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Knee arthroscopy versus conservative management in patients with degenerative knee disease: a systematic review

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KNEE ARTHROSCOPY VERSUS CONSERVATIVE MANAGEMENT IN PATIENTS WITH DEGENERATIVE KNEE DISEASE: A SYSTEMATIC REVIEW

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ARTICLE SUMMARY

ABSTRACT

Objective: To determine the effects and complications of arthroscopic surgery compared to conservative management strategies in patients with degenerative knee disease

Design: Systematic review

Main Outcome Measures: Pain, function, adverse events

Data sources: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar and Open Grey up to August 2016.

Eligibility criteria: For effects, randomized clinical trials (RCTs) comparing arthroscopic surgery with a conservative management strategy (including sham surgery) in patients with degenerative knee disease. For complications, RCTs and observational studies.

Review methods: Two reviewers independently extracted data and assessed risk of bias for patient-important outcomes. A parallel guideline committee (*BMJ* Rapid Recommendations) provided input on the design and interpretation of the systematic review, including selection of patient-important outcomes. We used the GRADE approach to rate the certainty (quality) of the evidence.

Results: We included 13 RCTs and 12 observational studies. With respect to pain, the review identified high certainty evidence that knee arthroscopy results in a very small reduction in pain up to 3 months (mean difference= 5.4 on a 100-point scale, 95% CI 2.0; 8.8) and very small or no pain reduction up to 2 years (mean difference= 3.1, 95% CI -0.2; 6.4) when compared to conservative management. With respect to function, the review identified moderate certainty evidence that knee arthroscopy results in a very small improvement in the short-term (mean difference= 4.9 on a 100-point scale, 95% CI 1.5; 8.4) and very small or no improved function up to 2 years (3.2, 95% CI -0.5; 6.8). Alternative presentations of magnitude of effect, and associated sensitivity analyses, were consistent with the findings of the primary analysis. Low quality evidence suggested a very low probability of serious complications after knee arthroscopy.

Conclusion: Over the long term, patients who undergo knee arthroscopy versus those who receive conservative management strategies do not have important benefits in pain or function.

Systematic review registration: PROSPERO CRD42016046242

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This in an update of previously published systematic reviews on the topic.
- This review is linked to a BMJ Rapid Recommendations project. We conducted the review directed by a guideline panel that included patient representatives. This guideline panel provided detailed input with regards to the patients, interventions and outcomes, and the interpretation of the results from this review.
- We included 7 new studies, analyzed data focusing on clinical interpretability, and explicitly assessed the certainty in the estimates of effect.
- We performed meta-analyses using different measures of effect, and conducted subgroup and sensitivity analyses that strengthened our conclusions.

WHAT IS ALREADY KNOWN IN THIS TOPIC:

- Although systematic reviews have failed to establish that knee arthroscopy has clear benefits over conservative management strategies, orthopaedic surgeons often offer this procedure to patients with degenerative knee disease
- Current guideline recommendations on managements of knee pain and associated functional limitation provide conflicting guidance and exclude many patients with degenerative knee disease (eg. those with meniscal tears with or without radiographic evidence of osteoarthritis)

WHAT THIS STUDY ADDS

- Moderate to high certainty evidence shows that there are at best only very small differences in pain, function, and quality of life of patients who underwent knee arthroscopy compared to those who received conservative management strategies over the short term, and no benefit over the long term.
- Patients can expect, on average, to achieve small but important improvement over the period of two years, irrespective of what treatment they receive.
- Patients and their health care providers must trade off the marginal short-term benefits against the burden and potential complications of the surgical procedure

INTRODUCTION

As a result of degenerative knee disease (osteoarthritis in the knee which can involve the joint lining and/or menisci), approximately 25% of people over 45 years experience pain and other symptoms that may be severe and negatively impact quality of life.[1 2 3] Total knee arthroplasty is the only definitive therapy available, but is reserved for patients with severe disease who fail conservative management.

In the United States, arthroscopic knee surgery in people with degenerative knee disease is the most common ambulatory orthopaedic procedure, and the ninth most commonly performed ambulatory procedure overall. [4] Such surgery results in transient increase in pain and the necessity for restriction in activities for a period of 2 to 6 weeks. Current guidelines recommend against arthroscopic lavage and/or debridement for patients with symptomatic knee osteoarthritis, but do not make specific recommendations for or against partial meniscectomy in those with degenerative meniscal tears (with or without other concomitant degenerative changes).[5 6] Further, many orthopedic surgeons suggest that patients with mechanical symptoms and meniscal tears – typically locking or catching of the knee – may benefit from arthroscopic partial meniscectomy.[7 8]

Our systematic review informs the second *BMJ* Rapid Recommendations,[9] a new *BMJ* series of trustworthy clinical practice recommendations published in response to potentially practice-changing evidence.[10] A trial that compared the outcomes of exercise therapy versus knee arthroscopic partial meniscectomy in 140 middle-aged patients with degenerative meniscal tears, published in July 2016 triggered this systematic review.[11] Previous systematic reviews addressing the impact of arthroscopic knee surgery did not consider all patient-important outcomes; did not consider patient importance when addressing patient-reported outcomes such as pain, function, and quality of life (QoL); and did not include all currently available randomized controlled trials (RCTs).[12 13]

To determine the effects and complications in patients with symptomatic degenerative knee disease, we performed a systematic review and meta-analysis of arthroscopic surgery with debridement, and/or partial meniscectomy compared to conservative management strategies.

METHODS

Readers can access the protocol of this systematic review in PROSPERO (CRD42016046242). According to the *BMJ* Rapid Recommendations process,[10] a guideline panel provided critical oversight to the review and identified populations, subgroups, and outcomes of interest. The panel included eight content experts and front line clinicians (three orthopaedic surgeons, one rheumatologist, one epidemiologist, one general practitioner and two physiotherapists), four methodologists (three of them whom are also front line clinicians and general internists) and three patients with lived experience of degenerative knee disease.

All patients received personal training and support to optimize contributions throughout the guideline development process. The patient panel members led the interpretation of the results based on what they expected the typical patient values and preferences to be, as well as the variation between patients. We also considered patients' values and preferences by using the minimally important difference (MID) to interpret the results obtained in the meta-analyses. These MIDs were obtained from a systematic review of studies in which patients were directly asked about the magnitude of change they had experienced, and whether that change was trivial, small but important, or larger.[14] Clinical experts who were part of the team of that systematic review judged the applicability of such studies to the target population and raised no concerns.

Eligibility criteria

For the effects of arthroscopic surgery, we included RCTs comparing arthroscopic surgery, including any or all of debridement and/or partial meniscectomy to any conservative management strategy (exercise therapy, injections, drugs, sham surgery) in patients with symptomatic degenerative knee disease (defined as persistent knee pain that affects the patient's quality of life and does not respond to conservative treatment), with or without osteoarthritis, of any age. We excluded studies that enrolled patients with acute trauma and those that enrolled fewer than 10 patients. For the complications of arthroscopic surgery, we also included observational studies (cohort studies, registry studies, and case series) in patients with degenerative knee disease undergoing arthroscopic surgery, with or without a comparison group. We excluded studies published before the year 2000 when considering complications (but not effects).

Literature search

We performed an update of a previously published systematic review[13] including MEDLINE (Pubmed), EMBASE (Ovid) and CENTRAL (See Appendix 1) from January 1 2014, to August 16, 2016. In addition, we constructed specific search strategies for these three databases for one outcome not studied in the previous review (nerve damage), with no date limits. We also searched for grey literature using the first 500 hits from Google Scholar and Open Grey. We did not limit any of the searches by language of publication.

Study selection and data abstraction

Teams of two reviewers, working independently, performed all study selection and data abstraction using standardized forms, and reviewed the titles and abstract of all the references resulting from the searches. We retrieved and reviewed the full text of all references identified as potentially eligible by at least one reviewer. We also reviewed the full text of all references excluded at the full text screening stage in the prior review.[15] We included all studies judged as eligible by the two reviewers. Reviewers resolved disagreements by discussion.

Reviewers abstracted characteristics of eligible studies including study design, number of patients enrolled, age and sex distribution, number of patients followed-up, whether partial meniscectomy was performed, co-interventions, and outcomes, including pain, function, quality of life, and knee replacement. When authors reported results from more than one measure of pain or function, we decided a priori to use only the measure ranked highest in a hierarchy of patient-reported outcomes specific to the patients of interest.[16] When studies had more than two arms, we only used the data from the arms relevant

to this study. The review addressed these outcomes at 3 months or less, and at the longest follow-up reported.

The review addressed complication outcomes of mortality, venous thromboembolism (VTE), infection, and nerve damage. Reviewers abstracted the absolute number of patients who experienced the outcomes over the follow-up period. When studies did not report VTE but reported pulmonary embolism and deep-vein thrombosis separately instead, we used these numbers to estimate the number of VTEs, considering the potential overlap due to patients experiencing both.[17] We examined these outcomes over the three months following surgery.

