Author's response to reviews

Title: Web-Based Therapeutic Exercise Resource Center as a Treatment for Knee Osteoarthritis: A Prospective Cohort Pilot Study

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Author's response to reviews: see over
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Version: 2   Date:

Authors’ response to reviews as follows: see over
Reviewer 1 report:

Title: Web-Based Therapeutic Exercise Resource Center as a Treatment for Knee Osteoarthritis: A Prospective Cohort Pilot Study

Version: 1  Date: 8 November 2013

Reviewer: Soren Thorgaard Skou

This manuscript focuses on the effects of an Internet-based intervention in knee osteoarthritis. The strengths of the study are the improvements in clinical outcomes and the applicability of the Internet-based intervention while the major limitations are the short-term follow-up and the lack of control group. Several other limitations should be addressed before the manuscript can be considered for publication.

Major Compulsory Revisions (MCR)

MCR1: Background. The background is well-written, however it could benefit from being a bit shorter, thereby leading to the purpose faster.
   The background has been shortened.

MCR 2: Background, fourth paragraph. If possible please be more clear on how TERC is different from the previous studies on Internet-delivered treatment in knee OA you mention. This is not clear at this point.

   The following has been added to the fourth paragraph of the Background for clarification on how the TERC is different from previous interventions.

   “Although internet-based physical activity resources are currently available, these are not geared toward patients with lower extremity OA and do not include patient-specific tailoring based on consideration of pain and functional limitations. The TERC is the first comprehensive web based system designed to evaluate, prescribe, monitor and adjust exercise programs for knee OA patients.”

MCR 3: Methods, second paragraph. The following inclusion criteria is a bit strict “living independently; considered themselves in general good health; able to walk without an assistive device” (and the exclusion criteria “a fall more than 2 times in past 6 months”), since you would think that all people with knee OA, perhaps especially those without the possibility to leave their home to do exercise, would benefit from internet-delivered treatments. Please discuss this lack of ability to generalize your findings to all patients with mild/moderate knee OA in the Discussion.

   This limitation has been added to the Discussion: “For the purposes of the research study, the eligibility criteria eliminated lower functioning patients such as those with a history of falls or walking with an assistive device, and thus the findings may not be generalizable to all patients with mild/moderate knee OA.”
MCR 4: Methods. Second paragraph. You need to be more specific on how the participants were enrolled. It is not clear to me, if the participants contacted you if interested or if you contacted them or both.

Both procedures were used. The enrollment procedure has been clarified.

MCR 5: Methods. You end up with 65 participants, how many were screened, and due to which criteria were they excluded. Preferably do a figure showing this. You could find inspiration for the figure in the CONSORT statement.

A figure illustrating this information has been added as Figure 2.

MCR 6: Methods. Even though your study is not a RCT, using the CONSORT checklist could in general improve the manuscript further, since it would assure that every part of the study was reported thoroughly.

We have adapted the CONSORT checklist to our cohort study design in order to thoroughly report all parts of the study.

MCR 7: Methods. TERC Intervention. The exercise is individualized, however to improve the strength and reproducibility of the study a more comprehensive description of the exercise is needed. Which exercises, focus, intensity, how many times a week etc.

Additional details regarding the exercises have been added.

MCR 8: Methods. TERC Intervention. How did you ensure that the participants performed the exercises according to your description of each individual exercise routine. Perhaps a lack of improvement in symptoms was simply due to the fact that the participant performed the exercise wrongly?

We cannot directly ensure that participants performed the exercises correctly. However there is substantial published evidence that direct clinician-patient interaction is not necessary to achieve effective exercise instruction. [Refs 38-42] While the majority of patients reported symptomatic improvement on GRC, it is possible that those that did not performed the exercises wrong. This has been added to Discussion.

No MCR9 in Reviewer Report

MCR 10: Methods. Your sample size calculation shows that 37 participants are needed to detect the changes you expect a priori. However, you include 65 participants, why? Is it to account for drop outs/missing data? This needs to be clarified.

This statement has been added for clarification: “To account for possible drop outs and missing data, an additional 28 participants were enrolled.”

MCR 11: Results, first paragraph. Only 80% (52 out of 65) completed both the baseline and 8-week follow-up. Please address this as a potential limitation to the results. Perhaps the last 20% did not improve in symptoms and was not satisfied
with the internet-based intervention?

This statement has been added to the Discussion: “We do not have information on why 13 of the 65 patients did not complete the 8-week follow-up questionnaire.”

