Author’s response to reviews

Title: DOES COGNITIVE/PHYSICAL SCREENING IN AN OUTPATIENT SETTING PREDICT INSTITUTIONALIZATION AFTER HIP FRACTURE?

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Author’s response to reviews:

Dear Editor,

We are very excited to have been given the opportunity to revise our manuscript. We revised our paper in response to the comments and questions raised by the reviewers. We hope that this revised manuscript will be considered suitable for publication and we look forward to hearing from you. Please find attached a revised version of our manuscript and point by point -answers.

Yours sincerely,

Markus Hongisto
1. Could the authors clarify why patients with high trauma fractures were excluded? They may also be at high risk of transfer to full care institutions. You may wish to do a supplemental analysis including these patients.

Older patients with a high-energy hip fracture, such as those resulting from pedestrian or traffic accidents, bicycle accidents, and falls from a chair will certainly increase the risk of institutionalization. Our intention, however, was to clarify the risk of institutionalized living arrangements in the most common hip fracture type, a low-energy hip fracture among frail community-dwelling patients. Further, a high-energy hip fracture often occurs outside the home, suggesting that these patients have better physical activity prior to injury compared to patients with a low-energy hip fracture. In addition, the number of patients with a high-energy hip fracture was relatively small (63 patients), thereby limiting the statistical analysis.

2. Please add a Flow diagram figure that describes the study population with eligibility and ineligibility criteria.

A flow diagram has been added.

3. I think it would be important to separate out the patients who are in rehabilitation institutions versus in long term care (full care) institutions. It is expected that a significant proportion of patients will go to rehab for 2 to 6 weeks post fracture and then return home. The primary outcome of interest is transfer to full care institution and I think it is misleading to present the results with rehab institutions in the same category as long-term care institutions.

The primary outcome describes the living arrangements 1 year after hip fracture and at the mentioned time-point, we believe the most interesting issue is to determine whether the patients survive at own home/assisted living accommodation or in units providing 24-h care. Further, we believe patients who are still living at an institution that provides 24-h care 1 year after hip fracture represent a population who are no longer able to be comprehensively rehabilitated.

The setting could be misleading at 1 and 4 months after hip fracture, because some patients may still be in a rehabilitation unit while others are living in nursing homes. There is no other way to categorize these variables, however, because the variables should be categorized in the same way at all time-points (1, 4, and 12 months). The key is to divide the groups into older people who live in the community on their own or with assisted living arrangements and those taken care of in nursing homes or corresponding units providing 24-h care.

We have added this as a limitation in the Discussion.
4. Other than the living arrangements, it is unclear what data were collected during the phone interviews. Would it not be possible to evaluate IADLs and MMSE over the telephone (there are telephone versions for MMSE) and use the 1-month data to predict the primary outcome? It seems that the earlier we (the healthcare system) has this information, the better for resource allocations. If not possible, it would be important to state what data were collected in the interviews.

In our orthogeriatric care model, we routinely arrange clinical examination 4-6 months after hip fracture and perform numerous clinical tests to evaluate rehabilitation capabilities and problems. Telephone interviews at 1, 4, and 12 months after surgery are the only supportive action in the integrated care pathway. We think only “simple” questions are suitable for telephone interview and IADLs and MMSE acquired over telephone are not sufficiently reliable to draw further conclusions at this point. We do acknowledge that a better test for identifying patients who are at risk of institutionalization should be available immediately after hip fracture. The first few weeks after hip fracture surgery, however, may significantly affect the measured variables. Living arrangements 1, 4, and 12 months after hip fracture were obtained by a telephone interview and the other statistical variables in this study were obtained on admission and at the 4-6 month geriatric outpatient visits.

5. Because IADL and MMSE are (likely though data not shown) closely correlated, it would be appropriate and expected to explore potential interactions between these variables in the multivariate model analysis. Similarly, living in an institution at 4 months is likely to be correlated with these 2 measures of functional autonomy.

We conducted a correlation matrix with the multivariate binary logistic regression. It seems that living in an institution 4 months after hip fracture is only weakly correlated with the IADL (r=-0.051) and MMSE (r=0.133) scores in the model. IADL and MMSE were weakly correlated in the multivariate model (r=-0.138).

6. Competing mortality is important to consider in this population. It would be interesting, if possible, to perform survival analyses for the primary outcome taking competing mortality into account, using the respective cut-off values of IADL and MMSE identified by the authors.

This study aimed to identify patients at risk for institutionalization. We considered conducting a survival analysis using IADL and MMSE as a covariate in this study, but the study already contains several statistical analyses and a survival analysis would lengthen the manuscript.
unnecessarily. Further, Reviewer 2 commented that even the current mortality analysis was too much.

