Author’s response to reviews

Title: Comprehensive Geriatric Assessment Pilot of a Randomized Control Study in a Swedish Acute Hospital: A Feasibility Study

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Author’s response to reviews:

Pilot and Feasibility Studies

Dr. Thabane, Editor

December 20, 2017

Dear Dr. Thabane,

The authors would like to extend sincere gratitude to you and the reviewers for making the effort to provide such valuable suggestions and comments regarding this pilot study manuscript. We appreciate the important and helpful remarks. The manuscript entitled Comprehensive Geriatric Assessment Pilot of a Randomized Control Study in a Swedish Acute Hospital: A Feasibility
Study has now been revised in accordance with both the editor’s and reviewers’ comments and suggestions.

Please see below. All changes to the manuscript are in track changes.

Editor's comments:

The paper requires major overhaul to make it acceptable for publication.

1) The reporting of the paper has to adhere to new CONSORT extension for pilot trials for both the abstract and the full text.

As per the editor’s recommendation above, we have tried to adhere to the CONSORT extension for pilot trails for both the abstract and manuscript’s full text.

2) The analysis description should describe clearly how feasibility outcomes are analyzed with clear criteria for assessing success of feasibility.

As suggested by the editor, the analysis description for the pilot study has been rewritten to clarify how the feasibility outcomes were assessed (for both the primary and secondary/surrogate outcomes)

3) Given that the study combines both proof-of-concept and feasibility assessment, it is important for the design to be clear on what the primary focus is between the two.

The reporting of the design needs to be consistent with the primary aim.
As suggested by the editor our pilot objectives are now more clearly described in the abstract and text throughout the manuscript, where the primary objective was on recruitment and retention rates.

Typically, proof-of-concept studies are designed based on surrogate outcomes with appropriate power to detect differences between groups.

As suggested by the editor the proof-of-concept is more clearly described in the abstract and text throughout the manuscript, where the secondary objective was focused on the surrogates related to risk assessments and safety. Furthermore, this data is now presented in tables 4 and 5, highlighting the differences between the intervention and control groups.

On the other hand, feasibility studies for phase III trials are designed appropriately based on feasibility objectives with clear justification for the sample size.

As highlighted by the editor a phase III trial is not relevant nor the case for our CGA pilot study. Therefore a design based on the feasibility objectives is not justified in the text.

4) Provide the appropriate CONSORT diagram showing how many patients were used for the analysis of each feasibility objective.

As per the editor’s recommendation a CONSORT flowchart has been added.

5) Delete p-values reported in both Tables 4 and 5. Report estimates of the difference (and corresponding 95% confidence intervals).

In lines 404-408 we clarify the statistical analysis for the pilot and have added mean difference and (CI) in tables 4 and 5 as suggested. Lastly all p-values have been deleted.
Reviewer 1 Comments:

Thank you for the opportunity to review this interesting manuscript.

This paper describes the protocol and pilot study of a planned large trial.

Generally, I think that this is an interesting topic and a large body of work that should be published. The flow of the order of information, however, is confusing with the authors moving rapidly and repeatedly from current to past and then future tense.

Reviewer 1, thank you for the valuable and helpful comments. Referring to the broad comment above, and in regards to the flow of the order of information, the authors have done a major overhaul on the current, past and future tenses. Furthermore, we have read all the comments and revised the text as you have suggested. Without referencing to every line we edited in the abstract and manuscript, the authors were attentive in attempting to clarify the past and future tenses in the pilot versus the full scale study.

I think that the pilot study has been undertaken, and the therefore the results presented, but even in the abstract this is not clear Lines 34 to 36 'A pilot study exploring frail people aged 75 years or older will …The pilot study was…'

Lines 39 and 40 have been rewritten to clarify the past tense.

This is repeated numerous times throughout the paper, and some separation of the protocol and data from the pilot study is needed for this paper to be clear to the new reader.

There are several examples of word use that are not clear Abstract: Line 31 'secured' does not make sense in this context to me. Is it 'carried out'?