Summary measures and data synthesis

We summarized continuous outcomes (pain, function and quality of life) at the study level using the difference in change from baseline between groups. When baseline mean and standard deviation per group at baseline and follow-up, but not change measures, were available, we assumed a within group correlation of 0.5 to estimate the standard deviation of the change from baseline per study arm. If arm level data were not reported, we abstracted the difference in change from baseline between the groups. When standard deviations at follow up were not reported, we assumed the same standard deviation as at baseline. When no standard deviations were available, we used the weighted average from all the other RCTs measuring the outcome with the same instrument. When studies reported medians and interquartile ranges, we converted to means and standard deviations.[18]

We performed meta-analyses, and present results for patient reported continuous outcomes in two ways. First, we transformed all scores to the scale of an index instrument, the highest in the hierarchy, and pooled results of all studies using the mean difference as the summary measure. This resulted in scores that could range from 0 to 100, in which higher scores signified better outcomes (less pain, better function, better quality of life). Second, we used the minimally important difference (MID) of each of the instruments to determine the proportion of patients who reached a change in the outcome that was larger than a MID. To inform this analysis, a parallel team performed a linked systematic review to establish the most credible MIDs for each of the instruments used to measure pain, function, and QoL. The most credible MID was the median of all the credible MIDs. Details of this review are available in a publication related to this *BMJ* Rapid Recommendation.[14] We then estimated and pooled the difference in the proportion of patients between groups achieving this difference.[15] When no credible MID was found for a particular instrument, we used the MID of the index instrument. Data for time-to-knee replacement was not available, so we summarized the data for knee replacement using the proportion of patients who

had the outcome per group and pooled those data using relative risk as the summary measure. These meta-analyses were performed using random effects models using the Hartung-Knapp-Sidik-Jonkman method.[19 20] All analyses were performed using an intention-to-treat approach. When authors did not report data in a way that allowed incorporation it in the meta-analyses, we summarized the results narratively.

For complications, we used the number of patients having the event and the total number of patients undergoing knee arthroscopy, and pooled these data using a generalized linear mixed effects model that allowed inclusion of studies with no events without a continuity correction.[21]

We planned to perform four subgroup analyses for the outcomes pain and function: trials in which there was more than 50% of patients with radiographic osteoarthritis (defined as Kellgren-Lawrence grades 2 to 4) versus trials with equal or less than 50% of patients with radiographic osteoarthritis; trials in which patients were blinded versus not blinded; trials in which meniscectomy was performed versus those in which it was not; and trials in which a control group received an active intervention (e.g. exercise therapy, injections) versus control groups without such interventions (e.g. waiting list, no treatment). We performed sensitivity analyses for calculating the difference in patients who achieve a change higher than the MID in two ways: 1) using the lowest and highest value of the MID of each instrument, based on the range of the MIDs that were deemed credible, and 2) calculating the standardized mean difference and then transforming the standardized mean difference into a risk difference[15] (this method does not use an MID). All data analyses used the package *meta* in the software R, version 3.3.1.[22]

Certainty of the evidence assessments

We assessed the certainty of the estimates of effect (quality of evidence) using the GRADE approach.[23] We considered potential limitations in risk of bias, inconsistency, imprecision, indirectness, and publication bias. [24-27] We used a modification of the Cochrane Risk of Bias tool[28] to assess the risk of bias of the studies informing on the effects of arthroscopic surgery, and the relevant items of the Methodological Index for Non-Randomized Studies (MINORS) tool[29] to assess the risk of bias of the studies informing on the complications of knee arthroscopy. All authors, in consultation with the parallel *BMJ* Rapid Recommendation guideline panel[30] participated in, and came to consensus regarding, certainty of estimates ratings.

The median of the change in score in the control arm from the studies that reported this information and did not use sham surgery as a control provided estimates of expected outcome in the control group (which

is the equivalent of the baseline risk in dichotomous outcomes), which informed calculation of absolute estimates of effect. Summary of findings tables[31] created using MAGICapp[32] summarized key information for all patient-important outcomes.

RESULTS

Of 710 unique references screened in title and abstract, 149 articles underwent full text screening, of which 13 RCTs informing the effects of knee arthroscopy[11 33-45] and 15 studies informing the complications of knee arthroscopy (12 OS[46-57] and 3 RCTs[11 37 42]) proved eligible (Figure 1).

Effects

Study Characteristics

The 13 eligible RCTs were published between 1993 and 2016, recruited a median of 119 patients, and enrolled patients with mean age from 48.9[43] to 62.8[33] years old, and a sex distribution from 5%[39] to 81.7%[41] women. Two studies performed sham surgery in the control group,[39 42] while most of the other studies used exercise therapy.[11 34 35 37 38 40 43 45] Table 1 presents details of study characteristics.

Table 1: Characteristics of randomised clinical trials included in systematic review of effects

Study	Number of patients enrolled	Comparator	Patients age (mean)	% females	ROA > 50%[1]	Pain measure[2]	Baseline mean intervention (SD)	Baseline mean control (SD)	Function measure[2]	Baseline mean (SD)	Baseline mean control (SD)
Chang, 1993[33]	34	Close needle joint lavage	62.8	71.6	Y	AIMS pain	65 (20)	61 (21)	AIMS physical function	23 (16)	17 (10)
Gauffin, 2014[34]	150	Exercise therapy	54.5	27.3	N	KOOS pain	55 (18)	58 (18)	KOOS ADL	65 (18)	68 (22)
Herrlin, 2007,[35] 2013[36]	96	Exercise therapy	54	38.9	N	KOOS pain	56 (18)	63 (21)	KOOS ADL	68 (21)	73 (20)
Katz, 2013[37]	351	Exercise therapy	58.4	56.7	Y	KOOS pain	54 (16)	53 (16)	WOMAC function	37 (18)	38 (18)
Kirkley, 2008[38]	188	Exercise therapy	59.6	62.9	Y	WOMAC pain	52 (21)	43 (24)	WOMAC function	51 (21)	43 (23)
Kise, 2016[11]	140	Exercise therapy	49.6	39	Y	KOOS pain	68 (15)	63 (21)	KOOS ADL	80 (16)	75 (22)
Moseley, 2002[39]	119	Sham surgery	52.8	5	Y	SF-36 body pain	39 (19)	38 (18)	SF-36 physical function	42 (22)	47 (23)
Osteras, 2012[40]	17	Exercise therapy	49.7	23.6	N	VAS	37 (10)	35 (17)	NM	-	-
Saeed, 2015[41]	120	Hyaluronic acid injection	NR	81.7	NR	Knee society score[3]	NR	NR	Knee society score[3]	NR	NR
Sihvonen, 2013[58]	146	Sham surgery	52	39	N	VAS	58 (20)	61 (20)	Lysholm knee score[3]	NA	NA
Stensrud, 2015[43]	82	Exercise therapy	48.9	35.4	N	Ordinal scale	NR	NR	Ordinal scale	NR	NR
Vermesan, 2013[44]	114	Steroid injection	58.4	79.2	NR	Oxford knee score[3]	NR	NR	Oxford knee score[3]	NR	NR
Yim, 2013[45]	108	Exercise therapy	56.8	79.4	N	VAS	52 (18)	49 (15)	Lysholm score[3]	NA	NA

ROA: Radiographic osteoarthritis, NR: not reported, NM: not measured, NA: not applicable

1. Based on Kellgren-Lawrence classification. Grades 2-4 were considered radiographic OA
2. All measures were converted to 0-100 scale. Higher scores mean less pain and better function
3. Instrument combines pain and function together

Effects of knee arthroscopy

Table 2 presents the GRADE Summary of Findings for effects of knee arthroscopy compared to control. Patients who underwent arthroscopic surgery had a change in pain scores larger on average than patients who received control, both in the short (5.4 points on a 100-point scale, 95% CI 2.0; 8.8, n=10 studies, 1231 patients, Appendix Figure 1), and long-term (3.1 95% CI -0.2; 6.4, n= 8 studies, 1097 patients, Appendix Figure 2). The minimally important difference for this outcome measured with the index instrument (KOOS pain subscale) was 12 points. [59] Using the MIDs specific to each instrument,[14] 12.4% more patients receiving arthroscopy achieved an improvement in pain greater than the MID (n=11 studies, 1102 patients) in the short-term.

Over the first three months of follow-up, the median average of improvement in pain was 15 points in patients who received conservative management versus 20 points in patients who underwent knee arthroscopy; over the long term, the median average improvement 19 points in patients who received conservative management, versus 22 points in patients who underwent knee arthroscopy.

