PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([http://bmjopen.bmj.com/site/about/resources/checklist.pdf](http://bmjopen.bmj.com/site/about/resources/checklist.pdf)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Cost-Effectiveness Analysis of Arthroscopic Surgery compared to Non-operative Management for Osteoarthritis of the Knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Marsh, Jacquelyn; Birmingham, Trevor; Giffin, J.Robert; Isaranuwatchai, Wanrudee; Hoch, Jeffrey; Feagan, Brian G.; Litchfield, Robert; Willits, Kevin; Fowler, Peter</td>
</tr>
</tbody>
</table>

VERSION 1 - REVIEW

| REVIEWER            | Raine Silvonen
|                     | Hatanpää Hospital, Tampere, Finland
|                     | Tampere University, Tampere, Finland |
| REVIEW RETURNED     | 25-Sep-2015 |

GENERAL COMMENTS

General comments:
As the authors state, in theoretic point of view, there should be no need for cost-effectiveness studies after no efficacy or effectiveness have been found for arthroscopic surgery for degenerative knee in trials with low risk of bias. However, as there are published studies (non-controlled) to suggest that knee arthroscopy may be cost-effective and the number of knee arthroscopies, even for those with established knee OA, has not decreased, I found this study to be well justified and with considerable interest.
I found the paper well written and without major flaws. However, some minor comments and suggestions:

General comment:
As stated (p7 lines 34 to 35) by authors, arthroscopic surgery provided no additional benefit beyond three months after surgery. Is it possible that surgery is associated with more rapid improvements in knee pain than non-surgical management? This phenomenon is argued often by the advocates for knee arthroscopic surgery for degenerative knee and also, in a recent publication (Scillia et al. Arthroscopic Partial Meniscectomy for Meniscal Tears: A Review and Commentary on Study by NEJM. The Journal of Knee Surgery 2015). Would you like to comment on the possibility for more rapid recovery after surgery vs. conservative treatment? Does the 3-month period with fewer symptoms make the procedure cost-effective, possibly for those younger patients who could return to work earlier?
I suggest commenting the issue in the discussion.

Methods:

p12 (lines 46 to 53)
What was the method for eliciting patients’ mechanical symptoms? Did you use a standardized question?
p10 (lines 3 to 11) "We also calculated quality adjusted life years (QALY) using the Standard Gamble technique. Scores on this health utility measure range from 0.0 (death) to 1.0 (perfect health). QALY
is calculated as the product of the utility score and the duration of
the corresponding health state."

I suggest making it clearer whether WOMAC score or other separate
general quality of life -score (health utility measure) was used to
calculate the score for quality of life and further to QALY. Was the
used time frame for QALY two years or did you make presumption
that the result will last longer?

Discussion:

p 22 (lines 20 to 25).
In the original article (flow chart) there is numbers for those excluded
from the trial. According to flow chart, 3 participants was excluded
for: “had other reasons”. Were those patients with bucket handle tear (and excluded for that reason) among those three? If so, I
suggest mentioning the actual number for those patients in the text.

If there were only three of those patients, the next concern is not
meaningful, but if there were bigger number of those:
I also suggest presenting the “suspicion criteria” for bucket handle tear more clear. Was it based on acute loss of extension (line 22 to
23) or "detected by clinical examination or, in a minority of cases, by
magnetic resonance imaging” as stated in the original article.

p22 (line 39)
I suggest omitting two references (16 and 17, Thorolund and Khan)
from here as the sentence is referring to the original trials.

REVIEWER
Colin R Howie
Orthopaedic Department
Edinburgh University
Orthopaedic surgeon and recent publication on rates of arthroscopy
surgery for OA Past president British Orthopaedic Ass.

