Author's response to reviews

Title: The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip fracture: randomised controlled trial (Oslo Orthogeriatric Trial)

Authors:

Leiv O Watne (l.o.watne@gmail.com)
Anne C Torbergsen (a.c.torbergsen@medisin.uio.no)
Simon Conroy (spc3@leicester.ac.uk)
Knut Engedal (knut.engedal@aldringoghelse.no)
Frede Frihagen (ffrihagen@gmail.com)
Geir A Hjorthaug (geir.hjorthaug@me.com)
Vibeke Juliebo (v.juliebo@gmail.com)
Johan Raeder (johan.rader@medisin.uio.no)
Ingvild Saltvedt (ingvild.saltvedt@ntnu.no)
Eva Skovlund (eva.skovlund@farmasi.uio.no)
Torgeir Wyller (t.b.wyller@medisin.uio.no)

Version: 2
Date: 14 March 2014

Author's response to reviews: see over
To the Editor:

Thank you for the thorough and relevant comments from the reviewers as well as from the Editor. We have now revised the paper accordingly. All changes are underscored. We have also changed the abstract as requested, added four keywords, moved the ethics statement to the Methods section and re-organized the Competing interests, Authors’ contributions, Acknowledgements, References, Figure legends, Tables, and Description of Additional files to be in the order requested in author guidelines.

“Oslo Delirium Research Group” was added to affiliation number 1 in accordance with a re-organization of research at Department of Geriatric Medicine at Oslo University Hospital.

Responses to Referee # 1

Is the question posed by the authors new and well defined?
The objectives of this paper address an important gap in the literature; however, the aims could benefit from further definition through development of a more Comprehensive background section and review of the current literature. First, a comprehensive review in the Introduction section should clearly identify the gap that this trial addresses, followed by clear statement of the aims. In that section, I recommend that the authors include current and projected statistics on falls and hip fractures in older adults. Second, additional details and literature related to orthogeriatric services would strengthen this section. The readers may also benefit from a short definition and pathophysiology of delirium, particularly related to older adults. Finally, additional background information regarding how existing dementia impacts delirium in the peri-operative phase would highlight a strength of the study: the inclusion of patients with dementia.

Response: We have re-written the introduction and included statistics on falls and hip fractures in older adults.

Page 4, para 1, line 43 - 47: More than 30 % of individuals aged 65 years or older experience at least one fall each year, and the prevalence increases with age [1]. Ten percent of falls result in serious injuries [2], with hip fracture as one of the most feared consequences. In the European Union it was estimated 615,000 new hip fractures in 2010, and the number of hip fractures is expected to increase in the years to come [3].

We have also emphasized that dementia is a major risk factor for delirium, and that despite this are patients with dementia often excluded from studies on delirium.

Page 4, para 3, line 59 - 61: Delirium is particularly common in patients with pre-existing dementia [11], despite which patients with dementia are often excluded from studies [12].
Our suggestion is, however, not to expand the Introduction with details on different orthogeriatric models or delirium pathophysiology. We feel that this would imply broadening the Introduction too far outside the focus of trial, and making it long and less readable. We have, however, included a very recently published review (Grigoryan, reference # 7) that compares different orthogeriatric models. In the protocol paper for this study (reference # 17), we have described in more detail how our model fit with previously described models. If the Editor wants us to put more of this subject into the text, we will indeed do so.

**Are the methods appropriate and well described, and are sufficient details provided to replicate the work?**

The study methods were strong, particularly the stratified randomization, blinding, and use of motion sensors for assessment of physical activity. However, the authors should consider adding a few statements describing the intervention. I realize there is an existing publication that details the protocol, but a short description would clarify the context of the trial. Also, please explain if the study physician and study nurse were blinded to group assignment in data collection (line 143). The authors should reconsider the organization of sections in Methods. Readability could be improved if the primary outcome measures were discussed under the “Primary outcome” section (those related to cognitive impairment), and likewise with the delirium measures (under “Secondary outcome”).

Response: We have included some details describing the intervention (page 7-8, para 3, line 123 - 126): Details about the clinical routines have been published [17] and included medication reviews, early and intensive mobilisation, optimising pre- and postoperative nutrition and early discharge planning.

Data collection during hospital stay could not be done blinded as the patients were assessed in the ward they were allocated to. We have highlighted this as a weakness with the study. Page 19, para 2, line 356 - 357: As with all service evaluations, blinding of assessments during hospital stay was impossible and may have introduced bias.

We have considered different ways to reorganize the sections in Methods, but have ended up with keeping this unchanged. Since we used a combined primary outcome, we have to explain in detail how that outcome was constructed. Other cognitive measures were collected at the follow up controls (MMSE, Clock drawing test, IQCODE), but this was defined as secondary outcomes. We feel it might be confusing to add description of these under the primary outcome section.