Minor

1. Consider changing the title to reflect that the screening is done in the outpatient setting following discharge from the hospital.
   The title was changed accordingly.

2. Consider moving the last paragraph in the result section higher up in that section (after the first paragraph?) since it is mostly descriptive in nature.
   Thank you for your advice. The scope of this study was to explore whether IADL and MMSE scores predict institutionalization and these results are provided first in the section. A change in the living arrangements is important information, but not the main result of this study.

3. Suggest to change the headings of the columns in Table 1: Baseline: Entire cohort
   Analysed patients: Patients in Primary Analysis
   We revised the headings in Table 1.

4. Consider changing this sentence in abstract: An IADL score of ≥5 excludes institutionalization. To: an IADL score of ≥5 predicts the ability to remain in the community.
   Thank you for your advice. The sentence was changed accordingly.

Reviewer #2: Thank you very much for the opportunity to review the manuscript

"Does cognitive/physical screening predict institutionalization after hip fracture?"
General Comments:

It is an interesting and well-designed study about an important topic. The manuscript is well-written manuscript. But I am not sure about the relevance to predict institutionalization 1 year after trauma at the time point 4 month after trauma instead of immediately after trauma. Considering the fact that 4 month after trauma rehabilitation process is finished in most cases, it is not surprising that IADL predicts institutionalization at 1 year. Consistent with that is has to taken into account that the most predicting factor was neither the IADL nor the MMSE but institutionalization at 4 month after trauma. This restricts the value of the study.

On the other hand some changes in living arrangement where observed. I therefore would prefer to identify predictors for change of the living arrangements from 4 to 12 month (especially those patients who where send to nursing homes in this period). The knowledge of the risk factors for deterioration might be helpful in developing concepts for patients at risk for this deterioration. Please add such analysis and rewrite the whole manuscript accordingly.

Thank you for your review of our manuscript and comments, suggestions, and criticisms. We acknowledge the limitations of this study. The first weeks after hip fracture are often crucial for rehabilitation. It would be optimal to screen patients at risk of institutionalization at this point. Some patients recover slowly, however, and rehabilitation seems to proceed for months after hip fracture. Certainly, patients who are still living in facilities providing 24-h care 4 months after hip fracture are predisposed to a risk of long-term institutionalization. Our study was focused on screening patients who may benefit from comprehensive rehabilitation at this point, because generally all hip fracture patients should be rehabilitated immediately after fracture, but it is still unknown who will benefit from extensive rehabilitation months after hip fracture. First, we must be able to identify these patients, because extensive rehabilitation programs should not be allocated for all hip fracture patients 4-6 months after hip fracture. We consider that the primary objective for extensive rehabilitation is to avoid institutionalization, immobility, new traumas, and a poor quality of life. The changes in absolute living arrangements represent important information, but not the endpoint – living in an institution providing 24-h care. Therefore, we prefer to keep our analysis and the scope of the present study as written in the manuscript.
Abstract:

Introduction:

Although it might be of interest to examine the predictive value of IADL and MMSE, the link to rehabilitation allocation is not unambiguous. Consider rewriting.

The sentence has been revised.

Methods:

Please add some information about the parameters and statistical methods.

IADL is a well-known screening tool for determining independent functioning in the community. The MMSE is widely used to screen for cognitive dysfunction. Further information about these tests in the abstract would lengthen the abstract unnecessarily. The statistical method we used is described in the Results just before the numerical data (Age-adjusted univariate logistic regression and Multivariate logistic regression analysis).

Results:

ROC analysis should also be performed for the variable "institutionalization at 4 month after trauma".

ROC analysis was conducted only for MMSE and IADL, because institutionalization 4 months after hip fracture had a clear impact on more dependent living arrangements 1 year after hip fracture. The effect of institutionalization at 4 months on 1-year institutionalization was demonstrated in the univariate and multivariate logistic regression model. The only purpose of the ROC analysis was to determine the appropriate cut-off value for IADL and MMSE to predict institutionalization, not to identify and interpret positive and negative predictive values or odd ratios as a prognostic indicator.

Add information, in which direction living arrangements changed from 4 to 12 month.

We added this information to the Results section.

Conclusion:

Please do not just repeat the results but try to draw a conclusion.
We revised the Conclusion.

Main document

Introduction:

P4 L1ff: I would disagree that clinical tests are required….In my view it is more important to perform these tests at an earlier stage, because it is probably too late to improve patients outcome significantly 4 month after trauma

The sentence was revised.

P4 L 10-19: Please transfer into Patients and Methods.

IADL and MMSE are first introduced in more detail in this section. Neither of the tests was used to directly classify patients or as methods of the current study. We prefer to keep the text as in the original manuscript.

Methods:

- Was an ethics approval obtained? Gave all the patients informed consent? Please add such information?

