**PEER REVIEW HISTORY**

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

**ARTICLE DETAILS**

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| **TITLE (PROVISIONAL)** | The effect of frailty on Quality of Life in elderly patients after hip fracture: a longitudinal study |
| **AUTHORS** | van de Ree, Cornelis; Landers, Maud; Kruithof, Nena; de Munter, Leonie; Slaets, Joris; Gosens, Taco; Jongh, Mariska A C |

**VERSION 1 - REVIEW**

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| **REVIEWER** | KM Sanders<br>The University of Melbourne, Australia |
| **REVIEW RETURNED** | 05-Oct-2018 |

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| **GENERAL COMMENTS** | Comments:<br>• Methods: states demographic and baseline information was collected at 1 week or 1 month post Fx. I think the authors mean information was collected between 1 week and 1 month….<br>• Is it valid to dichotomise the scores from the EQ-5D? I was under the impression this was not a valid way to use the questionnaire. This loses the value of being able to compare overall utility score with that of an age-matched sample of the Dutch population.<br>• It would be clearer if the authors actually state Health State is the overall utility score from the EQ-5D using the algorithm from the Dutch population.<br>• The Method describing the ICECAP questionnaire should also state what population is most relevant or was used to compare scores from this study since there is not normative values for the Dutch population to date.<br>• In addition to the flow chart, can the authors show what proportion of values (EQ-5D, ICECAP etc) were imputed at each assessment time point?<br>• Results: Table 2 – The OR shown in the table – are they a summary odds ratio for all the time points assessed since the hip fracture?<br>• Results: The figures are clear but Table 2 appears to give a different pattern to the figure as only anxiety/depression is significantly more likely to be present between frail and non-frail after adjustment for relevant variables. Please comment. First paragraph of discussion also does not reflect this.<br>• The figures need to also state what time point each of T0 to T5 represents. They also need to legend to state mean and SD/ 95% CI. On figures it is usual to have 95% CI but the values on the figures look like there are very tight confidence around the mean. You would expect more variation.<br>• Discussion: The authors state HS and capability did not improve substantially in the first 6 months post Fx. This is difficult for the reader to see as the x-axis on the figures is T1 to T3 – is |

| | it(?). Although it is well documented that QoL does not generally fully recover within 12 mths of hip Fx, several studies have found that QoL substantially improves in the immediate post Fx period (2 weeks to 4 mths period) – see ICUROS papers eg Borgstrom F; Abimanyi-Ochom et al.<br>• Can the authors comment on differences between responses/ patients where a proxy was used vs self reported responses? |
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| **REVIEWER** | Jae-Young Lim<br>Seoul National University Budnang Hospital |
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| **REVIEW RETURNED** | 25-Dec-2018 |

| **GENERAL COMMENTS** | Dear authors,<br><br>I'm happy to have an opportunity for reviewing your study. It is a meaningful trial to find out whether frailty is a good predictor of QoL in patients recovering from hip fracture or not. This study was based on the data from a well-established cohort study and the manuscript is well written. However, the present manuscript has some issues to be clarified before determining whether the authors' conclusions are valid.<br><br>Please, describe the post-fracture rehabilitation and other care that the patients received after hip fracture. Rehabilitation and other medical treatments could be one of influencing factors on QoL in hip fracture patients. I'm concerned about the possibility of the difference in post-fracture treatments between frail and non-frail.<br><br>During the 1-year F/U period, significant numbers of patients were not followed up with no show in both groups. Furthermore, there were more no-show cases in frail group. I wonder how the authors handled no-show cases when the authors examined the pattern of changes over time in health status.<br><br>Thanks. |
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## VERSION 1 – AUTHOR RESPONSE

Reviewer #1; KM Sanders

1. Methods: states demographic and baseline information was collected at 1 week or 1 month

post Fx. I think the authors mean information was collected between 1 week and 1 month….

Answer authors:

We tried to include patients into our study at onset of the fracture and asked patients/proxy's to fill the questionnaires at one week. Sometimes, patients responded a bit later and we could include them at one month. So there were officially two measurement timepoints to collect baseline information. We tried to include patients as early as possible to gain insight in the early period after hip fracture.

2. Is it valid to dichotomise the scores from the EQ-5D? I was under the impression this was not

a valid way to use the questionnaire. This loses the value of being able to compare overall

utility score with that of an age-matched sample of the Dutch population.

Answer authors:

We agree with the reviewer and we deleted sentence 152-153, because we use the scoring algorithm is available by which each health status description can be expressed into an overall score using a published utility algorithm for the Dutch population.

3. It would be clearer if the authors actually state Health State is the overall utility score from

the EQ-5D using the algorithm from the Dutch population.

Answer authors:

We thank the reviewer for this comment. We stated in our methods section: “Health status was assessed with the utility score (EQ-5D™ utility), ranging from 0 representing death to 1 for full health. A negative utility score indicates a health status worse than death. The Dutch tariffs were used for this study to calculate EQ-5D-3L™ preference weights.” (ref. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies)

4. The Method describing the ICECAP questionnaire should also state what population is most

relevant or was used to compare scores from this study since there is not normative values

for the Dutch population to date.

