Author's response to reviews

**Title:** Exercise programme with telephone follow-up for people with hand osteoarthritis - protocol for a randomised controlled trial.

**Authors:**

Nina Østeraas (nina.osteras@medisin.uio.no)
Kåre B Hagen (k.b.hagen@medisin.uio.no)
Margreth Grotle (margreth.grotle@medisin.uio.no)
Anne-Lene Sand-Svartrud (anne-lene.svartrud@diakonsyk.no)
Petter Mowinckel (petter.mowinckel@diakonsyk.no)
Eline Aas (eline.aas@medisin.uio.no)
Ingvild Kjeken (ingvild.kjeken@diakonsyk.no)

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**Author's response to reviews:** see over
Study protocol
Exercise programme with telephone follow-up for people with hand osteoarthritis - protocol for a randomised controlled trial.

Dear Editor-in-Chief

Thank you for considering our study protocol manuscript for publication and for the opportunity to submit a revision of the manuscript. We would like to thank the reviewers for their thorough reading and for providing valuable input and relevant comments, which have helped to improve the manuscript. We have carefully read the comments from the reviewers, and have adjusted the manuscript accordingly. Please find below point-to-point responses to the comments and the changes that are made in the manuscript.

Sincerely,
on behalf of all co-authors,
Nina Østerås

Reviewer 1
1. Please state the hypotheses of the study.
   RESPONSE: We have included our hypothesis in the last paragraph on page 3.

2. Please clarify in the Methods and Figure when the baseline assessment will be conducted. Ideally, it should be before randomization.
   RESPONSE: Yes, the randomization was performed after the baseline questionnaire and tests. We agree that this information should be included and have added this in the Methods section and in Figure 1. On page 4, last paragraph, last sentence; “once” is replaced by “after”. A box with “baseline questionnaire and assessments” is now included in Figure 1.

3. The control group will not receive specialized OT intervention for 6 months. Please comment on the steps to minimize attrition during the waiting period.
   RESPONSE: No particular steps were made to minimize attrition in the control group except that we promised that they would receive the exercise equipment and instructions. Both groups received a postal letter 2-3 weeks before the assessment dates and a SMS reminder the day before.

4. The authors state that FIHOA and the PSFS will be performed at 3 months post-randomization. Please clarify if these primary outcome measures will be done at baseline, ideally prior to randomization, and at 6 months. If not, please explain why.
   RESPONSE: Yes, the FIHOA and the PSFS will be performed at all measurement time points. The baseline questionnaire is filled in before randomization. This is now indicated in Figure 1 and on page 4 (See #2 response). To be more clear on outcome measures and primary outcome, we have revised the text:
Page 9, 3rd paragraph:
“All outcome measures are collected at baseline, 3 months (post-intervention, primary endpoint) and 6 months (Tables 3 and 4). “

Page 9, 4th paragraph:
“The primary outcome measure is self-reported hand activity performance, as measured by the the Functional Index for Hand OsteoArthritis (FIHOA) [35] and the Patient-Specific Function Scale (PSFS) [36]. “

5. Health resource utilization – please clarify if an existing health resource utilization measure is used. If not, what steps will be taken to examine its measurement property?
RESPONSE: We do not know any standardised health resource utilization measure, suitable for Norwegian health care, but we have based our questionnaire on a validated cost diary (Goossens et al, 2000) and a questionnaire used in previous studies (i.e. Grotle et al, 2011). The questionnaire is also discussed with researchers in Health Economics at the University of Oslo. We have revised the section on page 12 regarding direct and indirect costs to incorporate this information.

6. What is the authors’ strategy for handling missing data?
RESPONSE: We have instructed the outcome assessors to screen the questionnaires for responder missing items while the participants are still present. Hence, we hope to keep the level of missing data low, and plan not to impute missing data as this is known to reduce the data variability. We will analyze whether eventual missing data is missing at random or not. One sentence about this is now included on page 5 in the section on training of the involved personnel.

7. Health Economics section – please clarify that incremental cost-effective ratio is calculated ‘between groups’. Also, it appears that the authors will construct cost-effectiveness acceptability curves, but the description of this analysis is somewhat obscure. Please revise.
RESPONSE: We have now added “between groups” in the sentences about that incremental cost-effective ratio and have revised the information about cost-effectiveness acceptability curves on page 15.

8. ‘Sample size’ section – I am a bit confused by the description of the MCID of FIHOA. Is the 10% change an established MCID for this outcome measure? If so, please remove ‘e.g.’
RESPONSE: Unfortunately, there is no established MIC or MCID for FIHOA. We have removed the “e.g” in the Sample size section.

9. Will the author register this study in an open RCT registry?
RESPONSE: The study is already registered at www.ClinicalTrials.gov, which is stated after the Abstract on page 2.

10. Under ‘Health Economics’, it should be ‘….applying both health system and societal perspective’ rather than a ‘health-care perspective’.
RESPONSE: We agree and have changed the text on page 15 accordingly.

The manuscript has been through professional proof-reading to improve the language. Suggested changes are marked in the manuscript.
Reviewer 2

Abstract
1. Background: The authors highlight that available research is very limited. It is also at times conflicting and this is worth stating here and later in the discussion.
   **RESPONSE:** We agree. This is now included in the abstract and in the discussion.

2. Methods: Participants are classified using Physician-confirmed hand osteoarthritis. They follow the ACR clinical criteria and this is worth stating in the abstract.
   **RESPONSE:** We agree. This is now included in the abstract. We have also slightly adjusted the inclusion criteria in Table 1 to specify that we also include those with uni-/bilateral CMC1 OA, who fail to fulfill the last three of the ACR classification criteria.

