PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

| TITLE (PROVISIONAL) | Efficacy of arthroscopic partial meniscectomy for patients with degenerative meniscus injury A protocol for a randomized, placebo-surgery controlled, double-blind trial with a novel ‘RCT within-a-cohort’ study design |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| AUTHORS            | Järvinen, Teppo; Sihvonen, Raine; Paavola, Mika; Malmivaara, Antti                                                                                                                                 |

VERSION 1 - REVIEW

| REVIEWER            | David Felson MD MPH  
                       | Professor of Medicine and Epidemiology  
                       | Boston University School of Medicine |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------|
| REVIEW RETURNED     | 30-Dec-2012                                                                                                                   |

THE STUDY

| GENERAL COMMENTS | The authors present the study design and rationale for a placebo surgery controlled arthroscopy treatment of partial meniscectomy. There are a number of concerns with this paper.  
                    | 1. This paper is too long by around 50%. (the instructions to authors recommend less than 4000 words and this article is over 7900 words). While it is well written, the introduction and the discussion text can be made much more concise. The discussion is 8.5 pages long and could be cut by more than 50%. Much of this section could be eliminated altogether with little effect on this paper. The discussion about the placebo effect is adequately dealt with in the introduction. Also, the IRB discussion should be moved earlier and the issues posed could be moved into the introduction which covers some of the same concerns.  
                    | 2. The distinction in other arthroscopy studies has been whether the patients are required to have mechanical symptoms (locking, buckling). Can the authors please comment on this. Were those with mechanical symptoms actually excluded? If so, how is this trial different from the Moseley et al and Kirkley et al trials which also excluded patients with mechanical symptoms.  
                    | 3. Generally, meniscal tear designation on MRI requires the MRI changes on two slices. Was that required in this case?  
                    | 4. What types of MRI/arthroscopy findings constituted reasons for exclusion? Given that these were degenerative tears, one would expect a large percentage of knees (even with normal x-rays) to show cartilage lesions—either erosions, fibrillation or loss. What happened when this was seen? How does a ‘chondral injury’ relate to these? What other MRI findings constituted reasons for exclusion?  
                    | 5. The authors write that degenerative meniscal tears are associated with knee pain but that is not a widely held notion and has been |
shown not to be the case by Englund et al Effect of meniscal damage on the development of frequent knee pain, aching, or stiffness. Arthritis Rheum 2007; 56: 4048-4054. They have shown that the relation of meniscal tears to pain is due to the relation of these tears to underlying OA which is itself associated with pain. If meniscal tears do not cause pain, then this trial will not be a productive endeavor, since its outcome measures are all related to knee pain.

6. One of the main concerns about the design is the specification of 3 primary outcome measures each assessed at P < .05. The authors should have prespecified either one of these as their primary or come up with a Bonferroni type adjustment for the multiple testing.

7. While the comparison with an external group is appreciated, it is not entirely clear how this will be analyzed nor how the external group will provide information on generalizability since it is from the same center and is evaluated for trial eligibility. This should be noted in the methods section. Will the external cohort have the same outcome assessment as trial patients?

REVIEWER
Martin Englund, MD, PhD, Associate Professor
Epidemiologist
Department of Orthopedics
Lund University, Lund
Sweden

REVIEW RETURNED
10-Jan-2013

GENERAL COMMENTS
This is report is the study protocol and discussion around ethics etc for a randomized controlled trial (RCT) for the treatment of a degenerative meniscus tear believed to be causing symptoms (placebo-controlled surgery vs. sham surgery). In parallel with the Moseley trial for knee osteoarthritis, a study with a sham surgical procedure is the only way to tease out the placebo-effect from the true effect of meniscus surgery. Hence, I welcome this study as it is highly needed. Over all this is a very well planned RCT.

