Author's response to reviews

Title: Study Protocol: Does isolated hip strengthening for Patellofemoral Pain Syndrome (Anterior Knee Pain) give better long term results than traditional quadriceps based training? A randomised controlled trial.

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Author's response to reviews: see over
Reviewer 1:
Thank you for your comments. We have revised the manuscript accordingly and it is our opinion that this will improve the study.

Comment 1
1. This is a three-limb study but the title implies only two. Having said that it is not clear what the purpose of the control group is until mentioned briefly in the Discussion and Conclusion section at the end. This should be justified in Methods.

We understand that the sentence: “A randomised controlled study” does not fully explain what kind of treatment/information that the control group will receive. We suggest changing the title to:

DOES ISOLATED HIP STRENGTHENING FOR PATELLOFEMORAL PAIN SYNDROME (ANTERIOR KNEE PAIN) GIVE BETTER LONG TERM RESULTS THAN TRADITIONAL QUADRICEPS BASED TRAINING OR FREE PHYSICAL ACTIVITY? A RANDOMISED CONTROLLED TRIAL.

We have included the following sentences in the method section under the heading: “Control group (free physical activity)”: The purpose of the control group is to assess whether specific hip strengthening or quadriceps training is better than free training. This is important if there is no difference in effectiveness between hip strengthening and quadriceps training and also for assessing whether any of the specific training regimens are better than free physical activity.”

Comment 2
2. The term Patellofemoral Pain Syndrome (PFPS) is not approved by the International Patellofemoral Study Group; Anterior Knee Pain is preferred. The problem is the definition of the patient cohort. This proposal makes a very good stab at it, and is pragmatic.

We do recognize the ongoing discussion as to the preferred terminology for this disorder, and that a change to the term Anterior Knee Pain may be coming. However, at the current time the vast majority of articles published on this topic still use the term Patellofemoral Pain Syndrome and thus we prefer to mainly adhere to this term, and recognize the term Anterior Knee Pain in our title and introduction.

Comment 3
3. Inclusion criteria – clinical examination: Patellar compression is painful in the normal knee if undertaken forcefully enough. How will this be controlled?

We agree that patellar compression may have poor validity and reliability, but have chosen in a pragmatic way to include this test as one of several criteria for inclusion.

Comment 4
4. I would exclude patients with severe trochlear dysplasia on imaging from the study as they have a direct mechanical cause for their AKP. The problem is that
The definition of “severe” is contentious, but is best described as “obvious” on plain lateral X-ray. Subtle trochlear dysplasia is known to be associated with AKP.

We have included obvious trochlear dysplasia on MRI examination as one of the exclusion criteria.

Comment 5
5. Hypermobility is a cause of AKP in around 35% of patients referred to secondary care. The Beighton score (or equivalent) should be measured and the patients excluded if, say, > 3, or included and tested in the subanalyses. I would include them, as the only therapy that has a chance of working is hip exercises. If patients are hypermobile then the severity of any concomitant trochlear dysplasia is less important.

It has been reported that patellar instability and dislocations are associated with hypermobility [1], but we have found no study specifically examining and reporting the prevalence of hypermobility in patients with PFPS and its effect on treatment response. It may be hypothesized that PFPS patients with hypermobility have a poorer prognosis. In order to examine this and to estimate the prevalence of hypermobility in patients with PFPS, we have revised the protocol and plan to register the Beighton score at inclusion. This will allow us to describe this in the baseline table and eventually to adjust for this in the final analysis of between-group differences in change between interventions.

Comment 6
6. Randomisation details are very important. Please confirm that it is a computer produced random-number generation, and that the nurse will take the envelopes sequentially in order, by number.

Your suggestion has been included in the description of randomisation.

Comment 7
7. The Kujala score (Ref 33) is not a 13-point score, the score is out of 100. The main problem with it is that a change from 10 to 20 is not the same as a change from 90 to 100.

The questionnaire consists of 13 questions, with a summed score from 0-100. We have clarified this in manuscript. In addition the comment refers to all types of questionnaires and questions the use of approximation of a linear scale. Most often, however, if data are normally distributed, parametric statistics are applied. Using non-parametric statistics partly solve this problem. Also the use of the number with at least 30% improvement may add information but do not solve the problem.

Comment 8
8. Is the primary endpoint at 3-months or 12-months? I would assume that it is 12-months.

The primary endpoint of the study is 3 months. We have clarified this in our protocol.
Copyedits:
It is worth standardising the number reporting style i.e. as words or as numbers. One system is to report all numbers greater than nine as numbers, and less than 10 as words except when the number refers to a measurement, grade, classification, figure or table.
L62: “patellar maltracking”
L73: “for a short-term”
L73, 74, 83, 134, 166: “quadriceps-based”
L97: “observer-blinded”
L191: “by standardised, validated questionnaires”
L215: “Likert”
L218: Louden et al Ref number
L300: “Conclusion”

Thank you for pointing these out, we have corrected them accordingly.
Reviewer 2:
Thank you for your comments. We have updated our manuscript accordingly and it is our opinion that this will improve the quality of the study.

Introduction L57: There are a few studies looking at the incidence and prevalence, also within closed populations. Consider revising and referencing a couple of the key papers that might reflect your study population.
Introduction: L61-67: This sections deals with the etiology of PFP but reference none of the most important prospective studies that examine risk factors for PFP. Consider looking at the review on risk factors by Lankhorst et al. This will help strengthen your arguments made here. Lankhorst et al. J Orthop Sports Phys Ther. 2012 Feb;42(2):81-94
Introduction: L68-L75. This sections deals with the treatment of PFP however, none of the recent systematics reviews on the treatment of PFP is mentioned. Please consider adding these, as this will help the reader seeing how your study builds upon previous research and how your study will fit into the literature.
Introduction: L80. "Women with PFPS have been found to be weaker in hip abduction and external rotation compared to healthy controls [26]”. The Prins review that you cite was recently updated by our group. Please consider referencing the new review which was published in the BJSM.

Introduction: L57, L61-67, L68-L75, L80 and Conclusion L308 (updating references):
Thank you for your suggestions, we have updated these references and text accordingly.

Introduction: L90: Please add your hypothesis.

Methods:
L156: The treatment protocol is very difficult to follow and replicate. Most basic descriptors of an exercise protocol are missing. Please add time under tension, range of motion, intensity (e.g. 10 repetition maximum), training to failure and pain during exercise. Please take a look at Toigo and Boutelliers paper “New fundamental resistance exercise determinants of molecular and cellular muscle adaptations”. They have a good description of which exercise parameters that should be reported.
L160: Please add a rationale for why you progress using increased number of repetition and not through e.g. increased intensity or number of sets.
L166. What is the rationale for using these quadriceps exercises? Also, please add more information on the exercise protocol.
L156-L166: What is the rationale for using these two exercise protocols and not some of previously used exercise protocols that have been tested in previous RCTs?
L308: “The inclusion of a control group is important, as there is conflicting evidence regarding the effectiveness of specific training
compared to patient education, natural course and placebo [52, 53].”
You reference a study protocol (Rathleff et al. BMC 2012). The results from this trial have been published recently in BJSM and show a better effect of patient education and exercise compared to patient education alone. Please consider adding the reference to this RCT.
L308. Recently a new RCT was published that compared quadriceps exercises with hip+core exercises. This is very similar to your trial. It would be good to add the results from their trial in your introduction. Ferber et al. J Athl Train. 2014 Nov 3

Methods: L156, L160, L166, and L156-L166 (exercise choice and dosage):
We have re-worked the descriptions of the exercises in accordance with your suggestions including the rationale for choice of exercise type and dosage and hope that this will now be satisfactory.

L271: How will you measure compliance to home-based exercises?
L271: Do you plan on using the compliance data in an analysis? It would be interesting to see if there is an association between compliance and effect.
Consider adding this as a pre-planned analysis.

L271 and L271 (regarding compliance):
We have included a short description of the compliance measures in the methods section and added this as one of our planned post-hoc analyses related to treatment response.
References