Patients who underwent arthroscopic surgery had an improvement in function score that was, on average, 4.9 points larger on a 100-point scale than patients who received control in the short-term (95% CI 1.5; 8.4, n= 7 studies, 964 patients, Appendix Figure 3), and 3.2 points larger (95% CI -0.5; 6.8, n= 6 studies, 843 patients Appendix Figure 4) in the long term. The minimally important difference for this outcome measured with the index instrument (KOOS ADL subscale) was 8 points.[59] The probability of achieving a change in function higher than the MID was 13.4% higher in patients receiving arthroscopy (n= 6 studies, 835 patients) in the short-term.

In the short term, patients who received conservative management achieved a median average improvement in function of 9 points, versus 14 points in patients who underwent knee arthroscopy; over the long term, the median average improvement was 10 points in patients who received conservative management, versus 13 points in patients who underwent knee arthroscopy.

We were able to perform subgroup analyses according to blinding of patients and proportion of patients with radiographic osteoarthritis >50% for both of these outcomes. None of the analyses showed differences in results between groups (Appendix Figures 5-12). All RCTs performed partial meniscectomy as part of the intervention when needed, and all used active comparators. Therefore, we did not perform subgroup analyses for these variables.

Sensitivity analyses showed that for both short-term pain and short-term function, results using the upper and lower limit of the MID estimate, and the approach using the standardized mean difference, in all cases yielded lower estimates of the numbers with important benefit from arthroscopy than did our primary analysis (Appendix 2).

Changes in QoL scores were similar between patients undergoing knee arthroscopy and patients receiving control. In the short-term, the difference in change from baseline scores was 6.0 points greater for knee arthroscopy (95% CI -1.5; 13.5, n= 1 study, 120 patients). In the long-term, the difference in change from baseline was 2.1 points (95% CI -1.0; 5.2, n= 2 studies, 269 patients, Appendix Figure 13). The MID for the index instrument (EQ5D) is 15 points.[60] The median average of improvement in QoL was 8.0 points in patients who received conservative management versus 14.0 points in patients who underwent knee arthroscopy in the short term; and 10.3 points in patients who received conservative management, versus 12.4 points in patients who underwent knee arthroscopy.

The risk of undergoing knee replacement up to 1 year after the intervention was 1.89 times higher in patients undergoing knee arthroscopy (95% CI 0.51; 7, n= 2 studies, 497 patients, Appendix Figure 14).

Table 2: Summary of findings for the effects of knee arthroscopy versus control in patients with degenerative knee disease

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conservative management	Arthroscopy	**Certainty in effect estimates** (Quality of evidence)	**Summary**
Short term					
Pain (difference in change from baseline) 3 months	Measured by: Different instruments converted to scale of index instrument (KOOS pain sub scale) Scale: 0-100 High better, Minimally important difference 12) Data from 1231 patients in 10 studies Follow up 3 months	**15.0 points (Mean)**	**20.0 points (Mean)** **Difference: Mean Difference 5.4 more** (CI 95% 1.9 more - 8.8 more)	**High**	On average, knee arthroscopy results in very small extra reduction in pain scores when compared to control
Pain (difference in patients who achieve a change higher than the MID) 3 months	Data from 1102 patients in 9 studies Follow up 3 months	**669 per 1000**	**793 per 1000** **Difference: 124 more per 1000**	**High**	Knee arthroscopy increases the number of patients with an important reduction in short-term pain by approximately 12 in 100
Function (difference in change from baseline) 3 months	Measured by: Different instruments converted to scale of index instrument (KOOS ADL sub scale, Scale: 0-100, High better Minimally important difference 8) Based on data from 964 patients in 7 studies Follow up 3 months	**9.0 points (Mean)**	**14.0 points (Mean)** **Difference: Mean Difference 4.9 more** (CI 95% 1.5 more - 8.4 more)	**Moderate** Due to serious risk of bias, borderline inconsistency, and borderline imprecision	Knee arthroscopy may increase function change slightly more than control
Function (difference in patients who achieve a change higher than the MID) 3 months	Based on data from 835 patients in 6 studies Follow up 3 months	**519 per 1000**	**653 per 1000** **Difference: 134 more per 1000**	**Moderate** Due to serious risk of bias	Knee arthroscopy probably increases the number of patients with an important improvement in short-term function approximately 13 in 100.
Quality of life (difference in change from baseline) 3 months	Measured by: EQ5D VAS- Scale: 0-100 High better Minimally important difference 15 Based on data from 120 patients in 1 studies Follow up 3 months	**8.0 points (Mean)**	**14.0 points (Mean)** **Difference: Mean difference 6.0 greater** (CI 95% 1.5 fewer - 13.5 more)	**Low** Due to serious risk of bias, Due to serious imprecision	Knee arthroscopy may have, on average, little or no difference on QoL change, compared to control.
Pain and function up to 3 months	Based on data from 316 patients in 3 studies Follow up up to 3 months	Three studies evaluated the effects of knee arthroscopy in pain and function using measures that combined these two outcomes together or that could not be pooled. One study reported a difference in change from baseline in the Oxford knee score that favoured arthroscopy by 4.9 points (95% CI 3.61; 6.20, 114 patients) over steroids		**Moderate** Due to serious risk of bias	Knee arthroscopy probably has little or no difference in pain and function when compared to control

		injections. A second study reported no differences in the median in an overall self- assessment based on a 7-point ordinal scale (82 patients) when comparing knee arthroscopy to exercise therapy. The third study reported that patients who received intra-articular hyaluronic acid injections reported less pain than patients who received knee arthroscopy (120 patients)		
Long term				
Pain (difference in change from baseline) 1-2 years	Measured by: Different instruments converted to scale of index instrument (KOOS pain sub scale- Minimally Important Difference 12) Scale: 0-100 High better Based on data from 1097 patients in 8 studies Follow up 2 years	**19.0 points (Mean)** **22.0 points (Mean)** **Difference: Mean Difference 3.13 more** (CI 95% 0.17 fewer - 6.43 more)	**High**	On average, knee arthroscopy results in no difference, or a very small reduction, in pain
Function (difference in change from baseline) 1-2 years	Measured by: Different instruments converted to scale of index instrument (KOOS ADL sub scale- Minimally Important Difference 8) Scale: 0-100 High better Based on data from 843 patients in 6 studies Follow up 2 years	**10.0 points (Mean)** **13.0 points (Mean)** **Difference: Mean Difference 3.16 more** (CI 95% 0.48 less - 6.8 more)	**Moderate** Due to serious risk of bias and bordeline imprecision	On average, knee arthroscopy probably does results in no improvement, or a very small improvement, in function
Quality of life (difference in change from baseline) 1-2 years	Measured by: EQ5D VAS, 15D (converted to EQ5D scale- MID 15) Scale: 0-100 High better Based on data from 269 patients in 2 studies Follow up 1 year	**10.3 points (Mean)** **12.4 points (Mean)** **Difference: Mean Difference 2.12 more** (CI 95% 0.96 fewer - 5.21 more)	**High**	On average, knee arthroscopy does not result in an important improvement in quality of life
Knee replacement 1-2 years	Relative risk: 1.89 (CI 95% 0.51 - 7.0) Based on data from 497 patients in 2 studies Follow up 1 year	**12 per 1000** **23 per 1000** **Difference: 11 more per 1000** (CI 95% 107 more - 6 fewer)	**Moderate** Due to serious imprecision	On average, knee arthroscopy does not result in an increase in the risk of knee replacement
Pain and function 1-2 years	Based on data from 114 patients in 1 studies Follow up 1 year	One study measured pain and function using a composite score. The study showed that patients who receive arthroscopy have a change in Oxford knee score 2.6 points higher than patients receiving steroids injections (95% CI 1.14; 4.06)	**Moderate** Due to serious risk of bias	Knee arthroscopy probably has little or no difference on pain and function

Certainty of the evidence

There was high certainty in the estimates of effects for the outcome pain and moderate certainty in the estimates of effect for the outcome function. Although risk of bias due to lack of blinding that could affect the patient-reported outcomes was a concern in most of the trials, and the proportion of losses to follow-up was higher than desirable (Appendix Figure 15), for pain, trials with a low risk of bias reported similar

results to those in which there were risk of bias concerns (Appendix Figures 5 and 7). For function, there was less evidence from trials at low risk of bias, so we rated down our certainty in evidence for risk of bias (Appendix Figures 9 and 11)). In addition, the estimates for this outcome were imprecise. There was no evidence of publication bias (Appendix Figure 16)

The certainty of the estimates of quality of life was low in the short term due to risk of bias and imprecision, but high in the long term. The certainty of the estimates for knee replacement was moderate due to imprecision. Table 2 presents the details of the assessments per outcome.

Complications

Study Characteristics

The studies included in the complications systematic review reported data from a median of 20,770 patients. Average patient age ranged from 42[51] to 62.4[55] years, and the proportion of females from 39%[11] to 64.6%.[48] Table 3 presents detailed study characteristics.

