Author's response to reviews

Title: Chronic disease and falls in community-dwelling Canadians over 65 years old: A population-based study exploring associations with number and pattern of chronic conditions

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Author's response to reviews: see over
Dear Dr. Helbostad,

Please accept this revised manuscript, now titled “Chronic disease and falls in community-dwelling Canadians over 65 years old: A population-based study exploring associations with number and pattern of chronic conditions” as an original article for publication in BMC Geriatrics. We appreciate the opportunity to make changes to the manuscript. We have responded to all of the issues noted by the Reviewers and feel that this version is improved and clearer for the reader. In particular, we have added additional detail on the Canadian Community Health Survey and cluster analysis methods, described our rationale for the covariates included in the logistic regression analysis, and clarified our use of the terms “multi-morbidity” and “chronic disease”. Changes to the manuscript text are noted in blue font, and a detailed summary of our changes is included in the attached Response to Reviewers that follows this page.

All authors have read and approved the submission of this manuscript. There are no conflicts of interest for any of the authors. Material in the manuscript has not been previously published and is not being considered for publication elsewhere.

Thank you for considering this revised submission. Please do not hesitate to contact myself or Dr. Jaglal if you have any questions or require more information. We look forward to your feedback.

Sincerely,

Kathryn Sibley, PhD
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We would like to thank Dr. Vu and Dr. Freiberger for their constructive comments and suggestions. We have responded to each comment below (in italics) and made the necessary changes to the manuscript. Changes to the manuscript text have been noted in the paper in blue bold font.

**Reviewer:** Trang Vu

**Reviewer’s report:**

**Major Compulsory Revisions**

**Methods:**

Page 5: The authors should provide key details about the Canadian Community Health Survey – Healthy Aging so readers can understand how the study population was selected, how the sampling was done and how data quality was assured.

*As requested, we have included additional detail about the population, sampling procedures, and data quality assessments, as well as referring to a link to the survey description on the Statistics Canada web page. These changes were added to the first methods paragraph on pages 5 and 6. We think these revisions provide the key details about the CCHS, but would be happy to provide more details if particular issues are still unclear.*

Page 6: Readers unfamiliar with cluster analysis would benefit from having the terms “centroid”, “average linkage” and “Ward’s clustering method” explained. This will enhance their understanding of the approach used to validate different clustering solutions detailed on page 7.

*Thank you for this suggestion. We have included additional detail on hierarchical agglomerative clustering approaches and distinctions between Ward’s, average linkage and centroid methods to assist readers who may be unfamiliar with cluster analysis (page 7 and 8).*

Page 7: Age and gender were included as covariates in the logistic regression model. Did the authors consider other covariates? For example, limitation in activities of daily living, use of walking aids, number of medications, use of psychotropic medications and living alone.

*Yes, we did consider including other covariates, however, a number of factors lead us to the decision to include only the relatively ‘fixed’ parameters of age and gender as covariates. First, data measurement issues with respect to the timeframe of some variables made it difficult to include them in the model. For example, the questions about mobility level, activities of daily living, number of medications, use of psychotropic medications and living status were all asked about their current status, relative to the last 7 or 30 days. In contrast, the falls question was asked relative to the past 12 months. As such, we do not feel it is appropriate to adjust for these “current” variables when*
modelling something that happened earlier, and elected to adjust only for age and gender that would not fluctuate. We have noted the temporal discrepancies between variables as limiting our ability to adjust for them in the discussion text on page 15.