Answer authors:

We used the study from Makai et al. to compare scores from our study and we add this to our manuscript; “and for this study the population of Makai et al. of post-hospitalized older people in the Netherlands was used to compare scores.” (ref. A validation of the ICECAP-O in a population of post-hospitalized older people in the Netherlands. Health and quality of life outcomes).

5. In addition to the flow chart, can the authors show what proportion of values (EQ-5D,

ICECAP etc) were imputed at each assessment time point?

Answer authors:

We thank the reviewer for this comment and added to our methods section: “There were no variables with 5% or more missing values.”

6. Results: Table 2 – The OR shown in the table – are they a summary odds ratio for all the time

points assessed since the hip fracture?

Answer authors:

Yes, with mixed model analyses we show the OR for frail patients compared to non-frail patients (=reference group) on average over time.

7. Results: The figures are clear but Table 2 appears to give a different pattern to the figure as only anxiety/depression is significantly more likely to be present between frail and non-frail after adjustment for relevant variables. Please comment. First paragraph of discussion also does not reflect this.

Answer authors:

We thank the reviewer for this comment and added this to our discussion, see line 237-241: “The pattern of recovery trajectories in the prevalence of reported problems in the domains of the EQ-5D during the first year period after hip fracture differed between the frail and non-frail patients. However, after adjustment for confounders, especially for the concerned pre-fracture status of the EQ-5D domain, the major differences between frail and non-frail patients disappeared.”

8. The figures need to also state what time point each of T0 to T5 represents. They also need to legend to state mean and SD/ 95% CI. On figures it is usual to have 95% CI but the values on the figures look like there are very tight confidence around the mean. You would expect more variation.

Answer authors:

We thank the reviewer for this comment and we stated what time point each represents and we also stated the mean (95%CI). We also adapt the dots so the confidence around the mean could better be interpreted.

9. Discussion: The authors state HS and capability did not improve substantially in the first 6 months post Fx. This is difficult for the reader to see as the x-axis on the figures is T1 to T3 – is it(?). Although it is well documented that QoL does not generally fully recover within 12 mths of hip Fx, several studies have found that QoL substantially improves in the immediate post Fx period (2 weeks to 4 mths period) – see ICUROS papers eg Borgstrom F; Abimanyi-Ochom et al.

Answer authors:

We agree with the comment of the reviewer. We adapted the sentence in our discussion into: “In our study, HS and capability wellbeing do not generally fully recover within 12 months after hip fracture for both frail and non-frail patients.” We thank the reviewer to point out the ICUROS papers of Borgstrom and Abimany-Ochum and adapted our comparison with existing literature.

10. Can the authors comment on differences between responses/ patients where a proxy was

used vs self reported responses?

Answer authors:

We thank the reviewer for this comment and adds a paragraph to our discussion: “Gabbe et al. published in trauma patients that differences in HS between patient and proxy respondents showed random variability rather than systematic bias. They concluded that group comparisons using proxy responses are unlikely to be biased.” (ref: Level of agreement between patient and proxy responses to the EQ-5D health questionnaire 12 months after injury).

Reviewer #2; Jae-Young Lim

1. Please, describe the post-fracture rehabilitation and other care that the patients received after hip fracture. Rehabilitation and other medical treatments could be one of influencing factors on QoL in hip fracture patients. I’m concerned about the possibility of the difference in post-fracture treatments between frail and non-frail.

Answer authors:

We thank the reviewer for this comment and add your suggestion in our discussion. Line 259-262: “In the Netherlands, there is no difference in post-fracture treatments between frail and non-frail patients. However, frail patients have already pre-fracture more problems with their mobility and selfcare, and therefore, this could have influenced their post-fracture rehabilitation possibilities.”

2. During the 1-year F/U period, significant numbers of patients were not followed up with no show in both groups. Furthermore, there were more no-show cases in frail group. I wonder how the authors handled no-show cases when the authors examined the pattern of changes over time in health status.

Answer authors:

We thank the reviewer for this comment and add this kind of selection bias, selective drop-out to our discussion. Second, frail patients showed a higher capability wellbeing score at one-week follow-up than at one-month follow-up. This is probably due to selection bias because frail patients in relatively good condition were able to complete the questionnaire at this early follow-up time point. Furthermore, there were more no-show cases in the frail group, resulted in selective drop-out. Therefore, the overall QoL of patients after a hip fracture, especially in the frail group, is probably worse than that presented in this study.

**VERSION 2 – REVIEW**

| **REVIEWER** | Jae-Young Lim<br>Seoul National University, Korea |
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| **REVIEW RETURNED** | 25-Feb-2019 |

| **GENERAL COMMENTS** | I appreciate the authors’ efforts to correct the manuscript as suggested. The quality of the manuscript has improved considerably in the revised form at this time.<br><br>Thanks. |
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