Table 3: Characteristics of studies included in systematic review of complications

Study	Design	Number of patients	Age (mean)	% females
Basques, 2015[46]	Retrospective cohort (registry)	17774	53	46.9
Bohensky, 2014[47]	Retrospective cohort (registry)	139031	NR	42.5
Cancienne, 2016[48]	Prospective cohort	173216	NR	64.6
Hame, 2012[49]	Retrospective cohort (registry)	314578	NR	62
Hetsroni, 2011[50]	Retrospective cohort (registry)	418323	45.5	46.8
Hoppener, 2006[51]	Retrospective cohort (registry)	335	42	43.3
Jameson, 2011[52]	Retrospective cohort (registry)	261446	46	40.7
Katz, 2013[37]	RCT	174	59	55.9
Kise, 2016[11]	RCT	70	48.9	39
Krych, 2015[53]	Retrospective cohort (registry)	12595	NR	NR
Maletis, 2012[54]	Retrospective cohort (registry)	20770	44	42.8
Sihvonen, 2013[58]	RCT	70	52	58
Wai, 2002[55]	Retrospective cohort (registry)	14391	62.4	49.9
Yacub, 2009[56]	Retrospective cohort (registry)	12426	NR	57.3
Yeranosian, 2013[57]	Retrospective cohort (registry)	432038	NR	NR

Complications of knee arthroscopy

Table 4 provides a GRADE Summary of Findings for the complications of knee arthroscopy. Patients who underwent knee arthroscopy have an extremely small risk of death that is (<1 in 1000 95% CI 0; 1, n= 7 studies, 454,086 patients, Appendix Figure 17); a risk of VTE of 5 in 1000 (95% CI 2; 10, n= 11 studies, 1 119 920 patients, Appendix Figure 18); a risk of infection of 2 in 1000 (95% CI 1; 4, n= 5 studies, 603 838 patients, Appendix Figure 19); and an extremely small risk of nerve damage (<1 in 1000 95% CI 0; 1, n=1 study, 12 426 patients).

Table 4: Summary of findings for the complications of knee arthroscopy versus control in patients with degenerative knee disease

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conservative management / Arthroscopy	**Certainty in effect estimates** (Quality of evidence)	**Summary**
Mortality 3 months	Based on data from 454086 patients in 7 studies Follow up 3 months	**0 per 1000** / **0 per 1000** **Difference: <1 more per 1000** (CI 95% 0 more - 1 more)	**Low** Due to serious risk of bias and serious inconsistency	Arthroscopy may have an extremely small risk of mortality
Venous thromboembolism 3 months	Based on data from 1119920 patients in 11 studies Follow up 3 months	**0 per 1000** / **5 per 1000** **Difference: 5 more per 1000** (CI 95% 2 more - 10 more)	**Low** Due to serious risk of bias, Due to serious inconsistency	Arthroscopy may have a small risk for venous thromboembolism
Infection 3 months	Based on data from 603838 patients in 5 studies Follow up 3 months	**0 per 1000** / **2 per 1000** **Difference: 2 more per 1000** (CI 95% 1 more - 4 more)	**Low** Due to serious risk of bias, Due to serious inconsistency	Arthroscopy may have a very small risk for infection
Nerve damage 3 months	Based on data from 12426 patients in 1 studies Follow up 3 months	**0 per 1000** / **0 per 1000** **Difference: <1 more per 1000** (CI 95% 0 more - 1 more)	**Low** Due to serious risk of bias, Due to serious indirectness	Arthroscopy may have an extremely small risk of nerve damage

Certainty of the evidence

The estimates of complications of knee arthroscopy had low certainty. All studies suffered from risk of bias concerns, mainly due to the retrospective nature of the data collection (using data that had not been collected for the purposes of the study) (Appendix Figure 20). The studies informing mortality, VTE and infection showed inconsistent results from both a clinical and statistical perspective, which resulted in rating down the certainty for the pooled estimate. Finally, the only study informing nerve damage included patients with arthroscopy of the shoulder as well,[56] and therefore warranted rating down this estimate for indirectness. There was no evidence of publication bias (Appendix Figure 21). Table 4 presents details regarding the assessments of the certainty of the complications of knee arthroscopy per outcome.

DISCUSSION

This systematic review provides high quality evidence that patients with degenerative knee disease who undergo arthroscopy experience, on average, very small benefits in pain, function, and quality of life over

periods of up to three months when compared to patients who receive a conservative management strategy (Table 2). Results up to two years failed to show benefits in pain or function, and excluded any but very small benefits (Table 2). The median of the average pain change in patients receiving conservative management was 15 points in the short-term and 19 points in the long term (MID 12 points). Thus, whether patients receive arthroscopy or not, the clinical trial experience suggests, on average, a small benefit in pain reduction over both the short and long term.

The results for function proved similar, with very small average differences in the short term, and no convincing evidence of benefit in the long term (Table 2). Patients who received a conservative management strategy had a median average change of 9 points in the short term and 10 points in the long term, corresponding (minimally important difference 8 points). Risk of bias limitations leave this evidence less secure (moderate quality) than for pain.

Study results provide high quality evidence that the benefits of arthroscopic surgery on quality of life over the long term are minimal, if they exist at all (Table 2). Low quality evidence raises the possibility of a higher risk of knee replacement with arthroscopic surgery.

We found a low risk of serious adverse effects in patients undergoing knee arthroscopy. The risk of mortality and nerve damage may be close to 0, while the risk of VTE and infection may be 5 and 2 in 1000 patients, respectively. We have low certainty in this evidence, however, because the studies included were likely to be biased and showed results that were inconsistent.

Our systematic review has particular strengths. First, it provides the most comprehensive and trustworthy body of evidence up to date, including 10 studies not included in the most recent prior review.[13] While the conclusions of our systematic review may not be qualitatively different from the conclusions of previous reviews addressing the same question, we believe that all the additions in terms of studies included and methods for summarizing, presenting, and appraising the evidence strengthen the conclusions derived from this body of evidence considerably. Second, this systematic review was developed in parallel with a BMJ Rapid Recommendation according to predefined standards, methods and processes.[10] Extensive input from content experts and patients in the guideline panel throughout the process secured appropriate selection of outcomes and analyses as well as appropriate interpretation of the results from the systematic review. The Rapid Recommendations published together with our linked systematic review should provide clinicians and their patients with optimal guidance in practice and will also allow other guideline organizations to re-use or adapt content to their contexts, if needed. Third, by converting all the

instruments to the scale of an index instrument we do not only overcome the potential limitations of using the standardized mean difference (namely, the analysis depending on a similar standard deviation across studies, and the resulting measure of effect being difficult to interpret), but also provide an estimate of the proportion of patients who would achieve a minimally important change per arm, and the difference between these proportions. This allows incorporating patients' values and preferences explicitly when interpreting the results. A rigorous linked systematic review of studies addressing the issue informed our estimates of the minimally important change[14] and our results were robust to accounting for the uncertainty in the MID, as well as to calculating the proportion who might benefit using an approach relying on the standardized mean difference. Fourth, we provide an explicit and transparent assessment of the certainty in the absolute estimates of effect, which considers limitations of the evidence with regards to risk of bias, inconsistency, imprecision, indirectness, and publication bias.[61]

Our review is limited by suboptimal reporting in many of the original studies, requiring imputing standard deviations and, in a number of studies, estimating correlations between baseline and follow-up. It is possible that there is a subgroup of patients – for instance, those with locking symptoms – who do achieve substantial benefit from arthroscopic knee surgery. The available studies do not, however, provide evidence of any such subgroup. The burden of proof now rests with those who claim that such a subpopulation exists, with compelling RCT evidence required to substantiate the claim.

In summary, our results provide low quality evidence that knee arthroscopy is a safe procedure with a low risk of complications and moderate to high quality evidence that the procedure provides very small benefits in pain and function over conservative therapy in the short term. The evidence fails to support a persistence of these benefits over the long term. Patients and their health care providers must trade off the marginal short term benefits against the burden of the surgical procedure (pain, swelling, limited mobility, restriction of activities, over a period of 2 to 6 weeks).

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CONTRIBUTORSHIP STATEMENT: GHG and POV conceived the study idea. RBP performed the literature search. SS, BS, YC, NE and RBP performed screening, data abstraction and risk of bias assessments. RBP performed the data analysis. RBP, RB and GHG interpreted the data analysis. RBP and GHG interpreted the data performed certainty of evidence assessments. RBP wrote the first draft of

the manuscript. GHG, POV, RB, and RP critically revised the manuscript. All authors approved the final version of the manuscript. RBP had full access to all of the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. RBP is guarantor.

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TRANSPARENCY DECLARATION: RBP affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

DATA SHARING STATEMENT: Extra data is available in the publication of the BMJ Rapid Recommendation in MAGICapp.

