the respondents positive response to that single condition for which treatment had not been received exclude while their remaining morbidities were included?

The last paragraph of page 4 has been deleted due to the decision to remove the hierarchical clustering analysis (HCA) methods in response to other reviewers, see comment 1, reviewer 1 above.

I do not have the statistical knowledge to review these methods. They require a statistician.

4.1 My comments in this section are therefore limited to the use of the English language. -- Everywhere you use ‘degree of co-occurring’, it should read ‘co-occurrence’. --“where kappa equals to zero’ should read ‘where kappa equals zero’.

These items are related to the paragraph mentioned above, which has been deleted.

5. Results:
The results for the clusters identified by the HCA method and the Factors identified by the EFA method are clearly stated.

5.1 Page 7, last three line: This belongs in the discussion, not in the results, as it is an explanation of WHY the different methods results in a different number of clusters/factors.

The last paragraph of page 7 has also been deleted due to the decision to remove the hierarchical clustering analysis. This in response to concerns raised by other
reviewers, see comment 1, reviewer 1 above. The methods section explains decisions related to the EFA method. Please let us know if further clarification is required.

5.2 What is a ‘loading’?

“Loading” is a measure of the association between an item and a factor. The size of a loading indicates the contribution of an item to the definition of a factor. This is a term commonly used in the discussion of exploratory and confirmatory factor analysis.

Major essential revisions

6. Discussion: The discussion needs major revision.

We have undertaken major revisions to the discussion based on the valuable feedback provided below.

6.1 The whole of the discussion relies on your opening statement, that the grouping of health conditions identified through both methods appear to be grouped loosely into organ system functioning. You further state that the groupings are consistent with the CIRS groupings. These statements are not really correct. The statements ARE correct for Cluster 7 and you could almost get away with Factor 2, though ‘allergies’ are often related to the skin, not the respiratory system. For the other cluster and factors the groupings are not to body system, as classified by the International Classification of primary Care, and are not grouped according to the CIRS. For example: Using ICPC-2 – the Australian and WHO recommended standard for reporting patient self reported and general practice morbidity – and which is based on body systems. In Cluster 4 you have back/neck pain (ICPC chapter L musculoskeletal) + injuries (what type?) if in injuries of the musculoskeletal system they also fit into ICPC chapter L, but there are other injuries related to other body systems) + migraine (ICPC chapter N neurological). Another example: Cluster 6: high blood pressure (ICPC chapter K circulatory) + high cholesterol and obesity (both in ICPC Chapter T – Endocrine, Metabolic Nutritional). Another: Factor 1 is a mixture of musculoskeletal and Urinary and Digestive ICPC chapters. Using CIRS (Ref: Jour Clinical Epi, 60 (2007) 212 Abbreviated guidelines for Scoring the Cumulative Illness Rating Scale (CIRS) in family practice. In Cluster 4 you have back/neck pain (CIRS Endocrine, metabolic, breast) + injuries (what type?) if injuries of the musculoskeletal system they also fit CIRS Musculokeletal and tegumental, but there are other injuries related to other body systems) + migraine (CIRS Neurological). Another example: Cluster 6: high blood pressure (CIRS Vascular) + high cholesterol and obesity (both in CIRS Endocrine, metabolic). Another: Factor 1 is a mixture of CIRS groups Musculoskeletal & Tegumental, Genitourinary and Lower gastrointestinal.

The first three paragraphs of the discussion have been completely re-written. See response to reviewer 1, item 8 above.

6.2 Page 9 first para, statement in relation to reference 6. The Saltman paper reports management frequencies not prevalence so I don’t think it should be included. Ref 23 adjusted for attendance rates by age-sex and for non attenders so the statement of not being representative is inappropriate.

This sentence has been removed.
6.3 Page 89: perhaps your use of the term ‘psychological distress’ may have mislead the respondents. The Britt et al paper compared their results with the patient self reported prevalence of ‘psychological problems’ and found the self report to be low. Other studies have demonstrated the same under-reporting by self report. Are you sure Fortan used the term ‘psychological distress’ or was it ‘Psychiatric problem’.

This paragraph has been removed in response to reviewer 1, point 7 above.

6.4 Limitations. There is a distinct lack of a section on limitations. This needs to be added. Limitations include:
--lack of generalisability to the population at large ( because subjects were ‘workers’
--You have offered only 28 common conditions or risk factors. The selective nature of this list will effect your results.
--Limitations of patient self report: there is wide ranging literature on this topic

A strengths and limitations section has been added and the above issues addressed (see response to reviewer 1, point 9).

– you could move the last sentence of the Methods section into the discussion, where it belongs.

This has been removed.

