Author’s response to reviews

Title: Early inpatient rehabilitation for acutely hospitalized older patients: A systematic review of outcome measures

Authors:

Patrick Heldmann (heldmann@nar.uni-heidelberg.de)
Christian Werner (christian.werner@bethanien-heidelberg.de)
Nacera Belala (belala@nar.uni-heidelberg.de)
Jürgen Bauer (juergen.bauer@bethanien-heidelberg.de)
Klaus Hauer (khauer@bethanien-heidelberg.de)

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Dear Dr. Tovah Honor Aronin,

Please find enclosed the revised manuscript #BGTC-D-19-0002, now entitled “Early inpatient rehabilitation for acutely hospitalized older patients: A systematic review of outcome measures” (original title has been modified).

We greatly appreciate the comments and suggestions provided by the editor and reviewers for improving the manuscript and have modified the manuscript accordingly. The major change covers the substantial reduction (about -1900 words) of the manuscript’s size (as requested by reviewer 2) to sharpen its main and primary message. For this, we decided to delete the sub-analysis for older patients with cognitive impairment from the manuscript which was initially defined as a secondary aim of our review (about -1600 words). However, if you as the editor would like to still see this secondary aim in the manuscript, we of course will be able to re-include the sub-analysis in the manuscript.

All changes in the manuscript are indicated using track changes and documented in a comprehensive point-by-point response to all comments (see below).

We hope that the revised manuscript meets all the requests made by the reviewers as well as the high-quality standards of BMC Geriatrics and will now be found suitable for publication. Thank
you very much for your consideration of our manuscript. If there are any further comments, questions, or requests, please do not hesitate to contact me.

Sincerely,

Patrick Heldmann

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.Point-by-point response

Editor comments:

In accordance with BioMed Central editorial policies, could you please ensure your manuscript reporting adheres to PRISMA guidelines for reporting Systematic Reviews and Meta-Analyses. This is so your methodology can be fully evaluated and utilised. Can you please include a completed PRISMA checklist as an additional file when submitting your revised manuscript.

Response: We added the information that our review followed to the PRISMA guidelines for reporting systematic reviews and meta-analyses on page 8, line 165-167 and included the completed PRISMA checklist as an additional file (Additional file 2).

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Reviewer 1

1. Clarify that you included rehab in acute medical units- ie not just after transfer to GEM/Aged Rehab units?

Response: As defined in the inclusion criteria for the search strategy and study selection, we only considered studies that included older patients admitted to an acute hospital medical ward (page 7, line 151-158). In contrast to other reviews evaluating the effect of physical rehabilitation interventions in older patients during hospitalization (e.g., Kosse et al.2013; Scheerman et al. 2018), we included only studies that were performed in the acute hospital setting and not in or after transfer to subacute hospital settings (e.g., subacute geriatric rehabilitation wards). Due to the international nature of our review and the associated inconsistent terminology of the acute care hospital setting among different countries, it was not always easy to determine if the studies and intervention programs were conducted in the acute care hospital setting. However, potential eligible study for inclusion with unclear setting definition were extensively discussed between the researchers and, if necessary, with third party consultation. After such discussions, only studies that could be clearly identified as being performed in the acute care hospital setting were
included. According to the reviewer’s comment, we revised the section on the inclusion criteria to clarify that we included only studies performed in acute hospital medical wards (page 7, line 155).

2. How exactly was a response to the intervention defined? - absolute change, percentage change, change in x of y variables (and how was that defined) etc. Look at Paul Maruff’s work in the dementia field for some suggestions?

Response: We did not define successful response to the intervention by absolute changes, percentage changes, or changes in x of y variables. Intervention effects of the included RCTs (i.e. response to the intervention to be evaluated in the RCTs) were evaluated based on the significance level of between-group differences in the primary outcomes, as reported in the included studies. P-values of ≤ 0.05 were considered as statistically significant. A similar approach was used in Scheerman et al. 2018. Each individual primary outcome defined by an included study (some studies included more than one primary outcome measure) was checked for statistically significant intervention effects and was subsequently related to the intervention contents. To clarify our approach for evaluating the intervention effects, we included more detailed information on page 9, line 191-193.

3. Best not to use the term "geriatric patients" - there are more pc terms.

Response: The term “geriatric patients” has been replaced by “older patients” across the entire manuscript.

4. Are you sure all relevant literature has been accessed? This reviewer is co-author on a paper that seems to have been missed.

Response: We assume that the reviewer refers to the paper Said et al. 2012, 2015, or 2018. Our search strategy had successfully identified Said et al. 2012 and 2015; however, both papers were excluded during the selection process due to not meeting our inclusion criteria. To be more specific, Said et al. 2012 describes a feasibility study, which was defined as an exclusion criteria in our review (see page 7, line 151-158), and Said et al. 2015 describes a study protocol. Both studies were excluded during the screening process of title and/or abstract. The RCT of Said et al. 2018 included patients admitted from acute hospital, home, or other settings to subacute geriatric rehabilitation wards and was also conducted in these units. Thus, this study also does not meet our inclusion criterion of being performed in acute hospital medical wards. Additionally, this study was published outside the search cut-off data of our review.
Initial search terms were compiled and iteratively refined before the final literature search was conducted in the electronic databases. In our point of view, we used a rather broad search term to capture the largest possible number of potential eligible studies, which might be also represented in the much higher number of studies identified through data-base searching (n = 17072) compared to other systematic reviews in this research field (e.g., Scheerman et al. 2018: n = 1654 studies; Martinez-Velilla et al. 2016: n = 6564 studies; Kosse et al. 2013: n = 772 studies; de Morton et al. 2007: n = 3138 studies). The manual search performed in the reference lists of other relevant review articles and in-cluded articles provides only a very small number of additional studies to be screened (n = 2). Thus, we are confident that all relevant literature has been accessed.