This information was presented on page 12, according to the journal’s instructions.

Please consider adding a flow chart of the study.

A flow diagram was added as Figure 1. To shorten the manuscript, the corresponding section was revised.

Delete decimals in percentages that were <10. (this applies to the entire manuscript)

We changed the decimals to ensure two significant digits for the range of values across groups, e.g., if the range was ≥10% we used whole numbers, if <1%, we used two decimal places, and otherwise one decimal place. In the tables, however, one decimal place was used to ensure accuracy and readability.
Please consider adding some subheadings (e.g. for the description of the IADL or the MMSE) for clarity.

Thank you for your recommendation. The IADL and MMSE are briefly described in the main text and we cite original studies for interested readers. Therefore, we prefer to keep the text without subheadings.

Do you perform a test for normal distribution? - If not: Please add such a test and perform the further tests accordingly.

The only continuous variables in this study are the IADL and MMSE scores. Neither of these variables was continuously distributed. The residuals on multinominal binary logistic regression analysis increased to over the limits (-2- +2), but this did not affect the final results. We decided to categorize IADL and MMSE in a dichotomous manner, however, using the best cut-off value from the ROC analysis in this study, but the ROC analysis did not provide an optimal cut-off value for the MMSE and thus we used a value that lies between mild and moderate cognitive impairment.

Please mention all variables that were considered in the multivariate analysis.

This information is presented under “Patients and Methods”. Further, the information is provided under the table (Statistically significant age-adjusted variables from the univariate logistic regression analysis were included in the multivariate regression analysis).

Please add β-values and R2 in the multivariate analysis.

β-values and R2 are presented in the linear regression analysis. Because the institutionalization variable is dichotomous, it could not be modelled using linear regression analysis methods. Thus β-values and R2 could not be calculated. “Negelkerke R Square” is referred to as pseudo R2-value in the binary logistic regression model. The Negelkerke R Square value of our model was 0.567.

I would prefer NOT adjust for age and gender in the (multivariate) analysis.

Otherwise the significant factors could not be called "independent".
Thank you for your opinion. We believe it crucial to take age and sex into account in the multivariate analysis because the hip fracture population comprises more women. Further, the hip fracture incidence increases dramatically according to age.

P6 L53ff: I would delete this analysis. It is beyond the scope of this study and enlarges the manuscript unnecessarily.

Thank you for your opinion. We think mortality is always within the scope when elderly people are studied. Further, another reviewer insisted that we provide even more analysis about the effects of different variables on mortality. Thus, we prefer to keep the current survival analysis in the manuscript.

Results:
this section should be changed according to the previous recommendations.
We completely revised the Results section, taking your suggestions into account.

Please add ROC curves.
ROC curves were added as requested.

Discussion:
this section should be shortened significantly (max. 2.5-3 pages).
The Discussion was shortened by approximately 10%. Further shortening require removing additional content.

as previously mentioned, it has to be discussed that institutionalization at 4 month after trauma was the most important factor for institutionalization at 4 month.

This issue is addressed in the Discussion.
- a further limitation is, that the results might be biased by the fact that the 841 baseline patients have different characteristics as compared to the analysed cohort (see table 1).

Thank you for this comment. The study population consists of real-life patients. Naturally, mortality and non-attendees affect the size and properties of the analyzed cohort. We have, however, comprehensively described the characteristics of the analysed patients’ cohort.

Thank you for your expert review. We believe these suggestions have helped us to dramatically improve the manuscript.

REVIEWER 3#:

The paper by Hongisto et al. focuses on the screening with IADL scale and MMSE test as potential predictors of institutionalization 1 year after hip fracture in a Finnish population.

The manuscript is overall well written, and the methods are stated clearly.

I have only minor revisions to suggest:

Page 3, line 22: The expression "due to the rapid growth in the population of older people" is quite uncommon; I suggest to rephrase it in order to make it more fluent.

The sentence was revised. “… due to the rapid growth of the older population …”

Page 4, line 10: there is a missing space between "arrangements" and "1".

The sentence was revised.

Page 4, line 19: I suggest to use "time-point" instead of "point in time".

The sentence was revised as requested.

Additionally, in the manuscript I suggest to use the expression "Patients' characteristics" instead of "patient characteristics", including the tables and captions. I suggest the same for "patients' age" (as in page 7, line 12).
We inspected the expressions and prefer to our version.

Page 12, line 1: please use "this investigation" instead of "this study", in order to avoid the repetition immediately after.

The sentence was revised. “…strength of the study was that the research material represented a population-based sample of…”.

Statistical revision: I suggest a statistical revision by an expert.

Statistical revision was conducted by a specialist in Applied Mathematics and Biostatistics.

Language revision: not necessary.