7 Conclusions. In light of my comments about the discussion, the conclusion needs to be changed, removing the statement that the clusters were around ‘body systems’ and that this was consistent with CIRS.

The conclusions has been re-written based on feedback from reviewers (see response to reviewer 1, point 10 above).

8. Tables and Figures. I have no comments on the Tables and figures as I have insufficient knowledge of statistical methods to judge their appropriateness.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests
As a result of concerns raised by this and other reviewers we made the decision to remove the hierarchical clustering analysis methods to focus on the question of how diseases cluster using the EFA method, see comment 1, reviewer 1 above.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
I cannot judge the statistical paragraph, because I’m not an expert in clustering techniques and factor analysis. Also the results are hard to understand, because it is very technical. I think it’s up to the editor to decide whether or not this is acceptable (in terms of readability of the journal). However, doing a quick search on the internet gives me the impression that you should have used tetrachoric correlations instead of polychoric in case of dichotomous variables.

This was an oversight; the correct term to be used is tetrachoric. This error has been fixed.

3. Are the data sound and well controlled?
The response rate in this study is extremely low, with 24.7%. Although it is stated that the participants might not be a representative sample of all working Australians, I think the authors should be a bit more critical. This should be further elaborated in the discussion.

This has been addressed in the new ‘strengths and limitations’ section in the Discussion. See response to reviewer 1, point 9.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
It is true that the terms co-morbidity and multi-morbidity are used interchangeably in the literature. However, I strongly promote that for individual studies, authors choose one way of handling the terms (preferable conform the definitions of Feinstein (1970) and of van den Akker et al (2001, JCE).

We have edited the first paragraph of the Introduction to clarify the use of these terms in this paper, as follows:
“The term ‘co-morbidity’ was first used in 1970 by Feinstein (as cited by Kessler et al., 2001 [1]) and by van den Akker et al. [2, 3] to refer to situations where an individual has two or more physical and/or mental health conditions. More recently the term multi-morbidity was introduced. [2-4] Although co-morbidity and multi-morbidity are both used to describe two or more health conditions, a distinction is made between these two terms; co-morbidity is used when an index condition of interest is being discussed and multi-morbidity is used when no reference condition is considered [4]. Although these distinctions are not so clearly applied with both terms being used interchangeably in the literature, we will use this definition of these terms in this paper. Sometimes health conditions can be co-morbid purely by chance; however, certain co-morbidity clusters can also occur at higher than chance levels.[1]”

5. Are the discussion and conclusions well balanced and adequately supported by the data?
In the discussion, the authors should pay attention to the fact that they make use of self-reports on disease. Possibly, this influences the results. Also, the low response rate should be discussed.

This issue is also addressed in the ‘strengths and limitations’ section mentioned above in response to item 3 of comments from Reviewer 3.

6. Do the title and abstract accurately convey what has been found?  
Yes

7. Is the writing acceptable?  
In general, yes. However, there are some specific remarks:  
-I cannot properly read figure 1 and relate it to the text at page 6.

This figure has been removed as we are no longer including results related to the HCA methods – see response to reviewer 1, comment 1; and reviewer 2, comment 3.3 for a more detailed explanation.

-It is not clear whether 28 (page 3) or 23 (page 4) health conditions were included in the analyses.

The ‘study measures’ section of the methods has been revised to clarify this and the next issue mentioned below, as follows:

“Study measures: The Health and Productivity Questionnaire (HPQ) from the World Health Organisation [14] was used to collect self-reported health status on 22 health conditions and the Kessler 6 [15], a validated measure of psychological distress which is included within the HPQ, was used to collect psychological distress data; totalling 23 conditions explored for multi-morbidity patterns in this study. The following health conditions were included in the analyses as these were available in the HPQ: arthritis, asthma, back/neck pain, cancers (excluding skin cancer), skin cancers, chronic obstructive pulmonary disease (COPD) (and included chronic bronchitis and emphysema), cardiovascular disease (CVD), psychological distress (being a K6 score of 13 and above [16]), drug and alcohol problems, diabetes, fatigue (including sleep problems), high blood pressure, high cholesterol, injury (workplace injury requiring medical treatment), migraine (and severe headache), and obesity (using self reported height and weight to calculate BMI), bladder problems, heartburn, irritable bowel disorder, ulcers, osteoporosis, or other chronic pain….”

-Please make sure the disease labels are similar throughout the manuscript fatigue or fatigue/sleep problems; COPD or COPD & bronchiectasis.

See revisions to the ‘study measures’ section of the methods provided above in response to the previous comment.
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: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interests.

Thank you for considering our manuscript for publication in your journal.

Kind regards,

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