Still, I have a few comments/suggestions as detailed below:

Abstract
Line 25:
Quote: “Patients with symptomatic degenerative medial meniscus tear,”
How do you know for sure that the tear itself is “symptomatic”? Isn’t it better described as a “degenerative medial meniscus tear in a patient with medial joint line symptoms” or “with a potentially symptomatic medial meniscus tear”? For instance, the symptoms could potentially arise from other structures or processes in the (medial side) synovium, capsule, or potentially the subchondral bone, structures all that may be involved in pre-radiographic osteoarthritis. (The clinical tests for meniscal tear are not that great (Solomon DH JAMA. 2001 Oct 3;286(13):1610-20))

Line 37: Why the choice of the Lysholm Knee Score as primary outcome? This instrument was originally developed to be administered by the examiner (with potential for bias) Hence, the patient-administered version has several drawbacks; items are relatively often missing as it lacks instructions, and holds many ambiguities. There are more valid and sensitive patient-relevant outcome measures in the field of knee osteoarthritis and knee surgery. Some articles pointing out problems with the Lysholm Knee Score: Risberg and Ekeland 1994, Bengtsson et al. 1996, Höher et al. 1997, Demirdjian et al. 1998, and work by EM Roos et al.

MAIN TEXT
Intro:
The introduction would benefit from pointing out that degenerative meniscal tears are highly prevalent in the general population (middle-aged and elderly), if for instance
screened by MRI (and most of tears seem not to cause much trouble to the persons) (Englund et al New Engl J Med 2008).

Methods:
Table 1 Shouldn’t “unresponsive to the appropriate conservative treatment” be added to the table? (as it is stated in text as one inclusion criteria, line 15). It is important point because patients included have already then tried conventional therapy. Hence the sample is somewhat selected on the basis of being "resistant" against conservative therapy. Could you also please detail what kind of therapy that was tried?

How are the MRI’s to be graded? (scoring system for meniscus etc?)

How are the meniscal tears, location and their extent classified at arthroscopy?

Discussion:
Page 22 Line 15; I suggest better to use original reports than reviews if possible. For instance, the original ref (Englund & Lohmander Arthritis Rheum 2004) support the sentence that lateral meniscectomy is “worse” (higher risk of development of radiographic knee osteoarthritis than medial meniscectomy; the first study to show so).

Please consider include and refer to the published abstract by Katz et al presented at the ACR meeting Washington DC 2012; prelim. results from the US-based MeTEOR trial:
"The Meteor Trial: Preliminary Results of an RCT of Arthroscopic Partial Meniscectomy Vs. Physical Therapy in Patients greater Than 45."
Link:
http://www.rheumatology.org/education/annual/2012_Abstract_Supplement.pdf#toolbar=r=1
(Abstract # 2650 on page S1123)

The authors concluded: “These preliminary trial findings suggest that in both the APM and the nonoperative arms, subjects experienced substantial improvement in functional status over six months, with no significant differences between the two arms in the ITT analysis. 30% of subjects randomized to nonoperative therapy underwent APM within the first six months. As with all RCT’s the results should be generalized cautiously to clinical populations. These findings will aid physicians and their patients over 45 who present with knee symptoms in association with meniscal tears and osteoarthritis as they decide whether to elect APM or nonoperative therapy.”

In summary: This study will be an exciting and very important trial. The protocol is in my opinion overall well written. I congratulate the authors for their initiative and I very much indeed look forward seeing the results!

VERSIO N 1 – AUTHOR RESPONSE

Reviewer: David Felson MD MPH
Professor of Medicine and Epidemiology
Boston University School of Medicine

No competing interests exist.

The authors present the study design and rationale for a placebo surgery controlled arthroscopy treatment of partial meniscectomy. There are a number of concerns with this paper.

We would like to thank Prof. Felson for his very insightful, attentive and constructive comments on our paper. It is rare indeed to receive comments from two undisputed leaders of a given field (and thanks to open peer-review, to know about it) and we feel very privileged in this respect as Profes. Felson and
Englund are among the few people who have contributed tremendously and aroused our interest in this important topic - degenerative meniscus injury - and also in many respects, ‘paved the way’ (with their seminal articles on degenerative knee disease and delineating the true nature of degenerative meniscus injury (Felson, Niu et al. 2007; Englund, Guermazi et al. 2008; Englund, Guermazi et al. 2009; Felson 2013) making it possible to perform a placebo-surgery controlled trials on this complaint.