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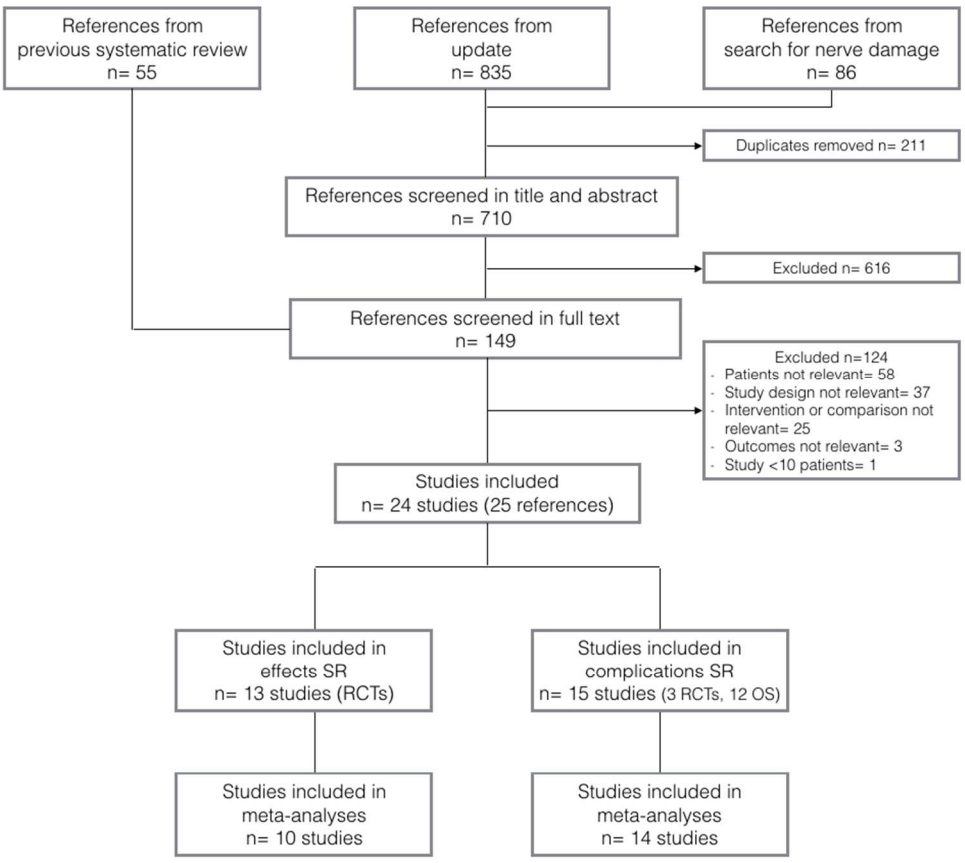
FIGURES LEGENDS

Figure 1: Study selection process



Study selection process
Figure 1
346x306mm (72 x 72 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3,5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5,6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	26-28
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9,25
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-10, 15-16
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15, 17, 41, 44
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	30-31, 39-40, 42-43
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-13, 16-17, 30-31, 39-40, 44-43
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15, 17
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-12, 29, 32-39
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17, 18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix 1: Search strategies

Update of effects and complications of knee arthroscopy

MEDLINE (Pubmed)

1. (((((("Menisci, Tibial/surgery"[MeSH Major Topic]) OR ("Menisci, Tibial/injuries"[MeSH Major Topic]) OR ("Degenerative meniscal tear"[Title/Abstract]) OR ("Arthroscopic lavage"[Title/Abstract]) OR ("Arthroscopic debridement"[Title/Abstract]) OR ("arthroscopic meniscectomy"[Title/Abstract]) OR ((arthroscopy[Title/Abstract]) AND knee[Title/Abstract]))
2. (("Randomized"[Title/Abstract]) OR ("Randomized controlled trial"[Publication Type]) OR ("randomized controlled trials as topic"[MeSH Major Topic]) OR ("Random allocation"[MeSH Major Topic]) OR ("Control group"[Title/Abstract]) OR ("Control groups"[MeSH Terms]) OR ("Cross-over studies"[Title/Abstract]) OR ("Cross-over study"[Title/Abstract])))
3. ((("Menisci, Tibial/surgery"[MeSH Major Topic]) OR ("Menisci, Tibial/injuries"[MeSH Major Topic]) OR ("Degenerative meniscal tear"[Title/Abstract]) OR ("Arthroscopic lavage"[Title/Abstract]) OR ("Arthroscopic debridement"[Title/Abstract]) OR ("arthroscopic meniscectomy"[Title/Abstract]) OR ((arthroscopy[Title/Abstract]) AND knee[Title/Abstract]))
4. (("adverse events"[Title/Abstract]) OR ("side effects"[Title/Abstract]) OR ("adverse effects"[Title/Abstract]) OR (complication*[Title/Abstract]) OR ("adverse effects"[MeSH Subheading])))))
5. 1 AND 2
6. 3 AND 4
7. 5 OR 6

EMBASE (Ovid)

1. Arthroscopic meniscectomy.ti,ab,kw.

2. Arthroscopic debridement.ti,ab,kw.

3. Arthroscopic lavage.ti,ab,kw.

4. Degenerative meniscal tear.ti,ab,kw.

5. knee meniscus/ or meniscus tibial.mp.

6. exp knee arthroscopy/

7. 1 or 2 or 3 or 4 or 5 or 6

8. randomized controlled trial/

9. randomized.ti,ab,kw.

10. randomised.ti,ab,kw.

11. Random allocation.mp.

12. randomised.mp.

13. "randomized controlled trial (topic)"/

14. Control group.mp.

15. control group/

16. crossover procedure/

17. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16

18. adverse events.mp.

19. side effects.mp.

20. adverse effects.mp.

21. complications.mp.

22. 18 or 19 or 20 or 21

23. 7 and 17

24. 7 and 22

25. 23 or 24

26. limit 25 to yr="2014-2016"

Cochrane Central Register of Controlled Trials

#1 MeSH descriptor: [Menisci, Tibial] explode all trees and with qualifier(s): [Injuries - IN, Surgery - SU]
#2 MeSH descriptor: [Arthroscopy] explode all trees
#3 MeSH descriptor: [Knee] explode all trees
#4 #2 and #3
#5 Degenerative meniscal tear:ti,ab,kw (Word variations have been searched)
#6 Arthroscopic lavage:ti,ab,kw (Word variations have been searched)
#7 Arthroscopic debridement:ti,ab,kw (Word variations have been searched)
#8 arthroscopic meniscectomy:ti,ab,kw (Word variations have been searched)
#9 #1 or #4 or #5 or #6 or #7 or #8 Publication Year from 2014 to 2016, in Trials

New search of outcome nerve damage

Medline Pubmed

("Peripheral Nerve Injuries"[Mesh]) AND ("Arthroplasty, Replacement, Knee/adverse effects"[Mesh] OR "knee arthroscopy" OR ("arthroscop*" AND "knee"))

Embase (Ovid)

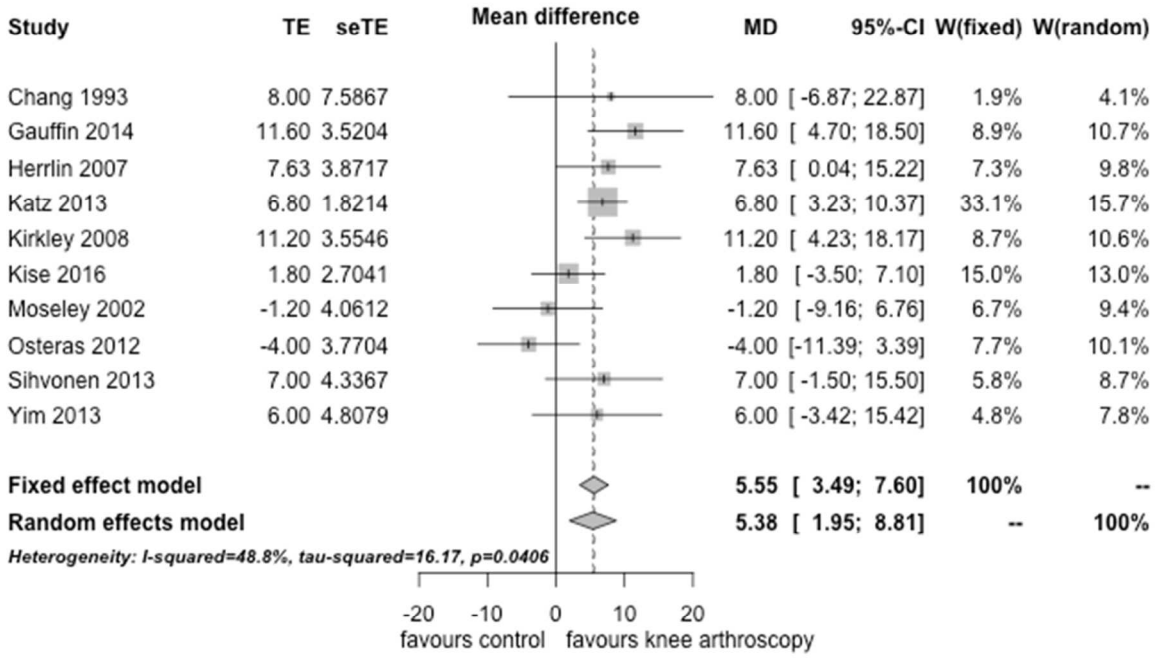
1. exp nerve injury/
2. exp knee arthroscopy/
3. 1 AND 2

