Author's response to reviews

Title: Screening for frailty in primary care: a systematic review of the psychometric properties of the frailty index in community-dwelling older people

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Author's response to reviews: see over
Dear Ms Olino,

Thank you for the reviewer reports on our manuscript (MS:1795672196102838) entitled ‘Assessing frailty in community-dwelling older people: a systematic review of the psychometric properties of the frailty index' and the opportunity to submit a revised version to BMC Geriatrics.

We have read the feedback of the reviewers with great interest and used their comments to improve the manuscript. Please find below a point-by-point response to all questions and comments. We have indicated after each of the reviewers’ points what textural changes have been made in the manuscript and referred to the line numbers in the revised manuscript.

We hope that we responded adequately to the issues raised by the reviewers. If more information is needed, please let us know.

We hope that the adjustments make the paper suitable for publication in BMC Geriatrics, and we look forward to your response.

Yours sincerely,

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Editor’s comment:

COMMENT:
This is an interesting paper. In the light of the first two major comments made by the first reviewer, it would be useful if the authors consider dropping the primary care and home-care studies (n=2) because their inclusion likely affects the clarity of their manuscript.

RESPONSE:
We kindly refer to our response to comment 1.1.

Reviewers comments:

# Reviewer 1

Major comments

1.1 COMMENT:
Overall it is not clear to me what the main purpose of this study was. There are some inconsistencies between the title, research question, and analysis. If the reader just looks at the title he/she will think the focus of the paper will be in community-dwelling older adults (the studies that you call “research studies”) and would expect other studies such as those using routine care data to be excluded. The intro focuses on primary care whereas in the results section the primary care data is only briefly mentioned. For clarity purposed it may have been easier to exclude the primary care data study (and possible home care studies) and focus only in community-dwelling older adults. In the discussion authors can talk about the possibility of using this tool in primary care and highlight this study there. It would also have been really nice if the authors would not have excluded studies based on the setting; this would have been a great summary of all the frailty index studies and would identify gaps where more research needs to be done (I understand that this was beyond the scope of this systematic review)

RESPONSE:
The main purpose of this study was to evaluate whether the psychometric properties of the FI in identifying frailty among community-dwelling older people would support the potential use of the FI as a screening and monitoring instrument for frailty in primary care. We thank the reviewer for pointing out the apparent inconsistencies between title, research question, and analysis. We realize now that the terminology of a study using ‘routine care data’ suggests that this study focuses on a specific subgroup of older people, while this is not the case. In the Netherlands, virtually every individual is enlisted with a general practice, and all inscribed individuals are included in the routine care datasets extracted from general practices. Consequently, it can be concluded that the study using routine care data does adequately represent the general population of community-dwelling older individuals, thereby matching the main purpose of our study. We also included studies specifically focusing on older people receiving home care and on people living in assisted living facilities, because GPs in many countries also provide care and are the main care coordinators for these subgroups of older people. Given the focus of our
review on primary care, we excluded studies of hospital or nursing home patients. To clarify the above outlined argumentation, we have modified the manuscript accordingly (lines 1-3, 110-114, 190-194)

1.2 COMMENT:
The authors need to tone town their statement about the difference between primary care vs research based studies. If only one study exists then the conclusion is that there is not enough evidence and not that primary care is different. In addition, in your results you mentioned that the rate of increase with age is different in the primary care study with a much lower score. This comparison is not possible since you are comparing a linear slope with logarithmic slopes (the ones reported in other studies). You need to calculate the logarithmic slope of your data in order to compare. With some briefly calculation looking at the figure 1 of your primary care data paper the logarithmic slope is around 0.03 which is similar to what other studies have shown. If this is true then actually the findings of this study are very similar to the other studies however I still believe that there is not enough evidence to support this comparison.

RESPONSE:
We agree with the reviewer that the statement about the difference between primary care versus research based studies should be modified, and we thank the reviewer for pointing out the error we made in the evaluation of the rate of FI increase with age. We have adapted the manuscript accordingly (lines 40-43, 291-292, 386 – 392).

1.3 COMMENT:
The section “3.4.3. Responsiveness, utility and interpretability” seems confusing. Especially the utility and interpretability part of it which is not really discussed. You cannot really conclude about how the frailty index can be used in clinical settings and what it means there when only one of the included studies was in clinical settings. The only thing that they can conclude is again that more studies need to be done in primary care settings in order to talk about "utility and interpretability" in this setting.

RESPONSE:
Taking comment 1.3 into consideration, as well as comment 2.8 from the second reviewer, we have deleted section 3.4.3, and moved the last two paragraphs of this section to section 3.4.2 on construct validity. Furthermore, we added a modification in the discussion section (lines 285-292, 306-308).

1.4 COMMENT:
In your discussion you mentioned many studies which reported FI changes which seems like evidence for “responsiveness” to me. Just because they did not compare the change in FI scores with other instruments does not mean that they did not examine the responsiveness of the FI. I would suggest including these studies in your review.