Second, many of these variables are related to one another, and as such we were concerned about risk of “over-adjusting” our model. Over-adjustment bias has been described as “statistical adjustment by an excessive number of variables or parameters, uninformed by substantive knowledge … it can obscure a true effect or create an apparent effect where none exist” (Breslow. Annu Rev Public Health 1982). Shisterman and colleagues define it simply as “control for an intermediate variable (or a descending proxy for an intermediate variable) on a causal path from exposure to outcome” (Shisterman et al. Epidemiology 2009). In the case of falls, there are a number of known interrelated, potentially proxy or intermediary factors, along a relatively fuzzy causal path. For example, age, mobility, and functional limitations are all risk factors for falls (Tinetti and Kumar. JAMA 2010), while age, falls, and chronic disease significantly predict personal and community mobility in large, population-based studies such as ours (Meyer et al. The Gerontologist 2013). Similarly, systematic review evidence indicates that chronic disease burden is associated with increased risk for functional decline and disability (Stuck et al. Social Science and Medicine 1999; Marengoni et al. Ageing Research Reviews 2011). And, population-based data illustrate links between chronic disease and medication use (Hagstrom et al. Scand J Pub Health 2006). Indeed, we examined correlations between all of the descriptive measures and clusters and found significant correlations between all measures (p< 0.05). Accordingly, we are of the view that chronic diseases and descriptive characteristics such as mobility, activities of daily living, and medication use, etc. are proxy indicators for one another. Therefore by accounting for chronic disease we are accounting for these issues at the same time, and to include them in the models will lead to over-adjustment. To address the reviewer’s concern, we investigated what would happen if we included mobility, ADLs, number of medications and psychotropic medications in the model, and indeed the magnitude of all trends and relationships were maintained, but reduced in amplitude. To us, this confirms that over-adjustment was a valid risk, and we have elected to keep our model that accounts for the cross-cutting effects of age and gender only. We still feel this is a valid analysis, as although chronic conditions and mobility or functional limitations may be considered proxy indicators of one another, the disease itself is the diagnosed condition and likely more in the ‘mindset’ of the healthcare provider. Our analysis adds to the literature by reframing the way that clinicians can conceptualize fall risk- in terms of diseases, rather than specific behaviors or characteristics. As discussed in the discussion text, we feel that this approach could be useful in terms of organizing clinical decision making for assessing individual fall risk.

Results:

Page 8: Influence of specific chronic disease patterns on falls: Would it be possible to include the dendrogram of the final clustering solution?
Yes, we have included the dendogram as an additional file to be included with the manuscript (Additional File 1).

Table 1: Please spell out abbreviations such as ADL in table footnotes.
This abbreviation has been defined in the table footnote as requested.
Table 2: Please spell out abbreviations such as COPD in table footnotes. Also, are the labels for the last two columns accurate?

The abbreviations have been defined in the table footnotes as requested. Yes, the labels for the last two columns are accurate, and refer to the 95% CIs for columns 3 and 4. We have added additional detail to the table to make this relationship clearer.

Table 3, first column: Please provide full label instead of “# CCs”.

We have changed the label to ‘Number of chronic conditions’ as requested.

Table 4: The cluster labels should be in the top row. Also, are differences between groups statistically significant? I think the “Heart disease” cluster should be labelled “Heart disease and hypertension cluster” because the prevalence of hypertension was quite high in this cluster (84.5%).

The cluster name labels have been moved to the top row of the table as requested. Yes, the differences between clusters are significantly different, and we have added Chi-square results to Table 6. In addition, we conducted post-hoc tests and determined that the low chronic disease cluster was significantly different than the other clusters on most variables (reported in results text on page 10, second paragraph). Thank you for the suggestion to name cluster #7 “Heart disease and hypertension” – we agree and have made this change in the table and where appropriate throughout the paper.

Discussion:

Page 9: Last sentence in the first paragraph: Suggest the authors revise this sentence once the issue of ‘other covariates’ (see my comments for the Methods section) is addressed. Also, could the authors please comment on the clustering structure in terms of the degree of overlap?

As we have not modified the covariates in the logistic regression, we have not modified the last sentence in the first discussion paragraph. With respect to the clustering structure, it was non-overlapping in terms of individuals, but as illustrated in Table 5, there was some overlap of conditions across each of the clusters. This finding is noted in the results section on page 9 (last paragraph). While each individual was assigned to one of seven clusters, the distribution of overlap in conditions across clusters was varied. Some conditions were relatively evenly distributed across all clusters (e.g. cancer), others were concentrated primarily in one cluster (e.g. diabetes). This has been described in the first discussion paragraph on page 10.

Page 9: Second paragraph starting with “Indeed, while our cluster analysis”: Suggest the authors revise this paragraph once the issue of ‘other covariates’ is addressed.

As we have not changed the logistic regression, we have not modified this sentence.

Page 12: The study population in Cornell et al (2007) is veterans affairs patients (95% males) and as such might not be comparable to a community-dwelling population. I suggest the authors consider revising the sentence.

Thank you for reminding us of this difference between the study populations. We have removed reference to this study in the text.
Reviewer's report
Reviewer: Ellen Freiberger

The manuscript addresses the very important issue of the impact of multi-morbidity on falls. The authors are to the opportunity of such an impressive data base and therefore the possibility of investigating such an important topic. Nevertheless some major and minor comments are to be addressed.

MAJOR comments:

Background Section:

1. The terms multi-morbidity (second paragraph in brackets (two or more chronic conditions) and chronic disease patterns (last paragraph and another explanation of multi-morbidity = chronic disease patterns) have to be explained better. Specially the last sentence has to be explained why the authors use now chronic disease AND multi-morbidity which is confusing for the reader.

