Author's response to reviews

Title: Operationalizing Frailty among Older Residents of Assisted Living Facilities.

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Author's response to reviews: see over
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Melissa Norton MD, Editor-in-Chief
BMC Geriatrics

Dear Dr. Norton:

Please find attached our revised manuscript entitled, “Operationalizing Frailty among Older Residents of Assisted Living Facilities” submitted for further consideration to BMC Geriatrics. All co-authors have reviewed and approved this revised version for re-submission.

We appreciate the comments provided by the three reviewers and welcome the opportunity to address them. As requested, we have provided a point-by-point response to each comment on the following pages. We have also highlighted (in yellow) the relevant sections of the text where we have made revisions in response to these comments.

Please do not hesitate to contact me if you have any concerns or questions regarding our re-submission. We thank you for your continued consideration,

Sincerely,

__________________________
Colleen Maxwell, PhD
Professor & AHFMR Health Scholar
Editorial Comments:

1. Please provide the names of all the authorities that gave ethical approval for this study and record this in the manuscript.

As requested, we have added the names of the authorities that provided ethical approval for the ACCES Study, see pg. 6.

Also, please note that we have replaced all instances of ‘predictive validity’ with ‘predictive accuracy’ as the latter term is somewhat clearer.

Reviewer 1: Peggy M Cawthon

Major Revisions:

1. “My biggest concern is that the reasoning that underlies this analysis appears flawed. Given the theoretical definition of frailty proposed by Fried, one would expect that the nearly all of the individuals in an assisted living facility would be classified as frail… Thus it is not clear that a frailty definition would have any utility in such a population where all the individuals are frailty. Thus testing whether such a frailty classification predicts poor outcomes in this population doesn’t necessarily have face validity. How could such a scale or index possibly “work” when everyone is considered “frail”?

Perhaps examining whether presence of each additional frailty criteria (i.e. having 3 criteria vs. 4 criteria vs 5 criteria) would be more important than just the presence/absence of frailty in this population would be more important….Perhaps revising the introduction section and providing a few more analyses could alleviate these concerns. For example, I might state as a conclusion that almost none of the AL residents were robust; nearly all were frail or intermediate; and the overall mortality and hospitalization rates were very high.

Additional methods that help divide this most frail population into groups based on the risk of hospitalization or death are needed and the CHS definition doesn’t do a great job of separating the somewhat frail from the very frail (which isn’t surprising since it was developed in community dwelling individuals.)”

We thank this reviewer for these very thoughtful comments.

(i) With regard to the rationale underlying our analyses, an important aim with this paper was to initiate a discussion about the concept of frailty in residents of AL facilities - a rapidly growing, yet poorly understood population of seniors. These residents are characterized as ‘at-risk’ and in need of a protective environment, careful monitoring and targeted interventions directed at improving their quality of life, psychosocial engagement and functional independence (with the aim of preventing or delaying adverse outcomes, including institutionalization). The effectiveness of such interventions will depend, in part, on the availability of a feasible and accurate approach to identifying the most at-risk segment of this vulnerable population. The concept of frailty offers a promising avenue for identifying and targeting care to those at greatest risk of a precipitous decline in their health. Yet, there is still no agreement on how best to identify frailty (although there is consensus that it is a worthy pursuit and clinically useful).
One may hold the belief that all AL residents are frail, but this will depend very much on the criteria used to identify its presence. Regardless of the measure employed, the assumption that all AL residents are frail is best put to an empirical test. We feel the heterogeneous nature of the AL setting argues against the notion that all AL residents will be ‘frail’. At present, the CHS criteria represent the most favoured approach to defining frailty in older populations. These criteria are not without criticism. As noted in our Introduction, several of the concerns raised about these criteria may be particularly relevant to an AL population. Results from community-based populations may not be safely extrapolated to the AL setting. We feel that an essential first step is to directly investigate the feasibility and prognostic significance of the CHS criteria in this understudied at-risk population. We also attempted to study whether the use of relative (as opposed to CHS-specified) cut-points for the individual frailty criteria – in an attempt to capture the frailest of the frail - offered any prognostic advantage. This latter point speaks to the notion that there is likely to be a spectrum of frailty with varying degrees of vulnerability (as also noted by Walston et al, 2006 in their summary of current research priorities in frailty).