1. This paper is too long by around 50%. (the instructions to authors recommend less than 4000 words and this article is over 7900 words). While it is well written, the introduction and the discussion text can be made much more concise. The discussion is 8.5 pages long and could be cut by more than 50%. Much of this section could be eliminated altogether with little effect on this paper. The discussion about the placebo effect is adequately dealt with in the introduction. Also, the IRB discussion should be moved earlier and the issues posed could be moved into the introduction which covers some of the same concerns.

We thank the reviewer for these very attentive remarks regarding our paper. We fully agree with the reviewer that the paper is very long and after these suggestions, we have managed to shorten it substantially (by more than 1,000 words). Editor Sands also recommended looking at the newly published SPIRIT guidelines for reporting trial protocols (Chan, Tetzlaff et al. 2013), which we did. The paper is still slightly over 4,000 words, but we respectfully propose a slight exceeding of the recommended word count, as the Materials & Methods section alone (when written according to the SPIRIT guidelines) is almost 4,000 words. Further, we would like to point out that our paper actually contains two “interlaced” studies (the actual RCT and the “within-a-cohort” extension), as well as a treatment of the rather contentious issue of placebo surgery. In this respect, we also note that a recent protocol from the UK claims that placebo surgery controlled arthroscopic trials are not feasible (Campbell, Entwistle et al. 2011) and accordingly, we venture to suggest that a slight more thorough discussion (including a shortened version of the “Quantifying the placebo-effect” section) would be justified in our paper.

2. The distinction in other arthroscopy studies has been whether the patients are required to have mechanical symptoms (locking, buckling). Can the authors please comment on this. Were those with mechanical symptoms actually excluded? If so, how is this trial different from the Moseley et al and Kirkley et al trials which also excluded patients with mechanical symptoms.

As the reviewer correctly points out, the concept ‘mechanical symptoms’ is a difficult one, as there really exist no universally accepted criteria/validation means to define/classify them. In this study, the only exclusion was ‘present or recent episodes of a true locked knee’ (i.e. patient’s inability to fully extend the knee). Patients with a degenerative knee disease rarely have a locked knee, but may well present with symptoms referred to as "catching, buckling and locking" and patients with such symptoms were included in the trial. The elementary distinction between our trial and those of Moseley et al. (Moseley, O'Malley et al. 2002) and Kirkley et al. (Kirkley, Birmingham et al. 2008) is the existence of radiological OA: In these two pivotal trials, the patients had established knee OA, whereas in our trial, the existence of a clear knee OA is cause for exclusion. Accordingly, all our patients are classified as either K&L 0 or 1 (and further, stratified based on this).

3. Generally, meniscal tear designation on MRI requires the MRI changes on two slices. Was that required in this case?

All our images were assessed by both a musculoskeletal radiologist and an orthopaedic surgeon participating in the study. Yes, the ‘pathological’ meniscal signal had to communicate with the meniscal surface on two slices (this has now been added to the text). However, it needs to be recalled here that the MRI assessment was not a formal exclusion criterion, but rather a requirement to proceed to arthroscopy (confirmation of the clinical diagnosis of symptoms that could be attributable
to meniscus injury). The final decision whether or not to include the patient in the trial was made at arthroscopy, when the meniscus injury was visually and physically (probing) verified. We have now added a paragraph on this issue in the “Limitations” section of our Discussion.

4. What types of MRI/arthroscopy findings constituted reasons for exclusion? Given that these were degenerative tears, one would expect a large percentage of knees (even with normal x-rays) to show cartilage lesions---either erosions, fibrillation or loss. What happened when this was seen? How does a ‘chondral injury’ relate to these? What other MRI findings constituted reasons for exclusion?

Please our response above. As stated, MRI was used merely to confirm that the patients’ symptoms could be due to degenerative meniscus injury (and to exclude possible rare situations such as knee tumours). No cartilage lesions detected in MRI was thus considered formal reason for exclusion.