RESPONSE:
We presume that the reviewer refers to the two studies mentioned in line 375 [50, 60] of the discussion section. As these studies do not assess within person-change over time with pre-specified hypotheses
about the expected correlations between changes in the FI score and changes in other variables, whether it be other instruments, demographic, or clinical variables, we did not consider these studies as responsiveness studies (Terwee et al, 2007). For example, in reference 59 (Mitnitski et al, 2006), in figure 1, the probability of transition from n to k deficits in relation to the starting n deficits is shown. It is demonstrated that with a high starting number of deficits, there is a high probability of transition to a higher number of deficits, i.e., the change of becoming more frail increases with a higher level of frailty at baseline. Whereas this finding indicates that the baseline FI score is correlated with future FI scores, it does not demonstrate whether this FI score progression actually does measure change in people’s frailty status. Would the changes in FI score have been compared against changes other measures, such as the Frailty Phenotype criteria or the Edmonton Frailty Score, then we could have evaluated whether changes in the FI score over time would describe true changes in peoples’ condition. Findings of a high correlation between changes in the FI score over time and changes in other, presumably related measures, would support the hypothesis that the FI score is truly measuring longitudinal changes in peoples’ frailty status.

1.5 COMMENT:
In addition, including the studies that measured frailty using comprehensive geriatric assessments would have improved this systematic review especially if you want to focus on routine care. For example the Davis et al. 2011 paper included a frailty index based on comprehensive geriatric assessment using the Canadian Study on Health and Aging. This study does not look very different than those you included.

RESPONSE:
We agree with the reviewer that FIs based on data gathered in comprehensive geriatric assessments, such as presented in the Davis et al 2011 paper, could provide valuable additional information to support the use of the FI in daily clinical care. However, specifically in primary care, it is not feasible to perform such an assessment for each older patient within the general practice population because of limited time and resources. Therefore, because the focus of our systematic review lies with the perspective of the GP, we excluded the studies that measured frailty using comprehensive geriatric assessments. We had formulated this exclusion criterion in Appendix A, but to clarify our argumentation, we have added information about this criterion in the methods section of the manuscript (lines 114-116).

Minor Comments
1.6 COMMENT: You mention that one of the exclusion criteria is to exclude people from nursing homes but then you mention that “Ten studies were population-based and used a representative sample of independently living or institutionalized older people” and “and two studies focused specifically on home-care clients or older people in assisted living facilities”. Please clarify

RESPONSE:
We thank the reviewer for pointing out this use of confusing terminology. The aim was to exclude studies in which the entire study population was living in a nursing home, because in the Netherlands, care for these vulnerable older patients is provided by specialized nursing home doctors instead of GPs. However,
studies in which the population consisted of a mixture of both independently living as well as institutionalized people were included. As these studies aimed to adequately sample patients from various living situations according to real-life distributions, the majority of older people included in these studies was independently living. Therefore, despite the fact that a minority of the study population was admitted to nursing homes, we concluded that the results of these studies could be generalized to the population of older people that GPs provide care for, and we decided to include these studies. Furthermore, studies focusing exclusively on home care clients or older people in assisted living facilities were also included. As we mentioned in the response to comment 1.1, in many countries, GPs are the main care provider and care coordinator for patients in these living situations, so considering the aim of our review, we decided to include these studies. To clarify the above outlined argumentation, we have modified the manuscript accordingly (lines 115, 190-194).

# Reviewer 2
Reviewer's report:
This systematic review aimed at collecting information on the psychometric properties of the frailty index developed by Mitnitski et al (2002) among community-dwelling older people. This is a well written paper and methodologically well conducted review.

Minor essential revisions
2.1 COMMENT:
RESPONSE:
We have replaced reference 6 by the abovementioned reference (lines 445-446).

2.2 COMMENT:
P4, 2nd paragraph: “An FI comprises a predefined list of health deficits (e.g. symptoms, signs, impairments, and diseases)…” I do not agree with the term “predefined” as the list depends on the data. As the authors highlighted, there is heterogeneity in the construction of FI in terms of number of items, type of symptoms, diseases, and deficits. Therefore, reporting that “Different numbers and types of deficits may be used to construct an FI, which enables application in and comparison between different datasets” is a quite strong statement. In my opinion, this can only be tested using a same list of items in different databases.
RESPONSE:
We have removed the term “predefined”. We do agree with the reviewer that an exact one-on-one comparison can only be made applying the same list of health deficits in different databases. However,
previous FI studies have demonstrated that when at least 30 health deficits are considered, FIs constructed with different types and numbers of health deficits show comparable properties, for example, a mean rate of deficit accumulation across ages of about 0.03 per year on a log scale. It is not so much what problems individuals have, but how many problems individuals have that determine the properties of the FI. To clarify this, we have adapted the manuscript accordingly (lines 77-79).

2.3 COMMENT:
P7, end of section 2.3: “The FI should comprise at least 30 deficits and deficit prevalence should be at least 1%”. Where do these thresholds come from? Please give a reference.
RESPONSE:
We have provided a reference for this statement (line 164).

2.4 COMMENT:
P9, section 3.3: “Four studies showed a low risk of bias for each of the five domains considered…” Please list here the five domains.
RESPONSE:
We have listed the five domains (lines 207-208).