3. The description of the ‘treatment as usual’ can be refined as this is primary care treatment and participants are more likely to be exercised naïve.
   **RESPONSE:** We are not sure if we have understood this comment correctly, but we have slightly revised this paragraph on page 6 to include some more information about “usual care”.

4. ‘Participants will be instructed to perform the exercise programme at home’ rather than ‘will perform the exercise… at home’. Adherence will be captured using self-report. A measure of global improvement could also be included in the abstract.
   **RESPONSE:** We thank the reviewer for this correction and the suggestion that will improve the readers’ understanding. We have included the secondary outcome “Patient Global Assessment of disease activity” in the abstract as this is an important outcome that will be used to calculate the OMERACT-OARSI. Due to the abstract word limit of 350 words, we have deleted some words in this revision, but we could not include all outcome measures in the abstract.

Background
5. Additional references could support the statements on the consequences of hand OA and the resulting activity limitations and participation restriction.
   **RESPONSE:** We agree and have included 2 references in the 2nd paragraph on page 3.

6. The conflicting findings for the benefits of exercise in hand OA are worth highlighting.
   **RESPONSE:** That there are conflicting findings in previous studies are now mentioned once more in the background (and in the Abstract and Discussion sections)

7. **The study objective.** The direction of the effects of the intervention could be included in a hypothesis or study question
   **RESPONSE:** We have included our hypothesis under Study objective on page 3.

Methods
Participants:
8. Will participants from the two OA cohorts be naïve to hand exercises?
   **RESPONSE:** This is a thoughtful comment. The Ullensaker cohort will most likely be naïve to hand exercises, while some of the Oslo Hand OA cohort may have received instructions at Diakonhjemmet Hospital Outpatient Clinic in 2007/2008. We will ask about this, and also ask if the control group participants have performed hand
exercises in the past 3 months. We have added three sentences about this in the manuscript in the first paragraph on page 9.

9. **Eligibility criteria**: Participants are recruited from cohorts - will two members living at the same address be eligible for inclusion – they may get allocated to different arms of the study? Will participants having received occupational therapy or physiotherapy treatment in the previous six months be excluded?

   **RESPONSE**: The possibility that participants living at the same address will be included is very small, but some of them might live close and know each other. We have not planned any strategy to avoid this, but will instruct the participants to avoid “contamination”. No, we do not plan ask about OT or PT treatment in the previous months. There are very few OTs in primary care, and a referral to secondary care OT is rare. The Norwegian PTs normally focus their treatment on knee or hip joints as people with radiologically confirmed hip and/or knee OA can receive PT treatment for free (no out of the hand pocket money). Some of these patients may have hand OA as well, but it is not likely that the PT will instruct in hand exercises. At 3 and 6 months the control group will be asked if they have performed hand exercises in the previous 3 months.

**Randomisation and allocation concealment**

10. Will information be collected on individuals approached to be part of the study and those consenting to assessment?

   **RESPONSE**: Some demographic information on demographic variables will be available (i.e. gender, age, education for the Oslo Hand OA cohort, and also BMI, marital status, occupational status, years with the OA diagnosis, and comorbidity for the Ullensaker cohort)

**Blinding**

11. The statistician performing the main analyses will be unaware of group allocation. When will the statistician be un-blinded?

   **RESPONSE**: The statistician will be un-blinded during the last analyses, the per protocol analyses, since intervention adherence will be included here.

**Intervention**

12. The procedures for both intervention and control arms could be described in a table which may help the reader to navigate through the process.

   **RESPONSE**: We see the point and have expanded the information in Figure 1

13. The description of usual care could be expanded. ‘Treatment as usual’ is primary care management and this is worth noting. Does this mean that participants in the usual care arm get a referral back to the GP or is it a more ad-hoc or community-based usual care?

   **RESPONSE**: We have now included some more information about usual care in the 1st paragraph on page 6.

14. What written information do all participants get when entering into the study?

   **RESPONSE**: All eligible persons receive brief information about the purpose and the content of the study and “standard information” about data storage, withdrawal and more. The participants receive some oral information at the baseline measurements (mainly information about the measurement procedure and future assessments), but no written information is provided to all participants at this time point.
15. The intervention is detailed and well described. The illustrations are very helpful. How will attendance be reported? Is there a per protocol definition?

**RESPONSE:** Attendance at the group sessions will be recorded by the occupational therapists delivering the intervention, and home exercise will be self-reported in the exercise diary. Our per protocol definition is that the inclusion and exclusion criteria is “maintained” (i.e. no steroid injections in the hand joints during the study), that the intervention group participants have received the intervention (recorded 3 of 4 scheduled group exercise sessions and 22 of 36 of prescribed home exercise), and that the control group participants have not done any hand exercises during the study period.

**Outcome measures**

16. Why has 3 - months been selected as the primary endpoint rather than six months?

**RESPONSE:** In the American College of Sports Medicine’s (ACSM) recommendations for developing muscular strength and flexibility in older frail adults, a minimum training period of at least 12-15 weeks is recommended to achieve an optimal effect. We decided that the intervention period should last 12 weeks. Since benefits of exercise therapy are known to diminish over time if exercise is discontinued, we thought the 3 month assessment was the best time to assess eventual effects of the exercise programme, and then added a follow-up at 6 months to see if eventual effects sustain.

**Other measures**

17. These could be described as Tertiary outcome measures (also Table 4)

**RESPONSE:** Good idea. Changes are made in the text and Table 4.

**Data analysis**

18. Responders will be compared using the OMERACT-OARSI responder criteria. A brief description of how this will be done would be helpful e.g. which measures will be used?

**RESPONSE:** We agree that this information should be provided, and have added a detailed description on page 14.