Appendix 2: Results of sensitivity analyses to assess the robustness of the difference in the proportion of patients who reach a change higher than the MID

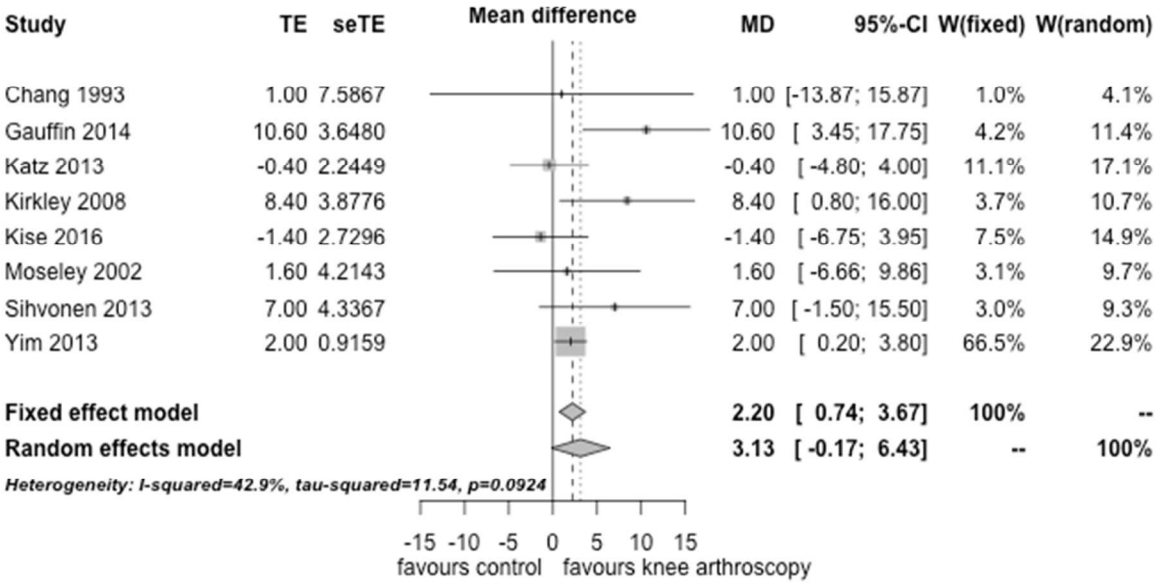
Outcome	MID (range)	Risk difference (95% CI))	Risk difference when using lowest value of the range (95% CI)	Risk difference when using highest value of the range (95% CI)	Risk difference based on the standardized mean difference* (95% CI)
Pain in the short term	KOOS pain[58] 12 (4; 20) WOMAC pain[61] 12 (2; 30)	12.4% (4.4; 20.4)	10.5% (4.3; 16.7))	11.3% (2.9; 19.7)	9% (1.7; 15.7)
Function in the short term	KOOS ADL[58] 8 (3; 9) WOMAC function[61 62] 13 (3; 34)	13.4% (4.4; 22.3)	11.3% (3; 19.5)	11% (2; 19.9)	7.3% (-0.06; 15.1)

*This method relies on the standardized mean difference. It does not use any specific threshold to calculate the risk difference.

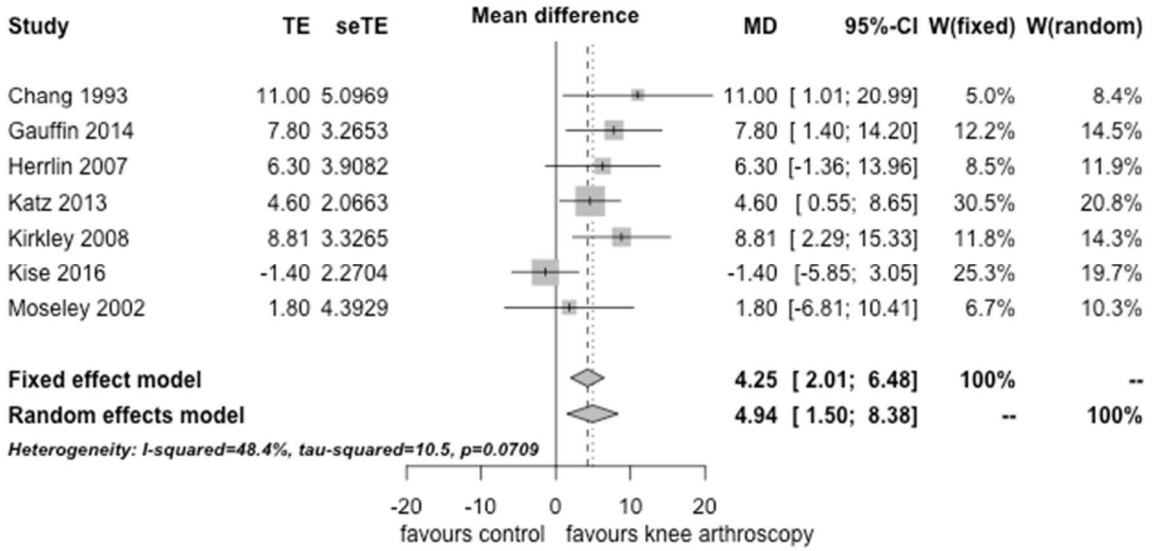
Appendix Figure 1: Meta-analysis of pain in the short-term (difference in change from baseline)



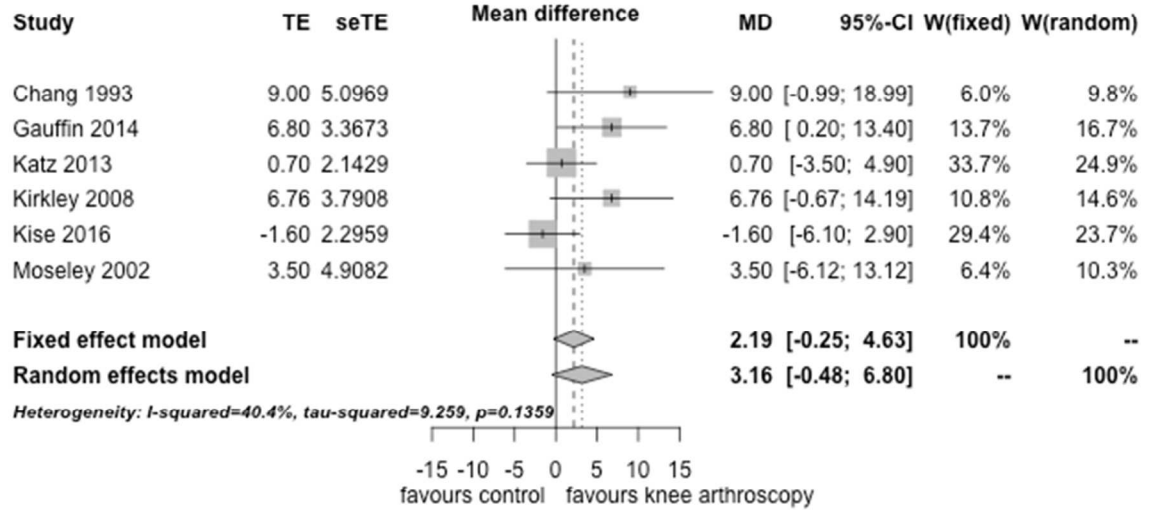
Appendix Figure 2: Meta-analysis of pain in the long-term (difference in change from baseline)