MCR 12: Results, first paragraph. If receiving physical therapy was an exclusion criteria, how was it possible that 21 participant continued exercising as prescribed by the physical therapy? How can you be sure that this was not the reason for their improvements?

The specific exclusion criterion was if the subject was currently under the care of a physical therapist. The wording in the text has been changed to reflect this.

Regarding the continuation of exercises previously prescribed by the physical therapist, the subjects reported this information at the start of the study. It does not indicate that these exercises were continued during the 8-wk intervention; however, the subjects may have done so. Despite this possibility, 42 of the 52 subjects reported symptom improvement from the GRC, double the number that reported doing exercises prescribed by their physical therapist.

MCR 13: Table 1. Please provide information on OA severity, specifically radiographic and symptomatic severity and duration of symptoms. Furthermore, I am not sure, why you present BMI distribution and not only mean (SD).

To better describe symptomatic severity, the sub-scales from mSF-WOMAC have been included in Table 1. Duration of symptoms is provided as mean (SD) in text; however we feel duration of symptoms does not necessarily reflect severity of symptoms. Our primary outcome is change in symptoms, and as radiographs do not correlate well with symptom severity, we have elected not to include radiographic severity nor to assess change in radiographs.

We have chosen to present the mean and standard deviation of BMI in the text only (first paragraph of Results section). We feel the inclusion of BMI categories is important given the high rates of obesity in the US and the strong relationship between BMI and knee OA. However we have changed the BMI categories in Table 1 to underweight, normal, overweight, obese as these are more clinically relevant.

MCR 14: Table 1. I guess the reason for presenting the distribution of age and education levels is to show that the use of Internet-delivered interventions is possible across age and educational levels? However, this is not mentioned in the discussion.

This has been added to discussion: “Additionally the range of participants in our study illustrates that an internet-delivered intervention is possible across age and educational levels.”

MCR 15: Table 2. Please explain what the mean is expressing in the table. Mean is expressing the average number of times the activity was performed per participant. This has been added as a column heading in Table 2.

MCR 16: Results, second paragraph. Please include educational level as a between subject factor in the analysis (as you have done with age) and discuss
it. Since your intervention involves educational aspects and “self-learning” the level of education could affect the results.

Educational level was also entered as a between subject factor and found to be non-significant. This text has been added to the manuscript.

MCR 17: Discussion, third paragraph. A recent meta-analysis by Fransen et al. (http://www.ncbi.nlm.nih.gov/pubmed/19447940) showed that supervised exercise sessions were twice as effective as non-supervised sessions. Please include this in your discussion.

Thank you for the reference. We have added this information to the Discussion section. [Reference 35]


Because the MCID for the mSF-WOMAC had not been previously defined, we chose to calculate it using the anchor based approach with the GRC from our own study. We have added a statement in the limitations regarding this.

Minor Essential Revisions (MER)

MER 1: Registration of the trial. Was this trial registered in a public trial registry or similar as supported by ICMJE: http://www.icmje.org/publishing_10register.html If so, please provide the registration number.

This pilot study was not registered in a public trial registry. Because of the small number of subjects, the NIH program officer did not feel it was necessary.

MER 2: Methods, Participants. Why did you set the inclusion criteria at 25 years? The ACR Clinical plus Radiographic Classification Criteria for OA, which you are referring to, are using 38 years as their age criteria.

The age of 25 was determined without regard for the ACR criteria, an oversight on our part. Thank you for bringing this to our attention. We will correct this for future trials. One person (age 33) was under age 38.

MER 3: Methods, Participants. It seems a bit redundant to have an additional inclusion criteria of pain, since The ACR Classification Criteria for OA, includes: “One must have articular knee pain for most days of the prior month”

The criteria “experiencing knee pain on most days” has been moved to make it less redundant and more clear that it is part of the ACR Classification.

MER 4: Methods, Outcome Measures. You are using the short-form WOMAC function scale (reference [37]). Please state this explicitly under outcome
measures and in the abstract. Currently you are only referring to it as: “a short form knee function scale”.

*We have eliminated the wording “short form knee functional scale” and stated explicitly throughout the manuscript that we used the mSF-WOMAC (Yang, 2007)*

**MER 5:** Results, second paragraph. You have already written this sentence in the methods: “Outcome differences were also examined with respect to patient gender, age, BMI, and duration of symptoms by including a between subject factor into a repeated measures analysis of variance model (ANOVA) examining baseline to 8-week follow-up scores.”

