Author's response to reviews

Title: Yoga for Managing Knee Osteoarthritis in Older Women: A Feasibility Study

Authors:

   Corjena K Cheung (corjena@umn.edu)
   Jean F Wyman (wyman002@umn.edu)
   Barbara M Resnick (resnick@son.umaryland.edu)
   Kay Savik (savik001@umn.edu)

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Author's response to reviews: see over
Dear Editor,

This letter is written in response to the comments and suggestions offered to the manuscript titled “Yoga for Managing Knee Osteoarthritis in Older Women: A Feasibility Study.” The comments from the reviewers along with how we addressed them are listed below.

Reviewer 1

1. **It is not entirely clear in what sense they are using the word “pilot” as their primary outcomes are treatment effects.**

   The word “pilot” is replaced with “feasibility.” This feasibility study was designed to test logistics and gather information, including eligibility, recruitment and retention rate, randomization procedure, adverse events associated with yoga and the effect sizes for a larger study. The purpose of the feasibility study is clarified in the background section.

2. **A potential limitation of this study, which was not noted, was that the randomization scheme would easily permit study staff to know the intervention group, as all those with odd-numbered study IDs were assigned to that group. Therefore, it seems unlikely that the study was in fact single blind.**

   The randomization procedure was clarified. Participants were assigned to an ID number based on the order of enrollment before they were randomized using a computer-generated random numbers. Those who received an odd number were assigned to the treatment group and those who received an even number were assigned to the wait-list control group. Their ID number does not correlate to their group assignment. However, although the research staff was not informed of the group assignment, the data collection schedule (data at 4 weeks were collected only from participants who were receiving the intervention) did not allow for blinding to be maintained, which is a limitation of the study. This limitation is added to the discussion section.
3. Additional details on the conduct of the study would be helpful

Additional details on the conduct of the study have been included in the Methods section: the process of designing the yoga intervention using an expert panel of five yoga teachers, and two yoga researchers, the setting including the class size and location, and yoga home practice instructions.

4. Introduction: The authors note that yoga is recommended by the Arthritis Foundation to promote joint flexibility and muscle strength. On what data is this recommendation based?

This statement is based on “Top 10 Yoga Myths Debunked” at http://www.arthritistoday.org/what-you-can-do/staying-active/activity-types/yoga-myths.php from the Arthritis Foundation (AF) website: Practicing yoga regularly can improve muscle strength and joint flexibility, while boosting mood and controlling stress. With regular practice, you can build up strength and flexibility, and try faster motions or more weight-bearing moves.

5. Please provide references for the statement that Iyengar yoga is not commonly practiced in the United States and Hatha yoga as the most commonly practiced style of yoga. Iyengar yoga is considered a type of hatha yoga.

The statement “Hatha yoga as the most common form of yoga in the United States” is from the National Center for Complementary and Alternative Medicine at http://nccam.nih.gov/health/yoga: Hatha yoga, the most commonly practiced in the United States and Europe. Although Iyengar yoga is a type of hatha yoga that is also commonly practiced in the US in general, the number of Iyengar yoga teachers who are qualified to teach students with disability is limited. This particular style of yoga has a rigorous certification process; only two Iyengar teachers have such qualification in Minnesota. This statement is clarified in the background section.

6. The authors cite 3 studies on yoga for OA management. There appears to be a broader literature, as evidenced by a Scoping Review by Haaz and Bartlett published in 2011; the authors may wish to consider these and studies of yoga in general populations with pain (including those with arthritis) in their introduction.

The scoping review of yoga for arthritis by Haaz and Barlett is included in the background section. The review further validates the need for more OA study because only two studies included in the review were OA focused. The differences between OA and RA are specified.

7. Methods: The authors indicate the lower age bound for eligibility. Was there an upperlimit?

Yes, the upperlimit is 90 years old which is added to the eligibility description.
8. Please clarify why the second screening for eligibility was performed in the home.

Participants were given a choice to meet at a location that was convenient for them for the second screening. Many chose to meet in their home.

9. Were all 18 intervention participants included in a single cohort/class?

No, only 9 participants were included in a single class, a total of four classes. The description of class size is added in the Intervention section on page 7.

10. More information on Tukey’s LSD method for handling multiple comparisons would be helpful.

An additional explanatory phrase was added to the mention of Tukey’s LSD on page 11: *Alpha levels for the multiple time comparisons were controlled for using Tukey’s LSD which computes the least difference between the possible pairwise comparisons that can be considered significant.*

11. Results: Please specify who was screened over the telephone. Was there an attempt to screen all participants? Was it only those who called the study line?

Although recruitment letters and flyers were sent or posted, we were able to screen only those who signed up during face-to-face recruitments or called the study line and left us their contact information (page 6).