To better highlight the above issues in our paper – we have expanded relevant sections of our text (see pp. 4, 16) and included the supportive reference by Walston et al., 2006.

In our opinion, when a population is likely to be further along the frailty spectrum (e.g., an AL population vs. relatively healthier community-dwelling older adults) - but where the primary goal is still to optimize health, function and quality of life - discussions of vulnerability become even more important, not less. This argument has also been supported by others (e.g., see Rockwood et al., How should we grade frailty in nursing home patients? Am Med Dir Assoc 2007; 8:593-603). Their study examined nursing home residents and specifically compared a frailty index they developed and a global assessment of frailty with a modified version of the CHS criteria (as the authors were unable to exactly replicate all the CHS criteria). Our study is one of the first to provide empirical evidence regarding the utility of various ways of detecting frailty and differentiating among levels of vulnerability in at-risk older populations.

(ii) With regard to exploring the relevance of a broader categorical variable (looking at risk associated with having different numbers of criteria) vs. yes/no measure, we appreciate this comment. In response, we have revised our key analyses to examine the predictive accuracy of a three level categorical measure of frailty for both our absolute and relative definitions (see pp. 7, 9, and our revised Table 4). We selected this three level measure to be consistent with the original description of the CHS index reported by Fried et al. and with work by other researchers. We have noted in our Discussion the potential limitations of exploring the utility of the CHS index in our AL sample (with regard to level of impairment and risk of death and hospitalization) (see pp. 15-17).

(iii) With regard to the need for additional approaches (beyond the CHS frailty measure) to help differentiate levels of vulnerability and risk of poor outcomes in the AL population, we agree with this statement. This was precisely a key conclusion of our work. We argued that the CHS criteria may have limited utility and prognostic significance in this specific population, and that frailty measures which capture other domains of vulnerability (beyond strictly physical characteristics) may be required. In response, we have expanded our discussion of these issues in our Discussion section (see pg. 17).
Discretionary Revisions:

2. “In the original CHS paper, three levels for frailty were considered – “frail” “intermediate” and “robust”. Did the authors consider frailty as this three level variable instead of just a “yes/no” state? What did such analyses show?”

As noted in our response to item (ii) above, we have revised our analyses to include a three level frailty variable (frail=3+ criteria vs. pre-frail=1 or 2 criteria vs. not frail=0 criteria) for our two different interpretations of the CHS criteria (see pp. 7, 9, and our revised Table 4). We agree that this provides a more comprehensive comparison of the relevance of varying degrees of vulnerability in our AL sample and further supports our argument that frailty may be best viewed as existing along a continuum.

3. “The authors should report the p-values for comparing the AUCs for the various models…”

We appreciate this comment. In response, we have provided 95% confidence intervals for AUC difference estimates (and associated p-values) for key comparisons highlighted in our revised Table 4.

4. “There is a large literature about the ability of gait speed to predict poor outcomes in various populations. I suggest the authors mention these other papers when discussing the gait speed results in the discussion section.”

We agree with this comment. In response, we have highlighted this past research in relation to our findings (with two key references, #19 and #32) in our Discussion section, see pg. 15.

Reviewer 2: Xiaowei Song

1. “Considering that many assistant-living older adults could have various extents of health problems and be at a relatively high risk for adverse outcomes, it would not be surprising that a model based on just a few health items could not be more accurately predict individuals for outcomes within a short period of time. This should be discussed.”