As both reviewers are obviously well aware of (as the world leaders in the particular topic), the differentiation of chondral injuries that require surgical procedure (such as microfracture) from the merely osteoarthritic lesions is difficult and there really exists no clear, objective classification system for this (at least to the best of our knowledge). In our trial, we considered chondral lesions osteoarthritic in patients with no obvious traumatic onset of symptoms. There really is no valid (RCT-based) evidence to show that surgery is indicated in these cases, and indeed the studies by Moseley et al. and Kirkley et al. suggest the opposite. However, if a large chondral flap or local deep osteochondral lesion was found, the surgeons were advised to carry out the surgical procedure they deemed appropriate and the patient was excluded. Finally, the only difference between our two allocation groups is whether a meniscus resection was carried out or not. Accordingly, if we made a wrong decision concerning chondral lesions, they should be evenly divided into the two study arms in a study as large as ours is.

In this context, as the primary objective of our study was to assess the efficacy of arthroscopic partial meniscectomy, we wanted to ‘simulate’ the prevailing clinical practice in the treatment of patients with degenerative knee disease as closely as possible. In essence, as the reviewers are obviously well aware, patients complaining of medial joint line symptoms are usually first referred to plain x-rays (to grossly visualize the extent of knee OA) and then (generally) to MRI. It is indeed true that most patients do display a wide range of cartilage lesions, but these are currently rarely considered a contraindication for knee arthroscopy (particularly if the x-rays show no or only mild knee OA, K&L 0 or 1). If the MRI shows a degenerative meniscus injury, knee arthroscopy is usually offered (after an attempt at conservative treatment) – as is also evident from the recent statistics on the incidence of knee arthroscopies in the US (and a similar trend seems to apply to the rest of the world).

Prompted by these very attentive remarks, we have now made the text of our inclusions/exclusions more unambiguous.

5. The authors write that degenerative meniscal tears are associated with knee pain but that is not a widely held notion and has been shown not to be the case by Englund et al Effect of meniscal damage on the development of frequent knee pain, aching, or stiffness. Arthritis Rheum 2007; 56: 4048-4054. They have shown that the relation of meniscal tears to pain is due to the relation of these tears to underlying OA which is itself associated with pain. If meniscal tears do not cause pain, then this trial will not be a productive endeavor, since its outcome measures are all related to knee pain.

It is very easy for us to agree with the reviewer that the knee pain perceived by patients with degenerative meniscus tears is not attributable to the tear per se, particularly with concomitant radiological (established) OA, as shown in the study mentioned by the reviewer as well as some other publications (Dervin, Stiell et al. 2001; Bhattacharyya, Gale et al. 2003). Prompted by this comment, as well as the suggestions of the other reviewer (Professor Englund), we have rephrased our
sentence “Patients with symptomatic degenerative medial meniscus tear” as “patients with symptoms consistent with a degenerative medial meniscus injury (pain on the medial joint line).” We have also added this reference to the Introduction (Ref. #6).

Regarding Prof. Felson’s contention that if meniscal tears are not causing the pain to patients with degenerative knee disease, then our trial will not be a productive endeavour, we would respectfully respond that APM is still the most common orthopaedic procedure, but there is a dire lack of evidence on its efficacy. If our trial suggests that APM does not produce benefits over those of placebo-surgery, we still consider our trial a success. Further, two of our primary outcome instruments, the Lysholm and WOMET scores, are not pain scores, but rather a generic knee score and a disease-specific quality of life instrument respectively. The reason why we feel that a pain score should also be included (and why it has been included) is that knee pain is still the most common (and debilitating) symptom in patients with degenerative meniscus injury (Noble 1975; McBride, Constance et al. 1984).

6. One of the main concerns about the design is the specification of 3 primary outcome measures each assessed at P < .05. The authors should have prespecified either one of these as their primary or come up with a Bonferroni type adjustment for the multiple testing.

We thank the reviewer for this very valuable comment. According to this suggestion, we will use the Bonferroni method to adjust the overall level of significance for the three primary outcomes, which all have been validated, and thus verification of effectiveness calls for statistically and clinically meaningful findings in all of them.