12. Discussion: It seems a bit strong to state that a 12-week assessment (4 weeks after the yoga intervention was completed) provides information on long term effects.

It was actually 12 weeks after the intervention was completed (20 weeks from the beginning of the intervention). This last data collection time point is clarified in page 5 in the Design section.

13. Figure 1. Additional information would be helpful to orient the reader. Consider stating that the control is a wait list control. The relevance of this is for the analyses, some which include both groups. Also, considering adding information about the duration of the intervention and when the follow-ups were conducted.

Figure 1 has been revised. The term “wait-list control,” the duration of the intervention and when the follow-up was conducted has been added.

14. It is not clear what additional information is presented in Graph 1 that is not included in Table 3. My other concern about the graph is that it does not provide information about the sample size for each analysis or confidence intervals around the assessment.

Graph 1 is deleted from the manuscript.
Reviewer 2

1. Abstract. Confidence intervals are reported in the abstract and throughout. Usually we see means and sdev. We see overlap between the mean WOMAC for yoga group, yet comparison is between groups, so CI could be meaningful if change was reported.

The CI is removed and the SE is added to the abstract, they are adjusted means from the ANCOVA.

2. Why are only women being studied? This is not well described or justified in the Intro. Info on feasibility in men would be valuable, so why forego that? There are many possible explanations, but unless I missed it, none were provided.

Reasons for including only older women are described and justified in the first paragraph of the background section on page 3. Statistics that indicate the high prevalence of OA in older women are provided.

3. Likewise, why only study knee OA? I know this is commonly done, but a brief statement of why it is better to isolate this group, even though many of them may have some degree of OA in other joints.

The reason for studying only the knee joint is partly because it is the most commonly affected joint. Isolating this group helped us to focus on the knee when developing the intervention program and included poses and sequence that would maximize the benefits to the knee. This statement is included on page 5 in the Methods section.

4. Introduction: Para 1. It states knee is most commonly affected joint by OA (needs reference)

The citation and reference for “knee is the most commonly affected joint by OA” is added.

5. Introduction: Reference 11 is for an Arthritis Center website. It would be much better to reference the scientific publications for the data or studies on which this statement is made. Overall, the manuscript has a higher number of citations than usual that are websites for foundations, books, organizations or other various agencies instead of peer-reviewed publications. Would be better to use these less frequently. (Ref #5,7,8,11, 13, 28, 31, 33, 34)

The citations and references for foundations, books, and organizations are reduced. Former references 11 and 28 are replaced with peer-reviewed scientific publications, and 34 is removed.
6. Two studies of Iyengar yoga are referenced and it states that this type of yoga is not available in the US. I don’t think that is necessarily true.

This is the same concern that reviewer 1 has. The difference between the type of yoga and the availability of qualified yoga teacher is clarified in the background section.

7. The description of the study design is confusing. It seems more like a cross-over design since outcomes appear to be measured for the wait-list group not only for 8-weeks while waiting, but again after that while they do yoga. Why are groups combined and data analyzed between 4-weeks and 12-weeks? How long did the wait-list group actually wait before starting yoga? Adding the schedule of assessments to Figure 1 may help show this. The second baseline is the same as the 1st follow-up assessment right?

The study design goes by several names, wait-list RCT, Step wedge design RCT, single group crossover, etc. In small studies, particularly, if time is controlled for or there is evidence that no change has occurred in the waitlist group during the phase where they have no intervention, the subsequent intervention data from the waitlist group may be added to the intervention group to increase the precision in the estimate of effect size. This plan was utilized in this study. The wait list group waited 8 weeks while the treatment group was having the intervention before receiving the same intervention. The second baseline is the true baseline for the wait list group before they received their yoga intervention. The schedule of assessment is clarified in the Design section on page 5.

8. Setting. “second screened” is not a good verb to use.

The term “second screened” has been replaced with “screened the second time.”

9. The description in the methods of the intervention does not say anything about the home practice. What were they told? This is partially mentioned in the results.

The description of what the participants were told about the home practice is added in the Intervention section on page 7.

10. The measures of safety are not adequately described. It says adverse events were recorded. By whom? At what time point? In the log or only at the end?

Safety measures are further described, the following paragraph is added to the safety section. Safety during group sessions was monitored by either the PI or research staff, who was presence in all yoga classes. Safety during home yoga practice was monitored by the participants themselves. They were asked to record the type and severity of any injuries happened during their home practice on the log sheet, and bring it to class every week.
11. The safety results say no practice related AE injuries reported, yet one person dropped out due to severe knee pain. Again was this asked only at the end? And who decided whether any problems were practice related? How were AE’s defined?

Although one participant decided to receive cortisone injection half way through the program due to severe knee pain, her knee pain was not caused by yoga practice. She joined the study with severe knee pain. She was due for her injection but decided not to get it so that she could be in the study. She actually wanted to remain in the study but was disqualified. This is clarified in page 13.