We appreciate this comment and agree that further discussion is warranted (please see our revisions on pp. 16-18). We would like to emphasize that our primary aim was not to develop and test a comprehensive prediction model for these outcomes in our AL population. This would have been a different research question than the one we addressed. Rather, we aimed to examine the feasibility and prognostic significance of two different interpretations of a well-established frailty measure that may provide a simple and practical approach to grading vulnerability in an AL population.

2. “I am not sure it is a good or even a valid idea to adjust an established standard, simply to better represent the norms of the study sample at hand. One obvious drawback of such adjustment would be a reduced usefulness of the product out of it. It is common place that at-risk population would be frailer. In my view, a valid measure of frailty would allow comparisons the differentiation of frail status among populations, instead of being restricted to discriminate people in certain specific settings.”

We appreciate this comment. While we agree that there would be advantages in having a frailty measure that would be applicable across care settings, depending on the measure selected, this might be problematic for several reasons. First, different vulnerable populations are likely to be at different
positions along a continuum of frailty. For example, there would be general consensus that nursing home residents would be considered further along the frailty spectrum than AL residents – who in turn would have a distribution shifted toward greater frailty than community-dwelling seniors. Our aim was to explore the utility and prognostic accuracy of the CHS criteria in our AL population. One of the considerations underlying our desire to compare an absolute vs. a relative operational definition of the CHS characterization of frailty was to explore if an approach recognizing the different “starting points” of AL residents compared to those in the community offered any advantages. Second, in view of the various operational definitions proposed for frailty and the lack of consensus on how best to define it, it is plausible that the selected domains that are captured by any one measure (e.g., physical, cognitive, and/or psychosocial measures of vulnerability) may differ in their relative importance in terms of predicting key outcomes of interest across different care settings (as also noted in Walston et al., 2006). In terms of identifying key areas for targeted interventions aimed at improving or maintaining the functional independence and quality of life of older adults, it may be desirable to have a measure that offers the best discrimination for that particular population.

In response to this concern, we have expanded our examination of the relative strengths and limitations of our study approach in our Discussion section (see pp. 16-17).

3. “I would think improved feasibility of a frailty measure may be better achieved by allowing inclusion of a less-restricted chose of health items in the frailty criteria. I was wondering whether the frailty index approach might be applied to this population (e.g., Rockwood and Mitnitski, 2007). The frailty index approach allows the use of multiple health measures of different domains to produce a continuous assessment of frailty that often does not require a subjective cut-point to apply. The authors may want to introduce/discuss this option in the paper and, even better, to test it.”

We absolutely agree with this comment. In response, we have expanded our discussion of other potential operational definitions of frailty that should be the subject of further research in the AL population (see pg. 17). Our primary aim with this first paper was to specifically address the feasibility and prognostic accuracy of the CHS frailty criteria in our AL cohort – as the CHS criteria currently represent the favoured approach to defining frailty (as a medical syndrome) in older persons. At the same time, we are presently engaged in ongoing research to examine and test other approaches to defining frailty with a particular focus on the predictive accuracy of more comprehensive frailty indices (e.g., which consider cognitive and social measures of vulnerability as well as physical ones) in an AL population.

Reviewer 3: Nader Fallah

1. “Because several measures of frailty are available, I would like to suggest keep them as they are, for prevent any confusion, I think it is better to use frailty phenotype for Linda Fried model, Frailty Index for Mitnitski/Rockwood model and so on. Therefore I recommend using “phenotype frailty “term instead of “frailty index”.”

Although we appreciate this comment, we do not feel that it is appropriate (at this stage) to equate the term of ‘phenotype’ with the CHS frailty measure. The term ‘phenotype’ implies a depth of understanding that we currently do not have about the concept of frailty. As defined, it requires the consideration of both genetic and environmental factors and the interactions between them. Many authors working in this area (including work by Fried et al., and Ensrud et al., see, for example, references #30, 31 in our current
paper) have used the term ‘index’ to refer to a number of frailty measures. The term “index” is not restricted to the specific measure published by Rockwood & Mitnitski.