Among the secondary outcomes are outcomes collected during hospital stay (e.g. delirium, length of stay) as well as outcomes from the follow up controls (e.g.
mobility, place of residence, ADL, weight changes). Instead of giving a description of how we measured the different outcomes when they are listed in the Method section, we feel it gives a better overview to first describe measures we did during hospital stay and next measures collected at the follow up controls. If the Editor prefers another way to organize the information in the Method, we will certainly do so.

**Are the discussion and conclusions well balanced and adequately supported by the data?**

The Discussion section was well supported by the data. However, I would hesitate to state “A likely explanation is that usual care was better in our study since the delirium rates both in the intervention and the control group were lower than in the Swedish study” (line 368). Is this because there are other interventions or organization of care in place in usual care that help prevent or reduce symptoms of delirium? If so, summarize the usual care procedures. Furthermore, I would recommend the authors review multi-disciplinary interventions that have a medical service or consultation component in the Discussion (e.g., Milisen, K., Foreman, M. D., Abraham, I. L., De Geest, S., Godderis, J., Vandermeulen, E., ... Broos, P. L. [2001]. A nurse-led interdisciplinary intervention program for delirium in elderly hip fracture patients. *Journal of the American Geriatrics Society*, 49[5], 523–532). Studies such as those have compelling findings related to delirium.

Response: We have added some details to support our argument that the usual care in our study were of high quality. Page 21, para 1, line 386 - 389: *The orthopaedic ward in our study provided short waiting time for surgery, similar staffing as in the geriatric ward, personnel with earlier experience with orthogeriatric models and delirium prevention, physiotherapy for most hip fracture patients, and an integrated post-operative care unit.*

As the reviewer points out, multidisciplinary team providing geriatric service in orthopedic wards have been shown to be effective in reducing delirium. In the discussion we have already mention two such studies (Dechods # 15, Marcantonio ref # 16.). The study from Deschods is from Milisens group in Belgium, and from the paper it seems to be the same hospital (Leuven) as in the reference from 2001 recommended by referee. The study from Deschod indicated that a multidisciplinary consultation could reduce delirium, and we feel that it is sufficient to refer to this latest report.

**Is the writing acceptable?**

Overall, this paper would benefit from critical editorial review due to multiple problems with language and readability. First, the authors use the term “endpoint” frequently throughout the paper (e.g. primary endpoint), although I presume the authors are referring the primary and secondary outcomes. Second, the authors
should consider the use of commas and punctuation to increase readability. Third, descriptions such as “best available evidence” (line 115) or “best available sources” (line 187-188) would be improved if supported by a statement of the evidence rather than these qualifiers.

Response: we have replaced endpoint with outcome throughout the manuscript. We have also expanded the description of “best available evidence”, Page 7, para 4, line 120 - 122: *Clinical routines were developed based on literature search, experience from earlier orthogeriatric models and the pilot phase prior to start of randomisation.*

With respect to CDR, it is recommended in the scoring guidelines that information should be taken from the best available source. We have not commented further on this in the manuscript.

**Minor issues not for publication:**
Finally, there are several issues related to clarity and grammar, including the following:

- Line 58 (“We evaluated this model by a RCT in which hip fracture patients receiving usual care...”; Introduction)
- Line 125 (“All patients included in the trial were offered a control in the orthopaedic outpatient clinic...”; Intervention and control section)
- Line 135 (“We used mobilisation after surgery as a process measure”; Measurements)
- Line 161 (“At each follow-up control were proxies interviewed...”; Measurements)
- Line 206 (“Based upon previous experience with the CDR”; Statistical analysis)
- Line 220 (To adjust for any inequality in the distribution...”; Statistical analysis)
- Figure 1 (“Not meeting inclusion criteria”)

Rather than providing each instance of these issues, I suggest that the authors critically review the manuscript for such problems.

Response:

The final version of the manuscript has been carefully reviewed by a native English co-author (Simon Conroy) and errors of spelling and grammar have been removed as far as possible.
Repsonses to Referee # 2:

The analyses appear to rule out an effect of the intervention on cognitive outcomes. The authors could consider further sensitivity analyses to determine what sample size would have been needed to rule out a clinical significant difference in cognition with the intervention. Another approach would be to provide confidence intervals with reference to the between group differences at the 4 and 12 month follow-ups for the primary outcome and major secondary outcomes.

Minor Essential Revisions
The only specific point about which the authors could respond is the issue of the precision of the estimates of the between group differences in outcomes and whether the possibility of clinical important differences have been ruled out.

Reponse: 95 % confidence interval is included for the primary outcome and the major secondary outcomes. SPSS does not give the 95 % confidence interval for medians, so an additional sentence had to be added in the Methods section: page 13, para 2, line 241 - 243: *All statistical analyses were performed using IBM SPSS Statistics version 20, except for median differences and corresponding 95% confidence intervals that were estimated by the Hodges Lehmann estimator using StatXact 8.0.*