12. In the yoga intervention description, it says “….series of poses was used with static stretching, balance, and strength exercises.” This is unclear and makes it sound like there may be additional exercises being added to the yoga. Or maybe this is a brief attempt to describe some of the mechanisms of the yoga?

The sentence is to briefly describe the mechanisms of the yoga intervention. This is clarified in the intervention section.

13. Please explain more about how pain medication is measured. It says number of pain medications used? How are these defined? Number of pills? OTC included? Number of medications used per day on average?

Pain medication was measured by the number of prescription and over the counter oral medications used per day on average. This is clarified in the outcome measures section on page 11.

14. The attendance results are very good. Can you say more about anything that was done to encourage attendance? Refreshments? More details on the setting would be good; was this all done in a larger city (Minneapolis?) how were transportation issues handled?

All intervention classes were held in the same yoga studio which is located in a city right near a city bus stop with sufficient parking spaces. No special strategies were done to encourage attendance. More descriptions on the setting are added to the intervention section on page 7.

15. I don’t think you have to list convenience sample as a limitation. Specific population groups must always agree to be in intervention research in the US, so never 100%

The comment of convenience sample being a limitation is removed.

16. Table 2 shows all the means and CI’s, but I don’t find this easy to read. Change scores are more comparable, and effect sizes would be important to see given the small sample.

Table 2 has been revised, change scores are now presented.
Reviewer 3

1. The trial should be reported in alignment with CONSORT guidelines using the standard required format.

A completed CONSORT checklist is provided. The report is aligned with CONSORT guidelines except the title. Although the study used a RCT design, the current title reflects the feasibility nature of the study. Please let me know if it is acceptable to keep the current title or we need to change it. If the title needs to be changed, we will make a request to our IRB which will take about 1-2 weeks to complete the process.

2. There is too much background information supplied.

The description of the physiological changes of OA is removed to shorten the background section.

3. There is no radiographic evidence used to support the Knee OA diagnoses of participants. This directly contradicts the fact that the study uses American College of Rheumatology diagnostic criteria, which require radiographic evidence.

This study used the American College of Rheumatology clinical classification criteria which does not require radiographic evidence. The criteria has a well-established validity and correlates well with articular cartilage damage in patients with OA.


4. Either a power calculation should be provided, or at least some justification should be given as to whether the study has sufficient power to detect an important difference between two groups.

This feasibility study did not perform a formal power calculation. The sample size of 36 was determined based on recruitment feasibility over the time frame for this study; not on providing adequate power to detect expected between group differences in mean efficacy outcomes. Results from this pilot study will provide the effect size needed for calculating the sample size for a future RCT which will be adequately powered to detect expected differences in efficacy outcomes. Significant results that were seen are adequately powered, or they would not be significant. This, however, was not the main goal of the study.

5. Intervention: How many therapists were used for the 1 hour weekly treatment? The abstract stated that yoga intervention program was developed by a group of 5 yoga experts (a statement which is not repeated in the text of the paper). This begs the question: how many years experience do the trainers have? Was there an association
between the length of the treatment and outcomes? How was the study quality controlled? What is the protocol that was used, specifically in terms of dosage, frequency, intensity and follow-up? Without standardized treatment protocol, the results cannot be replicated and generalized.

The yoga intervention program was designed by a group of five yoga experts. The program was reviewed by two yoga researchers and a yoga master. The intervention classes were taught by one yoga teacher who had ten years of yoga teaching experience. The association between the length of the treatment/adherence and outcomes will be reported in a subsequent paper. The quality of the study was controlled by two established research mentors who served as a mock data safety monitoring board members. The study protocol included 60 minute weekly yoga for eight weeks. The program is staged from easy to moderately difficult. Modified poses were included for participants with higher level of physical disability. This is clarified in the intervention section on page 7.

6. It is stated in the description of the Evaluation session: “Once initial telephone screening eligibility was established, the individual was screened for a second time at home to confirm the presence of knee OA symptoms using the ACR criteria”…. What is the justification for conducting the baseline evaluation at home? No data is supplied for the number of patients who had their knee OA diagnosis confirmed by X-ray.

These comments have been addressed in question #3 and question #8 (reviewer 1).

7. Data analysis should be presented in a way that is appropriate for an intent-to-treat intervention. Data presented in the tables in the results section should follow the standardized journal format.

Table 3 has been revised to show an intent-to-treat analysis approach, using mixed models and all 36 subjects. Mixed models are generally the preferred way to analyze intent-to-treat data.


Thank you for reviewing this manuscript. We hope that we have addressed all the reviewers’ comments satisfactory.

Sincerely,

Corjena Cheung, PhD, RN
School of Nursing, University of Minnesota