7. While the comparison with an external group is appreciated, it is not entirely clear how this will be analyzed nor how the external group will provide information on generalizability since it is from the same center and is evaluated for trial eligibility. This should be noted in the methods section. Will the external cohort have the same outcome assessment as trial patients?

In the previous version of the paper, we stated (Abstract…): “, in one of the five centers recruiting patients for the RCT, all patients scheduled for knee arthroscopy due to a degenerative meniscus injury (also those excluded from the RCT) will be prospectively followed up using the same protocol as in the RCT to provide an external validation cohort.”

And further: “all patients scheduled for a knee arthroscopy due to a degenerative meniscus injury but who bypassed the evaluation for eligibility (e.g., were assessed and scheduled for surgery by another orthopedic surgeon not involved in the trial or who were excluded from the trial) were followed up prospectively with a follow-up assessment protocol identical to that in the actual trial.”

As it seems readily apparent that this section is not entirely unambiguous, we have rephrased it as follows: “Additionally, in one of the five study centres (the initial site, in which over half of the participating patients were enrolled), all patients scheduled for a knee arthroscopy were followed up prospectively with a follow-up assessment protocol identical to that in the actual trial. Those with a degenerative meniscus injury (but who had somehow either bypassed our recruitment, were treated by an orthopaedic surgeon not participating in the trial or who were excluded from the trial) form a non-randomized, pragmatic, prospective cohort. This pragmatic cohort, together with the patients treated in the actual RCT (those randomized and also those who declined to be randomized), constitute the “RCT within-a-cohort” study population (Figure 2a).

In essence, this pragmatic cohort includes some 1,000 patients with degenerative meniscus injury with a wide range of baseline characteristics (age, sex, severity of knee OA, etc.) and these patients were treated by more than 10 surgeons with a wide range of experience in knee arthroscopy. Accordingly, by comparing the response to treatment in the RCT groups with the responses of the
distinct groups of patients with distinct prognostic factors (see Figure 2b), we should be able to address several interesting hypotheses regarding the efficacy and effectiveness of arthroscopic partial meniscectomy (APM). Some of these comparisons are showcased in Figure 2b. It is indeed true that this cohort might not enhance the generalizability of our findings with respect to other (different kinds of) healthcare systems, but in our opinion - the fact that the patients of this cohort are from the same centre as the majority of our RCT patients actually enables the comparison of the response to treatment under more pragmatic circumstances with those obtained under efficacy circumstances.

Reviewer: Martin Englund, MD, PhD, Associate Professor
Epidemiologist
Department of Orthopedics
Lund University, Lund
Sweden

This is report is the study protocol and discussion around ethics etc for a randomized controlled trial (RCT) for the treatment of a degenerative meniscus tear believed to be causing symptoms (placebo-controlled surgery vs. sham surgery). In parallel with the Moseley trial for knee osteoarthritis, a study with a sham surgical procedure is the only way to tease out the placebo-effect from the true effect of meniscus surgery. Hence, I welcome this study as it is highly needed. Over all this is a very well planned RCT.

We thank Prof. Englund for very constructive and highly professional comments.

Still, I have a few comments/suggestions as detailed below:

Abstract
Line 25:
Quote: “Patients with symptomatic degenerative medial meniscus tear,”
How do you know for sure that the tear itself is “symptomatic”? Isn’t it better described as a “degenerative medial meniscus tear in a patient with medial joint line symptoms” or “with a potentially symptomatic medial meniscus tear”? For instance, the symptoms could potentially arise from other structures or processes in the (medial side) synovium, capsule, or potentially the subchondral bone, structures all that may be involved in pre-radiographic osteoarthritis. (The clinical tests for meniscal tear are not that great (Solomon DH JAMA. 2001 Oct 3;286(13):1610-20))

As also pointed out by Prof. Felson, this suggestion is highly appreciated. We have amended our sentence according to this suggestion, thank you very much.