5. There are some English errors- eg line 96 on page 5.

Response: This error has been corrected. In addition, the entire manuscript has been checked once more for any English errors.

6. Please clarify that you have included rehab in acute medical units, rather than transfer to other units.

Response: Please see our response for comment 1.

7. Your prevalence of cognitive impairment/dementia is low- suggesting, as is common, that ascertainment was incomplete- and this would affect input and output values. Please clarify/expand.

Response: We agree with the reviewer that the prevalence of cognitive impairment (CI) identified in our review seems rather low, when compared to previous studies that sug-gest a higher prevalence of CI in acutely hospitalized older patients (40-70%) (Sampson et al. 2009; Torisson et al. 2012; Zekry et al. 2008). As it has been discussed on page 33, line 878-880, the lower mean prevalence rate in our review can be explained by our ap-proach in identifying patients with CI in studies that only provided information on the number of patients with premorbid or diagnosed dementia but not for those with CI. For these studies [36, 39, 42, 43, 56, 60], the subsample of patients with CI was defined based on the number of patients with premorbid or diagnosed dementia but not on the number of patients with CI, as information on such patients with CI was missing in these studies. In these studies, the prevalence rate of patients with premorbid/diagnosed de-mentia ranged from 11-33%, with a mean prevalence rate of 22%. As the number of premorbid/diagnosed dementia is certainly lower than that of CI in acutely hospitalized older adults, the inclusion of the studies for calculating the mean prevalence
rate of CI across all studies has decreased this prevalence rate. When considering only studies that explicitly distinguish between patients with and without CI by different assessment/screening instruments (e.g. MMSE, AMTS, SMSQ) and different cutoff values for CI (e.g., MMSE <26 or <24) [44, 45, 47, 48, 50, 54], the prevalence rates of CI is substantially higher, ranging from 14-65%, with a mean of 40%, which is similar to the prevalence commonly reported in acutely hospitalized older patients.

The prevalence rate of CI in our review might also be influenced by the different assessment/screening instruments and different cutoff values. For instance, Kimmel et al. reported the highest prevalence rate of 65% based on the MMSE cutoff <26 points, whereas other studies using a MMSE cutoff of <24 reported smaller prevalence rates (47-58%). As we were not able to standardize the definition of CI across the included studies but had to use the definitions of CI provided in the individual study, the prevalence rates are affected by these different CI definitions.

Overall, we do not agree with the reviewer that our prevalence rate of CI is affected by ascertainment bias but by our approach to define subgroups of patients with CI and the different CI definitions used by the studies included in this review. We are still confident that we accessed all relevant literature, as already discussed above for the reviewer’s comment 1.

In response to the comment of reviewer 2 that the manuscript “is far too long” and that shortening would sharpen the message, we decided to focus on the primary aim of our review (i.e., matching of primary outcome measures to the intervention, study sample, and setting & evaluation of the effects of matching on the main findings of the included studies) and deleted the secondary aim of analysing the subgroup of patients with cognitive impairment from the manuscript.

8. On page 22, lines 582 on, you have included discussion on results- please move to appropriate section

Response: We agree with the reviewer that this section included parts providing not only results but also some discussion. The section was removed by deleting the subgroup analyses for patients with CI.


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Reviewer 2

Through this extensive and carefully evaluation of the literature the authors examine primary outcome measures that have been used in randomized controlled trials on early rehabilitation in older hospitalized patients. The aim was to evaluate the effects of matching on the main findings in these randomized controlled trials. The authors identify 24 studies and a total of 33 different
outcome measures which were grouped into six categories. The review highlights the importance of being very specific in choosing outcome measures as this is crucial to reveal benefits to early rehabilitation. The authors conclude that outcome measures that specifically matched the results of intervention were more likely to document effect of the intervention. This review is a very helpful paper as it shows us the importance of choosing the right outcome measures. However, the paper is heavy reading and far too long. Reduction of the overwhelming number of details would sharpen the message. as well as a reduction of repetitions.

Response: According to the reviewer’s comment that the manuscript is far too long and that shortening the manuscript would sharpen the message, we decided to put the focus of the manuscript on the main and primary aim of our review, which was initially defined as the evaluation of the matching of the primary outcomes measures to the study characteristics (sample, intervention, setting) and the evaluation of the effects of matching on the main find-ings reported in the studies included in our review. We deleted the secondary aim of our re-view (subgroup analysis of patients with cognitive impairment) (e.g., page 6, 116-132; page 9, 204-216; page 21-23, line 534-609), as it has no impact on the conclusions that readers should draw from our review. The secondary aim rather directed the attention of the reader away from the key message of our review towards a research topic that could (or even should) be addressed exclusively and in more detail in a future study. We also revised the entire manuscript, trying to reduce the number of details and repetition. Overall, we reduced the word count of the manuscript from 10207 to 8316 words (-18.5%).

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Reviewer 3

1. Table 2: - The reference number of "Pitkälä 2008" is missing.

Response: The reference number was added in table 2.

2. Please double check missing/extra brackets (e.g. "Brown 2016" females percentage, "Jeffs 2013" Intervention paragraph, "Vidan 2005" Admission to discharge)

Response: Table 2 was checked once more and errors were corrected.