REVIEW RETURNED
04-Nov-2015

GENERAL COMMENTS
This is a timely revisitation of previously unpublished but relevant
data given the recent flurry of interest in arthroscopic surgery of the
knee for OA.
My only points marking no above relate to minor changes required
rather than a major disagreement with methodology or message.
Our understanding of the value of conservative treatments has
changed over the years since this study was undertaken and this
should be highlighted, many of the conservative treatments listed
are not currently supported other than by those who supply them
(Physicians cognitive dissonance?) McAlindon paper on OARSI
guidelines (quoted here) highlights this and further cost could be
taken out of conservative group which further supports the main
point of the paper.
A forthright contemporary and locally relevant reference may be the
UK NICE guidelines on the management of OA knee
(http://www.nice.org.uk/guidance/cg177/chapter/1-
recommendations#non-pharmacological-management-2).
Further support for the position taken by this paper could be derived
from looking at the supportive conservative treatments post
arthroscopy in this paper. I suspect they were no different from the
conservative treated group. Worth looking at if possible and
commenting.
Unclear whether subgroup analysis looked at KL gd 2 with locking and found no improvement... mentioned but I'm a little confused.
Small group of removal loose bodies noted then no further comment possibly too small but having mentioned them subgroup comment would head off criticism. On a similar vein worth commenting that 80% had a meniscal trim but no difference (I know it was in previous paper but worth hammering home).
The key thing in this paper, and the original trial, was that the patients had radiographic changes K_L gd 2 or above, it is mentioned in table 1 but not in the text. This point is important and should appear in the abstract and discussion (perhaps with the comment that a rush to costly MRI unhelpful though accept this reflects my prejudice).
There is randomised study in patients with no OA changes on plain radiograph showing benefit to arthroscopy over conservative treatments which is hinted at by excluding bucket handle tears in the text.(Osteoarthritis Cartilage. 2014 Nov;22(11):1808-16. doi: 10.1016/j.joca.2014.07.017. Epub 2014 Jul 30. Knee arthroscopic surgery is beneficial to middle-aged patients with meniscal symptoms: a prospective, randomised, single-blinded study.
Gauffin H, Tagesson S, Meunier A, Magnusson H, Kvist J) Threfore the discussion needs to be precise just having an age ban as such is unhelpful which has been the consequence of previous publications and has supported cognitive dissonance.
And then of course there is a more recent paper in BMJ from ourselves for the discussion.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Raine Sihvonen
Institution and Country: Hatanpää Hospital, Tampere, Finland; Tampere University, Tampere, Finland.

General comments:
As the authors state, in theoretic point of view, there should be no need for cost-effectiveness studies after no efficacy or effectiveness have been found for arthroscopic surgery for degenerative knee in trials with low risk of bias. However, as there are published studies (non-controlled) to suggest that knee arthroscopy may be cost-effective and the number of knee arthroscopies, even for those with established knee OA, has not decreased, I found this study to be well justified and with considerable interest. I found the paper well written and without major flaws. However, some minor comments and suggestions.

Response: We thank the reviewer for summarizing what we also believe to be appropriate rationale for this study, including the statement that rates of arthroscopy in patients with established knee OA remain high. We also appreciate the supportive comments and the opportunities to address the additional suggestions.

Comment: As stated (p7 lines 34 to 35) by authors, arthroscopic surgery provided no additional benefit beyond three months after surgery. Is it possible that surgery is associated with more rapid improvements in knee pain than non-surgical management? This phenomenon is argued often by the advocates for knee arthrocscopic surgery for degenerative knee and also, in a recent publication (Scillia et al. Arthroscopic Partial Meniscectomy for Meniscal Tears: A Review and Commentary on Study by NEJM. The Journal of Knee Surgery 2015). Would you like to comment on the possibility for
more rapid recovery after surgery vs. conservative treatment? Does the 3-month period with fewer symptoms make the procedure cost-effective, possibly for those younger patients who could return to work earlier?
I suggest commenting the issue in the discussion.

Response: We agree that the small difference observed at three months may be considered by some to be an indication that arthroscopy provides short-term benefits (regardless of its mechanisms) that may result in less time off work and therefore decreased costs. However, our data do not support that argument. There were no differences in direct disease-related costs between groups at the 3-month follow-up or any other time point over the 2-year study period. In fact, a significantly greater proportion of patients in the surgery group reported taking time off work in the first three months (which might be expected as most patients are required to take at least some time off to undergo and recover from surgery). We have added a brief description clarifying this finding to the first paragraph of the Discussion, as suggested (page 19, lines 6-8).

Methods:
Comment: p12 (lines 46 to 53)
What was the method for eliciting patients’ mechanical symptoms? Did you use a standardized question?

Response: Each patient underwent a standardized physical assessment and history exam with the orthopaedic surgeon at baseline, where the surgeon performed meniscal and stability tests. Although the specific wording of questions may have varied among surgeons, s/he was required to document on the standardized form whether or not the patient experienced mechanical symptoms of catching and/or locking.