Line 37:
Why the choice of the Lysholm Knee Score as primary outcome? This instrument was originally developed to be administered by the examiner (with potential for bias) Hence, the patient-administered version has several drawbacks; items are relatively often missing as it lacks instructions, and holds many ambiguities. There are more valid and sensitive patient-relevant outcome measures in the field of knee osteoarthritis and knee surgery. Some articles pointing out problems with the Lysholm Knee Score: Risberg and Ekeland 1994, Bengtsson et al. 1996, Höher et al. 1997, Demirdjian et al. 1998, and work by EM Roos et al.

We thank the reviewer for these helpful remarks. It is indeed true that the Lysholm score is not ideal for this purpose, but at the time we were planning this trial, it was the most commonly used outcome
instrument for evaluation of meniscal injury (at least, of which we were aware). Partly because of these apparent flaws, we decided to validate the WOMET. As also explained in our protocol, the WOMET has now been 'upgraded' as our third primary outcome measure.

MAIN TEXT
Intro:
The introduction would benefit from pointing out that degenerative meniscal tears are highly prevalent in the general population (middle-aged and elderly), if for instance screened by MRI (and most of tears seem not to cause much trouble to the persons) (Englund et al New Engl J Med 2008).

This has now been added to the Introduction.

Methods:
Table 1 Shouldn’t “unresponsive to the appropriate conservative treatment” be added to the table? (as it is stated in text as one inclusion criteria, line 15). It is important point because patients included have already then tried conventional therapy. Hence the sample is somewhat selected on the basis of being "resistant" against conservative therapy. Could you also please detail what kind of therapy that was tried?

The study was carried out in one secondary and four tertiary orthopaedic clinics and the patients were referred to our departments by GPs. According to a nation-wide guideline on the treatment of degenerative knee disease, GPs are instructed to attempt conservative treatment before referral to orthopaedic surgeons. However, there did not (and still does not) exist a standardized protocol for the proper execution of conservative treatment of these patients. Because of that, every patient recruited in the trial was met by a physiotherapist who instructed him/her on proper physiotherapy (ROM exercises and strengthening of the quadriceps muscle). This information was also given in writing. As also stated in our paper, if the symptoms subside during the waiting period before the operation, the patient was/will be excluded. We are well aware of the fact that there has been a recent surge in the attempts to develop effective conservative treatment of degenerative knee disease (meniscus tear), mainly by Prof. Ewa Roos and her group (Stensrud, Roos et al. 2012), but at the time of initiation of our trial, there really was no consensus of what the conservative management should be.

How are the MRI’s to be graded? (scoring system for meniscus etc?)
How are the meniscal tears, location and their extent classified at arthroscopy?

As far as we know, there exists no universal grading system for the MRIs. We had some preliminary discussion with Prof. Ewa Roos at a recent meeting to have them analysed by her team and she actually suggested that we should contact the reviewer (Prof. Englund). As you know, we have been unable to make this contact so far. However we repeat here that the MRI was used to confirm the existence of the tear, but the final classification/characterization of the tear was carried out at arthroscopy according to the system published by Cooper et al. (Cooper, Arnoczky et al. 1991). This system entails a drawing and a table to assess the size and the extent (circumferential zones 0-4 and radial zones A, B and C), as well as the type (longitudinal, bucket handle, flap, radial, horizontal or complex) of the tear.

Discussion:
Page 22 Line 15; I suggest better to use original reports than reviews if possible. For instance, the original ref (Englund&Lohmander Arthritis Rheum 2004) support the sentence that lateral meniscectomy is “worse” (higher risk of development of radiographic knee osteoarthritis than medial meniscectomy; the first study to show so).