*This sentence in Results section has been revised.*

**MER 6:** Discussion, Fourth paragraph. You state: “compliance with the recommended exercise regimen showed very high engagement with the program, with patients performing knee exercises on average 4-5 times per week.” How can you be sure about this? Since the exercise was not supervised, it would probably be better to write something like: “patients reported” instead of “patients performing” and even “soften” the sentence before a bit more.

*The word “reported” has been inserted to make it more clear that the exercise was not supervised.*

**Minor issues not for publication (MIP)**

**MIP 1:** Methods, second paragraph. In “American College of Rheumatology’s Clinical plus Radiographic Classification Criteria for OA” “s” should be deleted after Rheumatology.

*“s” deleted*

**MIP 2:** Methods, second paragraph. You state: “The radiographs were not conducted as part of this study but were been obtained as part of the patient’s routine care.” I think “had been obtained” is a better expression.

*“conducted” changed to “obtained”*

**Discretionary Revisions (DR)**

**DR 1:** Background, second paragraph. You are citing the EULAR recommendations. Later in the manuscript you are citing the updated paper on non-pharmacological core management (http://www.ncbi.nlm.nih.gov/pubmed/23595142; still recommending exercise). Why not cite the updated paper in the background.

*The updated paper has been added as a citation in the background. [Ref 16]*


**Level of interest:** An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests
Reviewer 2 Report:

Title: Web-Based Therapeutic Exercise Resource Center as a Treatment for Knee Osteoarthritis: A Prospective Cohort Pilot Study

Version: 1 Date: 28 November 2013

Reviewer: Daniel Bossen

This is a very relevant study. The paper provides interesting results from a web-based exercise intervention among patients with knee and hip osteoarthritis. The preliminary results underscore the importance of web-based exercise programs as self-management tools. Causality, however, cannot be drawn since this is a prospective cohort study without a control group.

Abstract Minor Essential Revisions:
- Results: “knee function scores decreased”. This is confusing.

For this outcome measure, a lower score represents better function as described in methods, paragraph 9. The phrase “(better function)” was added to abstract for clarification.

Background

Minor Essential Revisions:
- Paragraph 2: Reference 8 concerns only patients with hip OA.

We have removed previous reference 8: Hernandez, Arthritis Rheum 2008.

- Paragraph 3: The need for a web-based exercise intervention is highlighted by the fact that a low percentage of rheumatologist and physicians provide exercises. However, in my opinion (which is also described in the discussion section) physical therapists have a more important role in the provision of exercises. Can you elaborate on this? What is known about the provision of exercises in the physical therapy practice?

We agree that physical therapists likely have a more important role than in the provision of exercises. Studies indicate that up to 99% of physical therapists would use exercise in the treatment of knee OA (Holden et al. 2008, http://www.ncbi.nlm.nih.gov/pubmed/18703675). However, many individuals with chronic musculoskeletal conditions such as knee OA are not being referred to a physical therapist, and are oftentimes only referred when the condition worsens (Glauser et al, 2011 http://www.ncbi.nlm.nih.gov/pubmed/21293093).

- Last sentence introduction: “as part of treatment for knee OA” What do the authors mean with “treatment”? Is the application a tool to stimulate self-management or is it used as part of a treatment by healthcare providers?

Thank you for this question. We have replaced “treatment” with “management” to more accurately reflect how we utilize patient-centered self-management interventions to better address chronic disease. In the discussion we have also added that this intervention is meant to
be ongoing, lifelong which is another benefit of the TERC, as opposed to physical therapy which usually involves a very limited number of visits.

**Discretionary Revisions:**
- Paragraph 4: A suggestion for an up-to-date reference for the effectiveness of a web-based physical activity intervention in patients with knee and hip OA, see doi: 10.2196/jmir.2662.

Thank you for this reference. It has been added. [Ref 25]

**Methods**

**Minor Essential Revisions:**
- Paragraph 2: What do the authors mean with general good health? What kind of questions are used to measure this?

This is the question we asked in our screening form: “Do you consider yourself in good general health?” We did not provide patients with any additional details as to what was meant by this.

- The website www.helpmyknees.com is not accessible. Please, make a copy and archive the URL through WEbCite (www.webcitation.org).