2. “The authors used phenotype frailty (proposed by Linda Fried) and its modification (namely Frailty-absolute and Frailty-relative), although they explained them in RESULTS, but it should be define more clearly in METHODS section as well.

We appreciate this concern and have further clarified our measures of frailty (and two different interpretations) in our Methods section (see, pg. 7). As we have outlined our specific definitions for each of the five criteria in Table 1 - we have not repeated this again in the text as we feel this would be redundant and potentially confusing to the reader (in view of the extensive details required to explain and compare each of the criteria).

3. “Page 9 Analysis: The authors explained about modeling with “generalize linear models” but is not clear which type of generalized linear model they used (logistic regression, Poisson regression, etc). Moreover they mentioned about random effect model that they applied, but their explanation on page 12 is not clear.”

We thank this reviewer for both comments. In response, we have clarified the text to read “generalized linear models with binomial distribution and a log link” (see pg. 9). This should distinguish our modeling approach from logistic regression (which has binomial distribution and a logit link) and Poisson regression (with a poisson distribution and log link). This has been called binomial regression, but that is a misnomer as logistic regression is also binomial. It has also been called risk ratio regression. However, we feel that our revision is more specific.

In addition, we have updated the text of our Methods section to clearly describe how we examined the potential significance of clustering by facility and our justification for our analytical approach, please see pp. 9-10.

4. “In Table 3, separation of death and hospitalization and put similar result of each model in the same line can be useful. (Optional)”

As this comment is optional, we prefer to keep the current version of our Table 3 for clarity purposes. We feel our current Table 3 shows the key comparisons of interest (regarding the two interpretations for the individual criteria) clearly for both outcomes.

5. “In this paper authors compared Frailty-absolute and Frailty-relative in table 4 and concluded that frailty doesn’t have enough power to increase AUC values, but is not clear AUC is the best index for this purpose. Surprisingly the modified index (Frailty-relative) works worse than Frailty-absolute. It seems when data come from very frail people (AL) some ceiling effect can happen and this type of modeling might be inappropriate.”

Unfortunately, we are not sure what is meant by this comment. We do not agree with the comment that our analytical approach is inappropriate. However, as noted in our responses to Reviewer 1 (item (i)) and Reviewer 2 (item #2), we have revised our text to better highlight the rationale for approach and to clarify our findings (in relation to the comparison of the absolute vs. relative frailty measures) on pp. 4 and 16. Further, as we have since revised our measure of frailty to capture a three level variable
differentiation of degrees of vulnerability) we do not believe that the above statement applies to our revised findings.

6. “It would be useful to compare the results obtained with the frailty index (Mitnitski/Rockwood model) to see how it can improve model prediction.”

Please see our response to item #3, provided above for reviewer 2.

7. “In discussion they did not discusses about other available approach such as Frailty Index” or “Clinical Frailty Scale”.

Please see our response to item #3, provided for reviewer 2. As noted, we have revised the text of our Discussion to include mention of these other measures of frailty and the need for further research.

8. “The limitations of the study should be clearly discussed. It is also necessary to discuss advantages and disadvantages of the each frailty model.”

Please see our response to item #2, provided for reviewer 2.

9. “I would like to see more explanation about how they frailty modification was choose and used, especially more technical detail of cut points. In general, there is a problem with effects of many continuous variables such as age or sex issue. Consequently a naive percentile cutpoint might not be the best solution.”

Unfortunately, we are not sure what is meant by this comment. Generally, we agree that there may be concerns with employing specific cut-points for measures that may be better represented by continuous variables. However, an important aim of our study was to replicate the existing CHS criteria for frailty (using specific cut-points) and to compare this with an alternative (relative cut-points) interpretation of the CHS criteria in our AL population. In addition, in terms of application in the clinical setting, it may be desirable to have cut-points (albeit ones that are clinically relevant) available for relative comparisons and for targeting and evaluating intervention strategies. As noted on pg. 16, we have provided further discussion of the potential relevance of varying cut-points for selected measures (e.g., gait speed).