Comment: p 10 (lines 3 to 11) “We also calculated quality adjusted life years (QALY) using the Standard Gamble technique. Scores on this health utility measure range from 0.0 (death) to 1.0 (perfect health). QALY is calculated as the product of the utility score and the duration of the corresponding health state.” I suggest making it clearer whether WOMAC score or other separate general quality of life -score (health utility measure) was used to calculate the score for quality of life and further to QALY. Was the used time frame for QALY two years or did you make presumption that the result will last longer?
Response: We calculated QALYs using the standard gamble utility scores. We reported QALYs over the two year study period only. We did not predict QALYs past this time point for this analysis. We have clarified the method in the revised manuscript (page 7, lines 18-20, page 8, lines 4-8).

Discussion
Comment: p 22 (lines 20 to 25).
In the original article (flow chart) there is numbers for those excluded from the trial. According to flow chart, 3 participants were excluded for: “had other reasons”. Were those patients with bucket handle tear (and excluded for that reason) among those three? If so, I suggest mentioning the actual number for those patients in the text. If there were only three of those patients, the next concern is not meaningful, but if there were bigger number of those, I also suggest presenting the “suspicion criteria” for bucket handle tear more clear. Was it based on acute loss of extension (line 22 to 23) or “detected by clinical examination or, in a minority of cases, by magnetic resonance imaging” as stated in the original article.
Response: Thank you for the opportunity to clarify. Patients with bucket handle tears were not included in the study and were not reported in the flow chart. Although the statements in the original trial and the present study are accurate, the issue is that the target population we evaluated (i.e. those with knee OA) very rarely have bucket handle meniscal tears. If the surgeon suspected a bucket handle tear, even if in the rare event where the patient also had radiographic knee OA, the patient
would not have been referred to the study nurse for screening. Regarding “suspicion criteria” for a bucket handle tear, these were based on the surgeons’ clinical exam including the patient history (eg, most commonly twisting injury with acute loss of knee extension) and rarely an MRI. Importantly, as you noted above, the patients included in the present study are indeed representative of the population of patients that still very commonly receive arthroscopic debridement of degenerative meniscal tears associated with knee OA. We have added those details to the revised Discussion (page 20, lines 8-15). We have also added more detail to Figure 1 to match the original trial.

Comment: p22 (line 39)
I suggest omitting two references (16 and 17, Thorlund and Khan) from here as the sentence is referring to the original trials.

Response: We agree and have removed those references from this statement, as suggested (page 19, line 23).

Reviewer: 2
Reviewer Name: Colin R Howie
Institution and Country: Orthopaedic Department, Edinburgh University.

This is a timely revisitation of previously unpublished but relevant data given the recent flurry of interest in arthroscopic surgery of the knee for OA. My only points marking no above relate to minor changes required rather than a major disagreement with methodology or message. Our understanding of the value of conservative treatments has changed over the years since this study was undertaken and this should be highlighted, many of the conservative treatments listed are not currently supported other than by those who supply them (Physicians cognitive dissonance?) McAlindon paper on OARSI guidelines (quoted here) highlights this and further cost could be taken out of conservative group which further supports the main point of the paper.

Response: Thank you for the helpful comments and opportunity to address them. We agree that some of the non-operative treatments used are also not supported by evidence and are not included in present recommendations. We have expanded upon that issue in the revised Discussion (page 20, lines 3-8). Removing the costs of those treatments will not have an effect on our results, as both groups received the same course of non-operative management, and there were no differences in the non-operative treatments (both type and frequency of use) between groups at any follow up time period.

Comment: A forthright contemporary and locally relevant reference may be the UK NICE guidelines on the management of OA knee (http://www.nice.org.uk/guidance/cg177/chapter/1-recommendations#non-pharmacological-management-2).

Response: We agree and have added the suggested reference (UK NICE Guidelines), where appropriate.

Comment: Further support for the position taken by this paper could be derived from looking at the supportive conservative treatments post arthroscopy in this paper, I suspect they were no different from the conservative treated group. Worth looking at if possible and commenting.

Response: Consistent with comments from Reviewer 1, we agree that some may suggest that arthroscopic surgery might reduce the use of non-operative treatments and their associated costs. While understanding that there are limitations in the inferences we can make given our study design, we have emphasized that the present results show no differences in the treatments sought by patients after surgery, and an increase in indirect disease costs such as time off work, compared to the non-operative group (page 19 lines 5-8). We agree that some non-operative treatments used in
the study are not supported by current evidence, yet we felt it was important to include treatments commonly used and paid for despite the lack of supporting evidence (including arthroscopy). Because there were no differences in the use of non-operative therapies between groups, removing those treatments from the analysis would not change our results.