The URL www.helpmyknees.com was accessible only for the study and currently is not publicly available. The URL has been removed from the manuscript to eliminate this confusion. If a reviewer would like to access the web site www.helpmyknees.com, the following access code and email will only work once:

1. Access code 99-24-47
2. Use email: patient9924@helpmyknees.com

- In the description of the intervention, please explain how the initial level of Exercise difficulty is determined. how does this take place? Are aerobic recommendations also tailored to patient’s physical condition?

  We have added further detail regarding initial placement of exercise difficulty level. Aerobic recommendations were not tailored to the patient’s physical condition but instead were specific to the level of exercise difficulty in which they were placed.

**Discretionary Revisions:**
- Provide more details in the heading ‘study design’ (e.g. follow-up time, ethics approval)
  
  Eight week follow-up time and IRB approval added to this section.

- Primary/secondary outcomes are not indicated
  
  Methods revised to indicate primary vs secondary outcome measures.
- Statistical analysis: Most of the content in paragraph 3, 4 and 5 is redundant.

The content in the statistical analysis section in paragraphs 3, 4, and 5, which were redundant with text in the results section, now appears only once, either in the statistical analyses section or the results section.

**Results**

**Major Compulsory Revisions:**

- Are differences between the two measurements normally distributed? This is an important assumption for using a paired t-test.

  Prior to analysis all measures were examined for normality and no significant violations found. This was added to the manuscript.

- In contrast to GEE analysis or random coefficient analysis, t-tests can only analyze complete datasets. Of the 65 participants, 13 patients did not complete any of the two assessments. Please provide information about this group. Who are these people? (e.g. gender, age).

  The thirteen patients that did not complete any of the two assessments did not differ on sex or age, but they did have higher BMI scores. This has been added to the text.

**Minor Essential Revisions:**

- Please, provide a flow diagram illustrating the study design and flow of participants.

  A flow diagram has been added.

- First paragraph: “at the start of the study…..to some degree”, what do the authors want to say with this sentence? Are they excluded from the study? And, how many participants were excluded based on which criteria?

  See responses to Reviewer 1 MCR5 and MCR 12. We have added the flow diagram and changed wording in the text for clarification.

- In table 3 and results section, the total WOMAC score is presented. I think it is more informative when authors present both total scores and scores for subscales (stiffness, pain and daily function). Moreover, reductions in pain scores are described in the discussion and conclusion sections but not in the results section.

  The stiffness, pain, and daily functioning subscale scores have been computed and added to Table 3. In addition a description of the subscales scores (including pain scores) has been also been added to the second paragraph of the Results section.
- Were there any side effects captured? e.g. exercise related injuries
  
  No exercise related injuries were reported.

**Discussion**

**Major Compulsory Revisions:**

- The discussion needs to be considered more in the view of the study design, i.e. a non-randomized one arm pilot study.

  We are not sure exactly what reviewer is asking for here. We clearly state the study design is a limitation in the Discussion.

- Please, give suggestions for future studies in regard to your findings. What are the next steps. Implementation? A randomized controlled trial?

  We have revised the conclusion to better illustrate next steps: “Given the significant positive clinical outcomes of this non-randomized one arm pilot study, future studies may include a randomized controlled trial, and we expect to move forward with a larger trial comparing web-based TERC to more traditional office-based interventions.”

- Exercise adherence: Since program usage is strongly associated with drop-out (Eysenbach, The law of attrition 2005), it is obviously that adherence rates in this study are overestimated. Please, elaborate on this in the discussion.

  This was added to limitations: “As program usage is associated with drop-out, it is possible that adherence rates in this study may be overestimated.” [added ref 56, Eysenbach, The law of attrition 2005]

**Minor Essential Revisions:**

- Paragraph 3: What is meant with directed and non-directed. Guided?

  “Directed” has been replaced with “supervised” for better clarification that the exercises are guided in-person by a physical therapist.

- Exercise adherence: Adherence is a typical problem in this field (for example: Eysenbach, 2005). Given the fact that the TERC intervention is an unguided web-based intervention, adherence rates are high when compared to other non-guided interventions and even higher than most guided programs. Do the authors have an idea which intervention characteristics (e.g. communication with staff, design, email reminders) may have led to these high adherence rates?

  The intervention was tailored to each individual patient based on their self-reported pain level and function. We suspect that the high adherence rates may be due to the fact that patients were given an appropriate level of exercise difficulty that controlled for their baseline level of pain and function. This was added to the discussion.

**Level of interest:** An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests