Author's response to reviews

Title: Knee arthroscopy and exercise versus exercise only for chronic patellofemoral pain syndrome. A randomized controlled trial.

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Author's response to reviews: see over
Reviewer's report
Title: Knee arthroscopy and exercise versus exercise only for chronic patellofemoral pain syndrome. A randomized controlled trial.
Version: 1 Date: 27 June 2007
Reviewer: Sita M Bierma-Zeinstra
Reviewer's report: General
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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Introduction, Page 3:
It is not clearly stated why it is of importance to analyze the usefulness of arthroscopy in an randomized clinical trail to assess its efficacy because, as stated in the introduction, arthroscopy is used to make a specific diagnosis. From the introduction it would be more logical to emphasize the additional value of arthroscopy on the diagnostics of PFPS and testing the consequences of arthroscopy on the outcome. Please clarify this more in the introduction.

Authors response: We agree with the reviewer, and we have modified the text so, that it should be clear that the possible effect of arthroscopy is influenced both by diagnostics and possible operative procedure.

Methods, page 3,4 and table 1.
Inclusion criteria: PFPF pain during activities such as jumping, running etc. Did they have to have pain on all that activities or was pain during one activity enough to meet the criteria? Please specify.

Authors response: They did not have to have pain in all the activities (though many of them had). We have corrected “and” to “or” in table 1. They were asked together, so one is enough to meet this criterion.

Table 1: It is surprising that the word ‘possibly’ is used to define the inclusion criteria. Maybe it is clearer to leave both sentences out of the inclusion criteria because they are not inclusion/exclusion criteria on itself.

Authors response: We agree with the reviewer, and we have modified table 1.

Methods, page 6, data analysis:
What was the reason not to include all patients in the analyses by means of last value carried forward or imputation or repeated measurements? Please explain in the results or discussion.

Authors response: We agree with the reviewer, and have added “a worst-case scenario” analysis as also requested by the other reviewer.

Results, page 7 and 8:
Data is missing on possible interventions of included patients before the start of the study. It could be possible that some patients received physiotherapy, for example one month before this study. It would be interesting to be more specific on possible intervention in the previous year before the study. Because as mentioned in the introduction, chronic cases are included after failure of conservative treatment. Is this conservative treatment not the same as the home-exercises within the study? Please clarify.

Authors response: Our study sample consisted of patients with chronic PFPS, and usually most of them had been treated conservatively before they had been admitted to orthopaedic policlinics. We excluded subjects with previous knee surgery or those with physical therapy for PFPS within the previous 4 weeks from the study. These criteria are mentioned in table 1. It is unlikely that the patients had received similar exercise training advice previous to our study.

Previous knee surgery and physiotherapy within the previous 4 weeks were exclusion criteria, and we did not systematically record the long-term conservative treatment history of our patients.

Table 4, page 17:
Number of patients for each category is unclear. 17 patients did receive a surgical treatment, also mentioned in the text. For each patient the articular cartilage lesion grade is given (total 28), but how are the other arthroscopy findings distributed over the cartilage gradings? Please specify the 17 surgical treated patients. What treatment did each patient receive? This table is hard to understand, try to make it more clear.

Authors response: We agree with the reviewers, and we have modified table 4 accordingly.

Discussion, page 9:
Is there any data available on the compliance of the home exercises? It is generally known that the compliance of given home exercises is not quite high. So you should discuss this possible lack of compliance in your discussion.
Authors response: Manuscript pages 4 and 5: “compliance with the training protocol was similar in both study groups, the mean realized weekly exercise frequency being 5.0 in the arthroscopy group and 5.2 in the control group (P=0.52).” The reported weekly exercise frequency was quite high. Most of our subjects were active young adults and knee symptoms restricted their leisure time physical activities. It can be assumed therefore that they were motivated to follow the home exercise program.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Methods, page 4:
Three patients were excluded on the basis of the orthopedics surgeon’s examination. Figure 1 shows 5 excluded patients, but four of them did not met the inclusion criteria. Please explain.

Authors response: We agree with the reviewer, and we have modified our presentation style.

Page 5:
Text is not in correspondence with figure 1. All patients who were randomized into the arthroscopy group received the treatment (text), but figure 1 shows that one patient did not receive allocated treatment.

Authors response: Correct, and we have now written the text more clearly. All the patients in the arthroscopy group received arthroscopy, but one of them did not receive the home exercise treatment (refused to continue).

Results, page 7 and 8:
The mean in improvement on the Kujala score in the text is 12.9 in the arthroscopy group, but in table 3 the mean improvement is: 80.8 – 68.9 = 11.9. The mean improvement on the Kujala score of the control group in the text is 11.4, but in table 3: 86.3 – 73.8 = 12.5.

Authors response: We agree with the reviewer, and we have now corrected table 3.

Table 3:
What do you mean by ‘VAS during sitting up’?

Authors response: We admit that our translation was unclear - we have modified table 3.
Discretionary Revisions (which the author can choose to ignore)
Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

We thank the reviewer for valuable comments.
Reviewer's report
Knee arthroscopy and exercise versus exercise only for chronic patellofemoral pain syndrome. A randomized controlled trial.
1 29 May 2007 Version: Date:
Ewa M Roos Reviewer:

Reviewer's report:
General
This paper concerns the effect of knee arthroscopy for chronic patellofemoral pain syndrome, the design is randomized and controlled and the trial is unique and much needed not only within orthopaedics but also within primary care and sports medicine, and for this group of patients where evidence-based treatment is not available. The results indicate arthroscopy having no beneficial effect in addition to exercise which was effective in improving self-reported outcomes in both groups. My major comments relate to how the trial was reported and how the methods were described. An overall major comment is that I suggest the authors read the CONSORT statement and make sure they report their trial in conformity with this set standard for randomized controlled trials. This is important for the quality score of the trial and also for inclusion in future meta-analyses.

Authors response: We have tried to follow the CONSORT guidelines as far as possible when designing our study protocol, which we published earlier (Current Controlled Trials ISRCTN 41800323), and when reporting our results. Also, we have quality scored our trial (not shown) in order to be certain that all relevant information is available in our report. On the basis of very valuable comments of reviewers we have now modified the presentation style with respect to some details. If any specific points need modification, we will be happy to make additional revisions.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
P4,P1,L3 and Figure 1. The text is ambiguous. The inclusion/exclusion of patients has to be reported in an unambiguous way. Example: “All patients (64?) answered a structured questionnaire. Orthopaedic surgeon excluded 3 patients. All the patients who fulfilled the final inclusion criteria (61?) signed… In Figure 1, 61 met inclusion criteria as set by orthopaedic surgeon (in conformity with text), but then 5 subjects are excluded thereafter. By whom and for what specific reasons?
Authors response: We agree that this is a problem in our presentation. We thank the reviewer for the comment. We have corrected the text and written it more clearly.

P4, P3. Please give the exercise program as additional material to be downloaded from the journals webpage.

Authors response: We have included an additional file.

P5, P3. Please give the Kujala score. From the text it cannot be determined what items are included in this score and thus it is not known what is measured, pain, function, or what? Please also describe in detail how the score was administered since it is known from other knee scores that administration by a surgeon or an unbiased observer is associated with observer bias in relation to patient-administration. If the administration methods were different at the different time points, please be specific in your information.

Authors response: We have included an additional file (web extra), and we have described in detail how the score was administered.

P7, P2, L1. You state the analysis to be intention-to-treat. I would then suggest that an additional analysis of 28+28 patients with baseline results carried forward for patients not available for follow up (worst case scenario) is performed.

Authors response: We agree, and have added “a worst-case scenario” analysis.

P9, P2, L10. This statement has to be modified. Quite a lot is known regarding the placebo effect of surgical interventions. I suggest you review the literature, including the arthroscopy trial by Moseley et al. NEJM 2002 and the glucosamine trial by Clegg et al. NEJM 2005, improve your discussion and give appropriate references.

Authors response: We did not use placebo arthroscopy in our patients. According to our protocol during arthroscopy all the knee compartments were examined systematically and pathological findings were recorded, and the patients treated on the basis of the arthroscopic findings. All patients were awake during the operation, and the orthopaedic surgeon informed the patient about the findings and about the possible treatment. Interestingly, those with no abnormalities had the best outcome. One explanation may be that arthroscopy has a placebo effect, but this does not change our main conclusion. We now take up the possible placebo effect in the discussion.
P3, P2, L10. I suggest you expand the two lines discussing the effect of exercise in your trial. Actually, an alternative interpretation of your results is that exercise was effective both with and without the addition of arthroscopy. This has implications for clinical care and should be appropriately discussed.

Authors response: Our primary aim was not to investigate the effectiveness of exercise therapy in patients with PFPS. It is well known that most PFPS patients improve with time. Heintjes et al. (2003) concluded in their systematic review that there is some evidence that exercise therapy reduces anterior knee pain in patients with PFPS. Our result is in line with that view. But to study the natural course of the syndrome we would have needed a no-treatment group. Using such a protocol it would have been possible to investigate the effectiveness of exercise therapy compared to no-treatment. Because our patients had experienced prolonged knee symptoms, it would have been difficult and perhaps unethical to use a no-treatment control group. Also, the number of withdrawals and dropouts would have been higher among patients without any treatment. However, we have discussed about the possible speculative alternative interpretation of our results.

P10, P3, L7. Unless you can give appropriate references to support your statement that future studies should focus on subgroups determined by MRI or clinical examination, this statement should be deleted. To my knowledge, all available studies show poor correlation between measures at body structure level (x-rays, MRI etc) and activity and participation levels (patient-relevant aspects such as pain and function). If anything, you should focus on subgroups with less/more pain, less/more functional limitations when you outcome is pain and function (which I guess, but not know, that the Kujala score evaluates).

Authors response: We agree with the reviewer, and we have removed the sentence.

Figure 1. Please read the CONSORT statement carefully when designing figure 1. I guess that patients not receiving allocated treatment were really drop-outs not available for follow-up. One may interpret the current figure as the patients not receiving allocated treatment but were available for follow-up. The information given that 3/1 patients underwent arthroscopy from 2-9/9-24 months AND were included in ITT analyses is unclear. What does this really imply?

Authors response: We agree with the reviewer, and we have modified the figure.
Table 1. The first stage, I guess is prior to the 61 given in figure 1. But in the text you state 3 were excluded by orthopaedic surgeon, what stage was this, 1 or 2? In figure 1, 5 patients are excluded after seeing orthopaedic surgeon, what stage was this?

Authors response: We agree with the reviewer, and we have modified our presentation style.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

P5, P2, L8. Please clarify regarding meniscus resections. You state that 3 patients were excluded due to meniscal symptoms prior to randomization. Here you state that meniscus resections were performed, indicating that meniscus resections were performed in subjects not having meniscus symptoms. Is this correctly understood, and if so how was this justified?

Authors response: All the subjects with typical meniscal symptoms and signs were excluded at the baseline examination. Some patients shown to have meniscal pathology in arthroscopy reported only anterior knee pain symptoms. However, we cannot be sure whether these symptoms are due to meniscus pathology. These patients were treated according our preliminary pre-determined guidelines, which followed generally accepted recommendations.

P5, P2, L13. Please state how the time from arthroscopy to exercise was adjusted.

Authors response: Page 4, paragraph 4, lines 1-2: “The 8-week home exercise program started three weeks after randomization in all patients (two weeks after arthroscopy in the arthroscopy group)”. There was one patient who was unable to start the program at two weeks after the arthroscopy because of pain.

P6, P2, L4. The two anchors of the global rating scale indicate cross-sectional evaluation (asymptomatic knee) and longitudinal evaluation/change (marked worsening). Both anchors should reflect change. Have the anchors been correctly translated from the original language?

Authors response: As a secondary outcome measure we evaluated a global rating of change between baseline and follow-up (longitudinal evaluation) with a 6-point scale: 1) marked worsening, 2) moderate worsening, or 3) the same vs. 4) moderate improvement, 5) marked improvement or 6) asymptomatic knee. The scale was later dichotomized and analyzed as follows: 1) marked worsening, moderate worsening, or the same vs. 2) moderate improvement, marked
improvement or asymptomatic knee. At the baseline all subjects reported knee symptoms and at
the follow-up some subjects reported no knee symptoms (asymptomatic knee = change from
baseline). So, asymptomatic knee at follow-up is classified as improvement as there were no
asymptomatic knees at randomization. Some of our subjects reported no change in their symptoms
during the follow-up. Even if there is no change at follow-up, this part of the scale remains relevant.
However, we have modified “the same” into “no change from baseline”.

P7, P3, L6. Please clarify, 9-month follow-up?

Authors response: P7, P2, L1-2: “the primary follow-up time was nine months from randomization”.

P9,P1,L1. Since the content of the Kujala score is not given, it is not possible to interpret “overall
additional advantage”. Please clarify.

Authors response: The Kujala score is now given.

Table 3. Exchange “Before treatment” with “baseline”. Exchange “9-months after the
randomization” with “9 month follow-up”.

Authors response: We agree, and we have modified the text.

Table 3. VAS during sitting up. What is sitting up? Does it reflect change (sitting up to/from laying
down) or do you mean during sitting (without change)?

Authors response: Our translation was unclear, and we have corrected the text.

Table 4. Please help the reader by inserting “Kujala score” in a separate row over the last 4
columns instead of repeating “Kujala score” three times.

Authors response: We agree, and we have modified table 4.

Discretionary Revisions (which the author can choose to ignore)
P4, P3 I suggest you change header from conservative treatment to exercise protocol or
equivalent.

Authors response: We agree, and we have changed the header.
P6, P2, L2. Omit the word “symptoms”.

Authors response: We agree, and we have omitted the word.

P7, P3, L3. Please do not give percentage for single patients (1/28, 3/28), give absolute numbers only.

Authors response: We agree, and we have changed the text.

P7, P4, L3. Please do not give mean scores of 3 patients. If anything give absolute score improvements or median improvement.

Authors response: We agree, and we have given the absolute scores.

P8, P4. You state that at the 24 mo follow-up there was still no difference between groups. Was the improvement seen earlier maintained or not?

Authors response: The improvement was maintained in both groups. We have modified the text.

P10, P2, L3. Please omit the word “conservative”.

Authors response: We agree, and we have omitted the word.

Table 2. Tab inserted by mistake: …Duration TAB of symptoms…

Authors response: We agree, and we have single-spaced the text in the cell.

We thank the reviewer for valuable and detailed comments.