Thank you for this helpful comment. Amended as suggested.
Please consider include and refer to the published abstract by Katz et al presented at the ACR meeting Washington DC 2012; prelim. results from the US-based MeTEOR trial: "The Meteor Trial: Preliminary Results of an RCT of Arthroscopic Partial Meniscectomy Vs. Physical Therapy in Patients greater Than 45." Link: http://www.rheumatology.org/education/annual/2012_Abstract_Supplement.pdf#toolbar=1 (Abstract # 2650 on page S1123)

The authors concluded: "These preliminary trial findings suggest that in both the APM and the nonoperative arms, subjects experienced substantial improvement in functional status over six months, with no significant differences between the two arms in the ITT analysis. 30% of subjects randomized to nonoperative therapy underwent APM within the first six months. As with all RCT’s the results should be generalized cautiously to clinical populations. These findings will aid physicians and their patients over 45 who present with knee symptoms in association with meniscal tears and osteoarthritis as they decide whether to elect APM or nonoperative therapy."

Thank you for this reference. We have been eagerly waiting for these results to be published, but this abstract has avoided our radar. The paper has now been added to the text (REF #16).

In summary: This study will be an exciting and very important trial. The protocol is in my opinion overall well written. I congratulate the authors for their initiative and I very much indeed look forward seeing the results!

Once again, thank you very much for these constructive and positive comments (and attentive remarks that certainly improve our paper).

References

Bhandari, M., G. Guyatt, et al. (2008). "Study to prospectively evaluate reamed intramedially nails in patients with tibial fractures (S.P.R.I.N.T.): study rationale and design." BMC Musculoskelet Disord 9: 91.

Bhattacharyya, T., D. Gale, et al. (2003). "The clinical importance of meniscal tears demonstrated by magnetic resonance imaging in osteoarthritis of the knee." J Bone Joint Surg Am 85-A(1): 4-9.

Campbell, M. K., V. A. Entwistle, et al. (2011). "Developing a placebo-controlled trial in surgery: issues of design, acceptability and feasibility." Trials 12: 50.

Chan, A. W., J. M. Tetzlaff, et al. (2013). "SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials." BMJ 346: e7586.

Cooper, D. E., S. P. Arnoczky, et al. (1991). "Meniscal repair." Clin Sports Med 10(3): 529-548.

Dervin, G. F., I. G. Stiell, et al. (2001). "Physicians' accuracy and interrator reliability for the diagnosis of unstable meniscal tears in patients having osteoarthritis of the knee." Can J Surg 44(4): 267-274.

Englund, M., A. Guermazi, et al. (2008). "Incidental meniscal findings on knee MRI in middle-aged and elderly persons." N Engl J Med 359(11): 1108-1115.

Englund, M., A. Guermazi, et al. (2009). "Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The Multicenter Osteoarthritis Study." Arthritis Rheum 60(3): 831-839.

Felson, D. T. (2013). "Osteoarthritis as a disease of mechanics." Osteoarthritis Cartilage 21(1): 10-15.

Felson, D. T., J. Niu, et al. (2007). "Correlation of the development of knee pain with enlarging bone marrow lesions on magnetic resonance imaging." Arthritis Rheum 56(9): 2986-2992.

Kirkley, A., T. B. Birmingham, et al. (2008). "A randomized trial of arthroscopic surgery for osteoarthritis of the knee." N Engl J Med 359(11): 1097-1107.

McBride, G. G., R. M. Constine, et al. (1984). "Arthroscopic partial medial meniscectomy in the older
patient." J Bone Joint Surg Am 66(4): 547-551.
Moseley, J. B., K. O'Malley, et al. (2002). "A controlled trial of arthroscopic surgery for osteoarthritis of the knee." N Engl J Med 347(2): 81-88.
Noble, J. (1975). "Clinical features of the degenerate meniscus with the results of meniscectomy." Br J Surg 62(12): 977-981.
Stensrud, S., E. M. Roos, et al. (2012). "A 12-week exercise therapy program in middle-aged patients with degenerative meniscus tears: a case series with 1-year follow-up." J Orthop Sports Phys Ther 42(11): 919-931.

VERSION 2 – REVIEW

| REVIEWER         | Martin Englund, MD, PhD, Associate Professor Epidemiologist
|                 | Department of Orthopedics
|                 | Lund University, Lund
|                 | Sweden

| REVIEW RETURNED | 08-Feb-2013 |

- The reviewer completed the checklist but made no further comments.