We apologize that our use of the terms “multi-morbidity” and “chronic disease” were not clear. After reviewing the manuscript in mind of the reviewer’s concern, we now understand how our liberal use of the term multi-morbidity was confusing and have made changes throughout the text to address this issue. First, in the opening paragraph, our initial mention of multiple chronic diseases emphasizes that multi-morbidity is commonly described as the presence of two or more conditions. Then in the second paragraph we discuss the limitations of previous multi-morbidity studies that only considered the impact of number of chronic conditions, when in fact pattern of disease combinations may also play a role. Then, in the third paragraph of the background section, we have described how our study aims to expand the concept of multi-morbidity one step further by investigating the impact of both number and pattern of chronic conditions. We have also made edits throughout the text, using the term multi-morbidity only when we are referring to the general category of having two or more chronic conditions, and ensuring that the rest of the time we are specifying we are considering the issue of number and/or pattern of chronic conditions. We have also revised the title and abstract as appropriate. We think these revisions will remove confusion for the reader, but would be happy to make more changes if particular sections are still unclear.

2. As fall is a central topic the definition being used should be stated in the methods sections. In addition by looking at the cited references the number of falls without any injuries could not be found. Only INJ_Q10 “Was the injury the result of a fall?” was found. The authors should explain and state the database, probably the appropriate information missed the reviewer. If the Survey differed between 2008 and 2009 then the authors should state the differences. Furthermore the Fear of Falling item is a “yes-no” question which should also be stated because it differs from the present recommendation to use at least a graded question.

Falls were not defined for survey participants, which we have noted as a limitation in the discussion (page 14, third paragraph). We have included in the methods text on page 6 (second paragraph), the relevant question about falls used to define the study sample: “In the past 12 months, did you have any falls?” (FAL_Q01). The reviewer did not miss the injury data- this was unintentionally omitted from the manuscript and we apologize for this. 35% of fallers experienced no serious injury. We have added detailed data on fall characteristics, including specific injuries sustained, in an additional table (new Table 2). The question used to determine injuries was FAL_Q03: “What has been most
serious injury or problem due to a fall within the past 12 months?” We have also noted in the limitations paragraph the issue of the fear of falling question being only a dichotomous variable (page 14, third paragraph). The same survey was administered to everyone in the study and was administered only once (not in 2008 and 2009).

3. Based on the importance for clinical practice the mechanism of COPD acting on falls should be explained more in depth. In addition it should be stated why stroke does not seem to play an important role (chronic disease like Parkinson and dementia are explained but stroke is not addressed again).

Thank you for this suggestion. Increased fall risk in COPD has been recognized only relatively recently, and as such data is still emerging on the underlying mechanisms that may contribute to falls in this population. We have expressed this issue more explicitly in the discussion text on page 12 (first paragraph), and added mention of potential mechanisms of falling in COPD (skeletal muscle dysfunction and cerebral hypoxemia) that have been postulated in the literature. With respect to stroke, it should be noted that although it did not emerge as one of the seven dominant clusters, it was still associated with significant increases in falls compared to people without a stroke (Table 3). As such, we are not saying that falls are neither common nor important in stroke, as a multitude of evidence clearly suggests that it does. Rather, we are saying that when considering the Canadian community-dwelling older adult population, stroke does not seem to be the primary condition associated with falls. This could be related in some part to the relatively low prevalence of stroke, lower stroke severity, or greater functional recovery among community dwellers, and might be different if we were to explore individuals living in long term care settings. We have added emphasis that all but one chronic condition were individually associated with elevated falls (discussion paragraph 1, page 10) and that even if a condition did not emerge as a key driver of the chronic disease clusters, its individual contribution to fall risk should not be understated (page 12, first paragraph).

MINOR comments:

1. The authors should review the References because not all the Refs are cited right e.g.#14 was published in 2011 not in 2008.

We apologize for this error in the references. We have changed the Diederichs et al. reference to the correct year, and reviewed and corrected all other references as required.

2. The sentence in the discussion section (4th paragraph: First given the differences in fall rates between individuals with and without chronic disease, the data suggest that CD older adults is not a unified population”. This sentence does not seem appropriate based on the functional decline level in CD setting. The sentence would fit better eg“data underline the difference in a CD population with regard to fall risk and rising red flags”…

This sentence has been modified as suggested by the reviewer, and now reads “First, given the differences in fall rates between individuals with and without chronic disease, the data underline differences within the community-dwelling older adult population with regard to falls, and that both the presence of specific chronic diseases and the number of conditions affecting an individual contribute to fall risk” (page 12, second paragraph).