2.5 COMMENT:
P9, section 3.3: “and nine did not report the percentage of missing FI data or how missing FI data were managed [19, 20, 22, 24, 27, 30-32, 34, 36]”. I count 10 references. Please harmonise.
RESPONSE:
We thank the reviewer for noting this inconsistency. We have removed reference 27, which was incorrectly placed here (line 219).

2.6 COMMENT:
P9, section 3.3: “In total, 98 separate domains were assessed…” What do the authors mean by “domains”?
RESPONSE:
With “domains” we intended to refer to the domains of the QUIPS tool that was used for critical appraisal of the included studies. To clarify this, we have modified this section of the manuscript (lines 226-229).

2.7 COMMENT:
P12: “The FI score is almost inherently linked to comorbidity and disability because most FIs incorporated diseases and functional impairments as deficits.” This seems to be obvious; does this sentence deserve to be said?
RESPONSE:
We have removed this sentence from the manuscript.
2.8 COMMENT:
P12, section 3.4.3: I do not think this section is necessary. What do the authors intend to show reporting skewness of FI score distribution? In my opinion, 2 last paragraphs can be moved into section 3.4.2. Construct validity.
RESPONSE:
We have modified sections 3.4.2 and 3.4.3 according to the reviewer’s suggestions (lines 285-292).

2.9 COMMENT:
P13: “that its discriminative capability is poor to adequate”. How do the authors can conclude that? What thresholds did they use?
RESPONSE:
We have added the used thresholds to the methods section and inserted the associated reference (lines 128-130).

2.10 COMMENT:
P13: “The FI score increases steadily with age towards a maximum of 0.60-0.70, indicating that no ceiling effect exists”. Is it “indicating that no ceiling effect exists with age”?
RESPONSE:
We intended to report two separate statements: that the FI increases steadily with age, and that, in general, no ceiling effect exists. To clarify this, we have modified this sentence in the manuscript (lines 299-301).

2.11 COMMENT:
P14: “the reported loss to follow-up was typically well below 20...». Do the authors mean below 20%?
RESPONSE:
We did indeed mean below 20%, and we modified this in the manuscript (line 326).

2.12 COMMENT:
P14: “However, the studies included in our review have been performed by various different research groups from all over the world indicating that publication bias is less likely.” I do not agree with this statement, the publication bias still exists even one takes into account all existing articles.
RESPONSE:
We have removed this statement from the manuscript.

2.13 COMMENT:
P15: “One may hypothesize whether this performance-based measure...” I think the verb “hypothesize” is not adequate. Maybe it can be replaced by “wonder” or “question”.

RESPONSE:
We have replaced “hypothesize” by “question” (line 343).

2.14 COMMENT:
P15: “Our results are consistent with previous FI reviews that also reported on criterion validity, construct validity and interpretability of the FI [7, 13, 43].” There are no results on interpretability in the manuscript; therefore, this small inconsistency needs to be amended.
RESPONSE:
We have modified this statement to “…FI reviews that also reported on criterion validity and construct validity.” (lines 350-351).

2.15 COMMENT:
P17: “there may be suboptimal data registration in the EMR [60, 61]”. Please indicate what EMR stands for.
RESPONSE:
EMR stands for Electronic Medical Record, which we indicated in the manuscript (lines 398-399).

2.16 COMMENT:
Table 2: Is it possible to provide some information on how “low”, “moderate”, and “high” risk has been defined?
RESPONSE:
We have added extra information on how “low”, “moderate”, and “high” risk has been defined (lines 630-631).

2.17 COMMENT:
Table 3: “Per increment FI” Can this be replaced by “Per one-unit increment in FI score”?
RESPONSE:
In table 3, we have replaced “Per increment FI” by “Per one-unit increment in FI score”.

2.18 COMMENT:
Both “FI” or “FI score” are used in the column “Interpretation effect measure”, this needs to be harmonised.
RESPONSE:
In table 3, we have replaced “FI” by “FI score” in the column “interpretation effect measure”.

2.19 COMMENT:
The footnote needs to be moved.
RESPONSE:
We have moved the footnote of table 3.

**Discretionary revisions**

2.20 **COMMENT:**
P8: “a Likert-scale [33].Two” Please add a space between “.T”

**RESPONSE:**
We have added a space between “.T” (line 199).

2.21 **COMMENT:**
P10: “(FI score < 0.07)) » Please remove the extra « ) ».

**RESPONSE:**
We have removed the extra ”)” (line 244).

2.22 **COMMENT:**
P11: “(CHESS)Scale » Please add a space between ”)S”.

**RESPONSE:**
We have added a space between ”)S” (line 269).

2.23 **COMMENT:**
P13: Please remove the space between “inter RAI-AL”.

**RESPONSE:**
We have removed the space between “inter RAI-AL” (line 304).

2.24 **COMMENT:**
P15: “and interpretability of the FI [7, 13, 43)” In references, ”)” should be replaced by ”]”.

**RESPONSE:**
We have replaced “)” by ”]” (line 351).

2.25 **COMMENT:**
P17: “Body Mass Index”. Capital letters here are not needed.

**RESPONSE:**
We have replaced the capital letters by lower case letters (line 402).