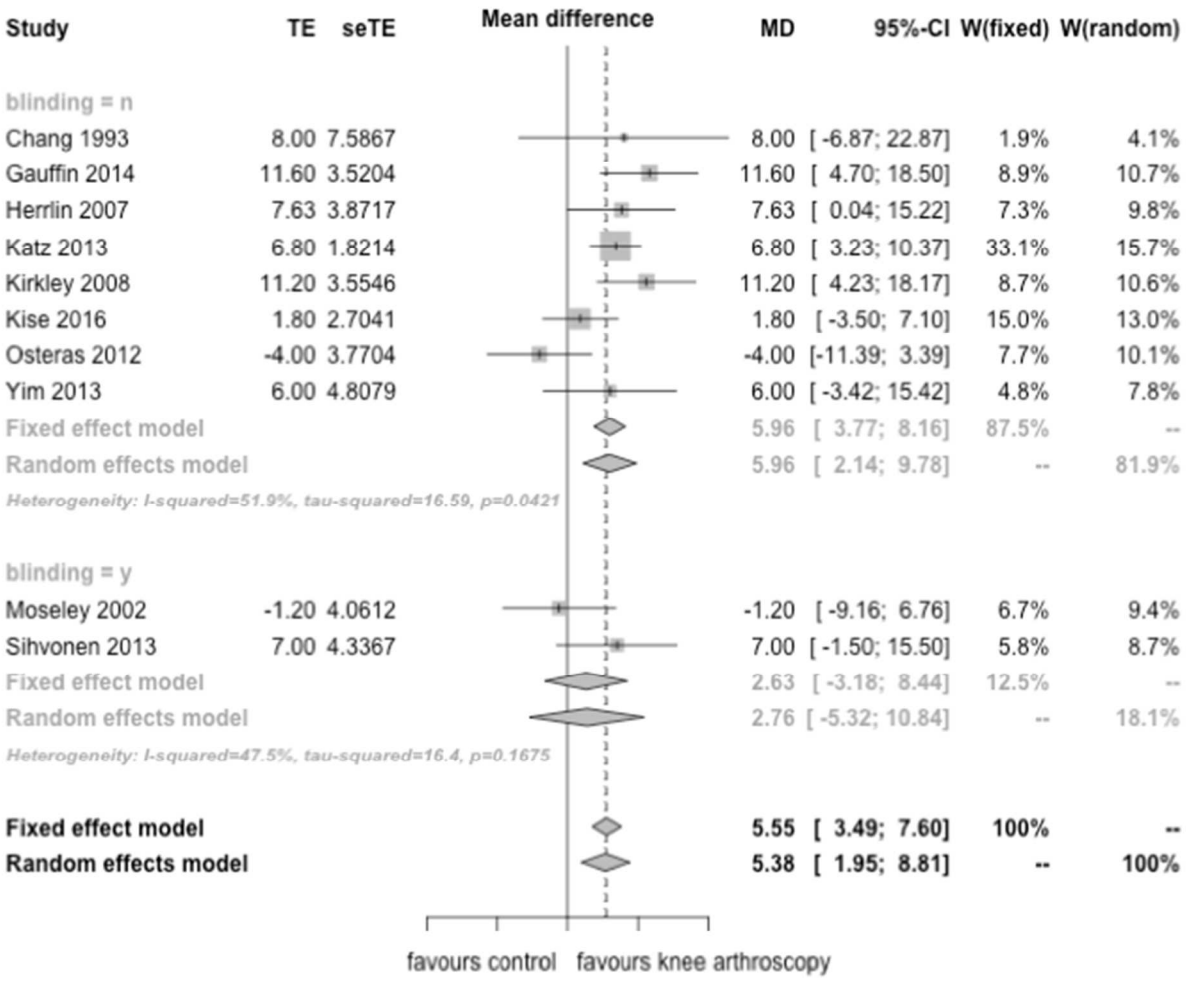
Appendix Figure 3: Meta-analysis of function in the short-term (difference in change from baseline)



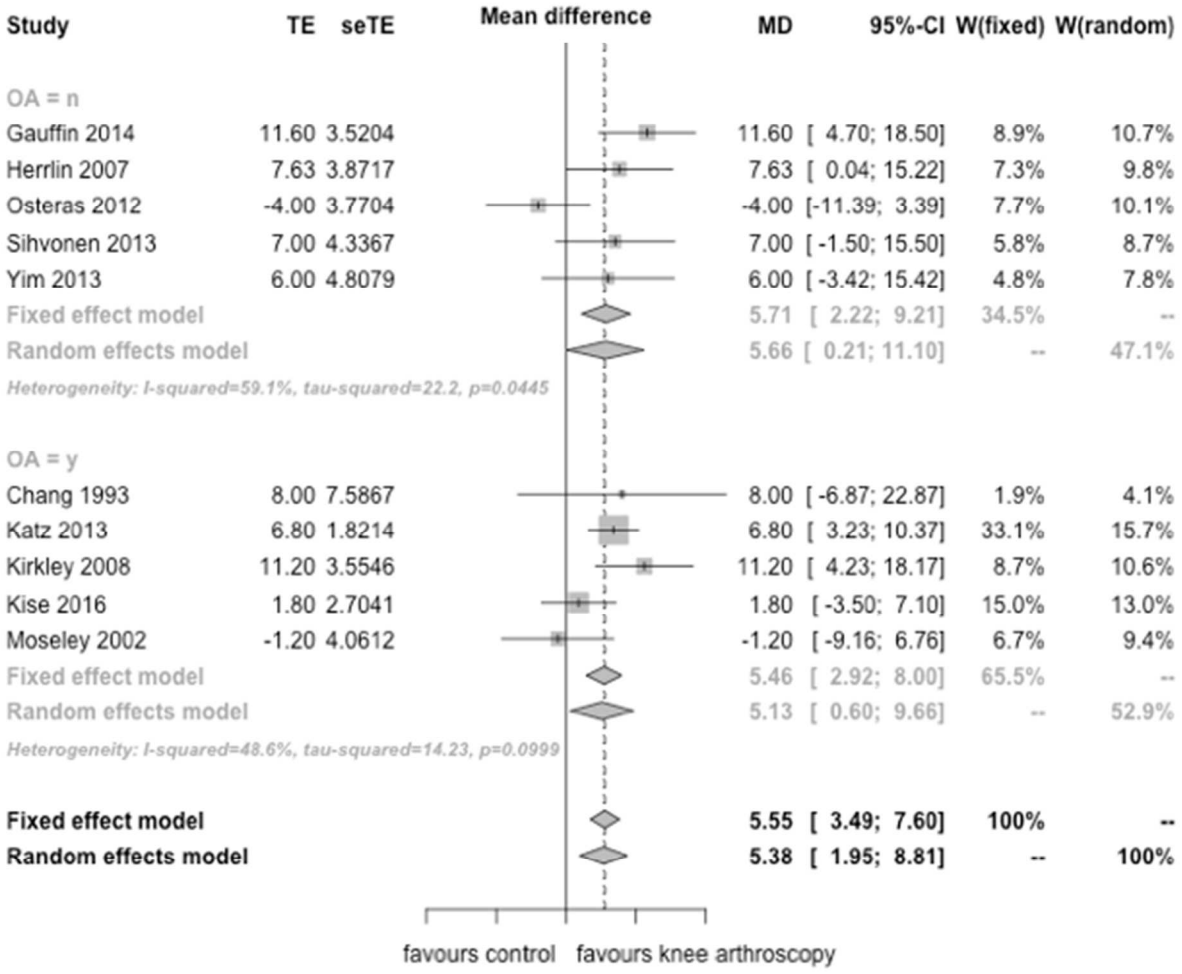
Appendix Figure 4: Meta-analysis of function in the long-term (difference in change from baseline)