Comment: Unclear whether subgroup analysis looked at KL gd 2 with locking and found no improvement... mentioned but I'm a little confused.

Response: We conducted two separate, pre-specified subgroup analyses; 1) patients with KL grade 2, and 2) patients reporting mechanical symptoms of catching and/or locking. We have clarified this in the manuscript, page 11, lines 1-4; page 20, lines 19-20.

Comment: Small group of removal loose bodies noted then no further comment possibly too small but having mentioned them subgroup comment would head off criticism. On a similar vein worth commenting that 80% had a meniscal trim but no difference (I know it was in previous paper but worth hammering home).

Response: While we agree that the number of surgical patients receiving removal of loose bodies is too low to perform a subgroup analysis, we have added further emphasis on the fact that patients did indeed receive trimming of the meniscus and the target population is indeed similar to patients often undergoing arthroscopy (page 20, lines 12-15)

Comment: The key thing in this paper, and the original trial, was that the patients had radiographic changes KL grade 2 or above, it is mentioned in table 1 but not in the text. This point is important and should appear in the abstract and discussion (perhaps with the comment that a rush to costly MRI unhelpful though accept this reflects my prejudice).

Response: We have emphasized KL grade 2 or above in the abstract and Discussion, as suggested (page 2, lines 6-7; page 20, lines 4-5). We agree that MRI's are typically unnecessary and have stated so in the revised Discussion where relevant.

Comment: There is a randomised study in patients with no OA changes on plain radiograph showing benefit to arthroscopy over conservative treatments which is hinted at by excluding bucket handle tears in the text.(Osteoarthritis Cartilage. 2014 Nov;22(11):1808-16. doi: 10.1016/j.joca.2014.07.017. Epub 2014 Jul 30. Knee arthroscopic surgery is beneficial to middle-aged patients with meniscal symptoms: a prospective, randomised, single-blinded study. Gauffin H, Tagesson S, Meunier A, Magnusson H, Kvist J)Therefore the discussion needs to be precise just having an age ban as such is unhelpful which has been the consequence of previous publications and has supported cognitive dissonance.

Response: We have added more detail to the Discussion about bucket handle meniscal tears (page 20, lines 8-12), which represent a different injury/patient population. We have also added to our comment about arthroscopy for degenerative meniscal tears in the absence of radiographic OA. Although we are careful not to generalize beyond the capabilities of our study design, we have emphasized in the revised Discussion that meta-analyses of all randomized trials evaluating arthroscopic partial meniscectomy in the degenerative knee, and a sham controlled trial in middle-aged patients with degenerative meniscal tears in the absence of radiographic knee OA, suggest that the procedure is not effective (page 21, lines 1-6).

Comment: And then of course there is a more recent paper in BMJ from ourselves for the discussion.

Response: We have added reference to the paper in the Discussion where appropriate, along with
others that suggest changes in the clinical care pathway are possible and needed (page 22, lines 8-13). We hope that adding cost-effectiveness data contributes to such changes.

VERSION 2 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Raine Sihvonen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hatanpää Hospital, Tampere, Finland; Tampere University, Tampere, Finland</td>
</tr>
<tr>
<td>REVIEW RETURNED</td>
<td>30-Nov-2015</td>
</tr>
</tbody>
</table>

GENERAL COMMENTS  The reviewer completed the checklist but made no further comments.
Cost-effectiveness analysis of arthroscopic surgery compared with non-operative management for osteoarthritis of the knee

Jacquelyn D Marsh, Trevor B Birmingham, J Robert Giffin, Wanrudee Isaranuwatchai, Jeffrey S Hoch, Brian G Feagan, Robert Litchfield, Kevin Willits and Peter Fowler

BMJ Open 2016 6:
doi: 10.1136/bmjopen-2015-009949

Updated information and services can be found at:
http://bmjopen.bmj.com/content/6/1/e009949

These include:

References
This article cites 41 articles, 11 of which you can access for free at:
http://bmjopen.bmj.com/content/6/1/e009949#BIBL

Open Access
This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Health economics (365)
Medical management (229)
Rehabilitation medicine (312)
Sports and exercise medicine (222)
Surgery (404)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/