Line 31 with the text “secured” has been further developed and written to clarify how the team works to make CGA unique.
Line 157 Pilot sample size - this should based on primary aim(s) of the study.

The authors have made a revision to clarify the primary objectives as noted in line 189 “aims”.

Regarding the confusion about the main trail, the power was calculated prior to the pilot based on the ADL, and the main study is not calculated from the pilot data findings.

Line 279 ’performs’ is written in current tense - will they do this or did they do this?

Line 320 has been altered from “performs” to “does” a chart review for clarity, as it was intended to written in past tense.

Line 370 differences between the two groups are well described Line 492 data from the pilot study will be used (correctly) to determine the sample size of the main study, however the number of participants in the main trial is not calculated from the pilot data and it is one of the most valuable outputs from the pilot study.

The authors have tried to improve and develop these parts further so that it is clear for the readers that lines 304-315 are for the main study. The pilot’s main aim was not to assess the output from ADL, but rather to insure randomization and retention and its surrogates regarding risk assessments and safety. As a result of this we have not used the results from the pilot to calculate the sample size for the main study, which might be a limitation. This has been added to the manuscript in the discussion as a limitation (lines 575-577).

Background.

This section is quite long and may be streamlined without losing the meaning I think. Please consider changing some of the following words or phrases to make the meaning clearer.

The background have been revised, shortened and significantly edited to make meanings clearer for reader.
Line 70 'the problem' Is this the problem that resulted in admission - please clarify.

Line 74 'the future of in-patient acute medical is going to be the care of’…Perhaps this will be a major focus, but not 'is'. Consider; 'a major focus in the future of …'.

Lines 92-94 have been rewritten to address the use of language and meaning.

Line 83 'tapped out' is a colloquial phrase that is not clear.

Line 108 “tapped out” has been replaced with severely limited.

Line 84 please provide a reference for this


I cannot see in the pilot study results where the data for the main trial is calculated (from the pilot data - a theoretical sample size based on ADL is presented in lines 255-267) ie results of adl (mean and SD) and how the actual dropout rate is used to calculate sample size. This is a significant issue that I believe needs addressing.

Furthermore, Reviewer 1 lifted an important issue regarding the theoretical sample and dropout rate (see lines 304-317). The headings texts have been edited to clarify that the sample size and calculated power are for the main study (not the pilot). Furthermore, the power calculation was created prior to the pilot for the main study’s primary outcome of the ADL. Lastly the calculation of loss was based on previous research on frail older people and was not determined as a result of or following this pilot.

Regarding the dropout rate, this was not higher than expected (lines 488-490), therefore the authors choose not to recalculate the sample size.
Reviewer 2 Comments:

I think that some more clarity around the protocol and pilot data would help make this easier to read. Perhaps it just needs the pilot to be written in the past tense for it to make more sense.

The authors fully agree with your comments and observations regarding the confusion in tenses when discussing the pilot and main study protocol. Thank you for bringing this to our attention. We have overhauled the entire abstract and manuscript with conscious efforts to clarify and address the main study (future tense) and the pilot study (past tense).

I think that the omission of the authors to use the actual pilot data for the sample size calculation is a problem, when they are presenting both the pilot data and protocol in one document.

Furthermore, we appreciate your insightful suggestion to use the actual pilot data to calculate the sample size, however in lines 304-317 we believe that we have discussed the authors approach for the main study and calculated power based on the primary variable (ADL), which was not tested or examined in this pilot.

As a result of this we have not used the results from the pilot to calculate the sample size for the main study, which might be a limitation. This has been added to the manuscript in the discussion as a limitation (lines 575-577).

Rather the purpose of the pilot study focused on the randomization, retention and surrogate outcomes (as they related to safety and risk). Hopefully now clarified in the text in Lines 189-204, where sample size is now better clarified in Lines 208-211 related to line 189-204.

Lastly data is now presented in tables 4 and 5, highlighting the differences between the intervention and control groups, relating to the proof of principle (mean difference (CI)).
Additional revision

• Four additional references have been added to further clarify text and meanings.

Sincerely,

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