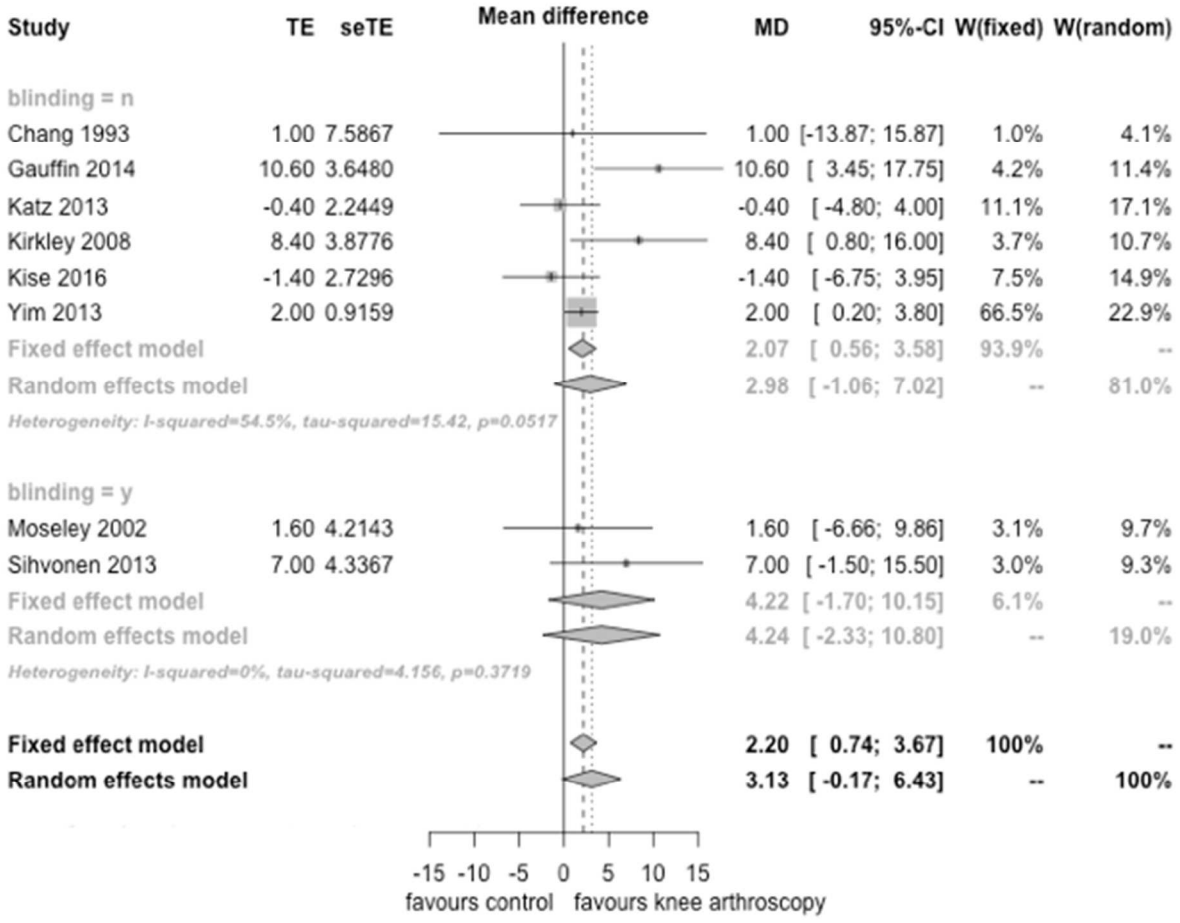
Appendix Figure 5: Subgroup analysis of pain in the short term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.48



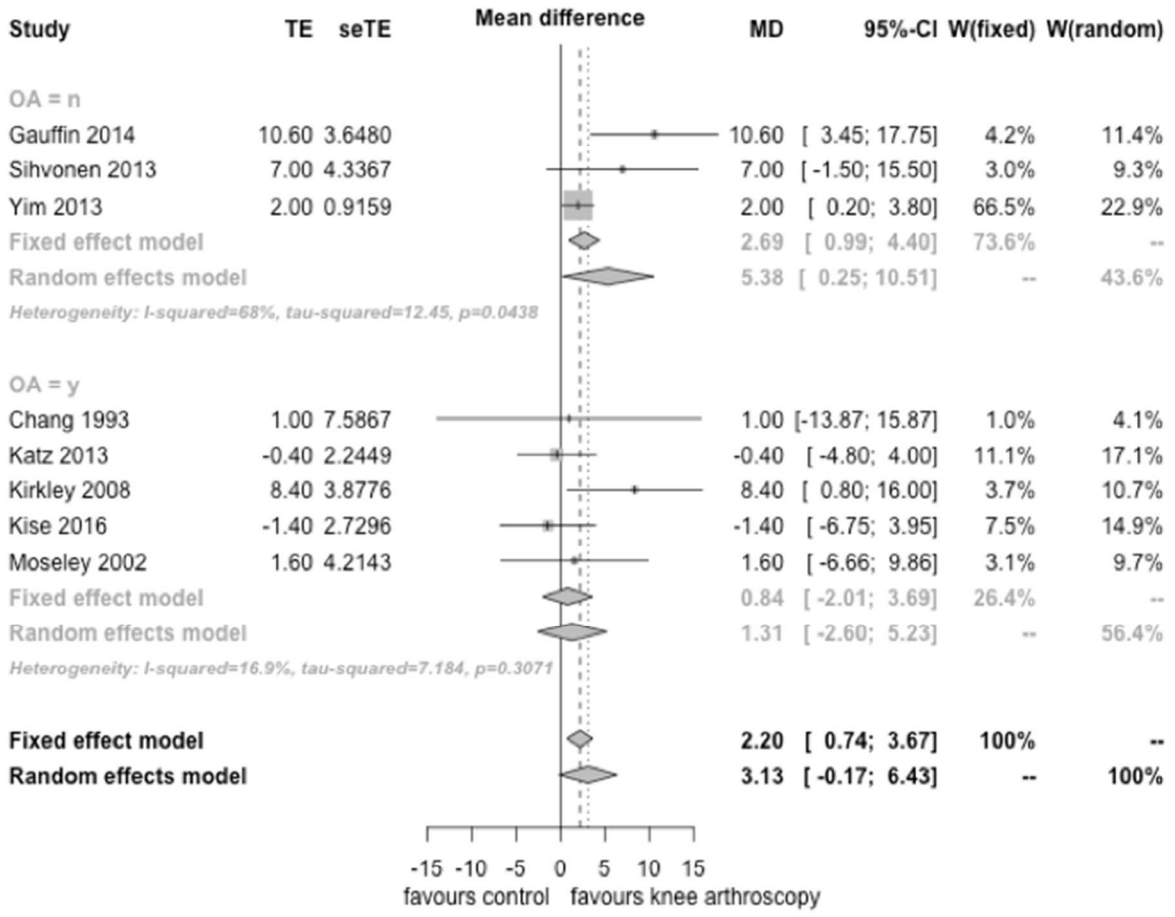
Appendix Figure 6: Subgroup analysis of pain in the short term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.88



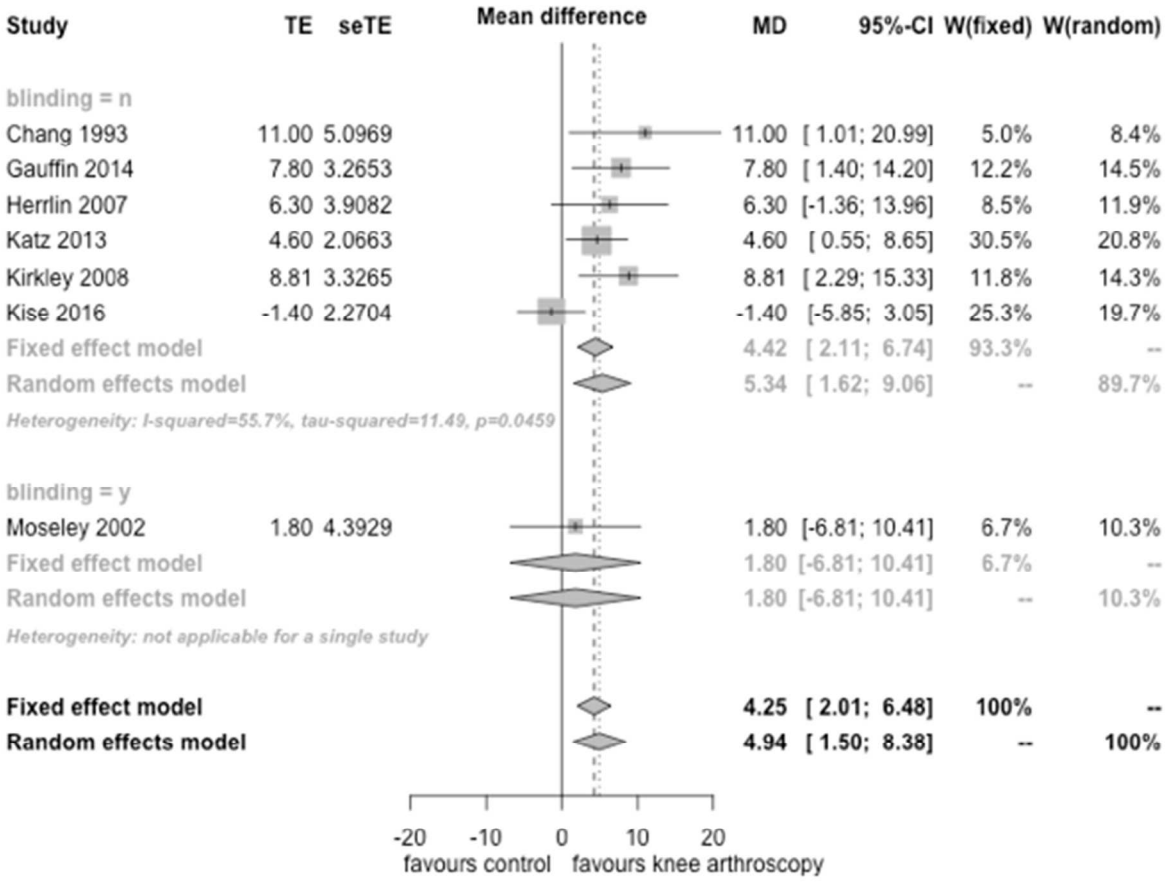
Appendix Figure 7: Subgroup analysis of pain in the long term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.75



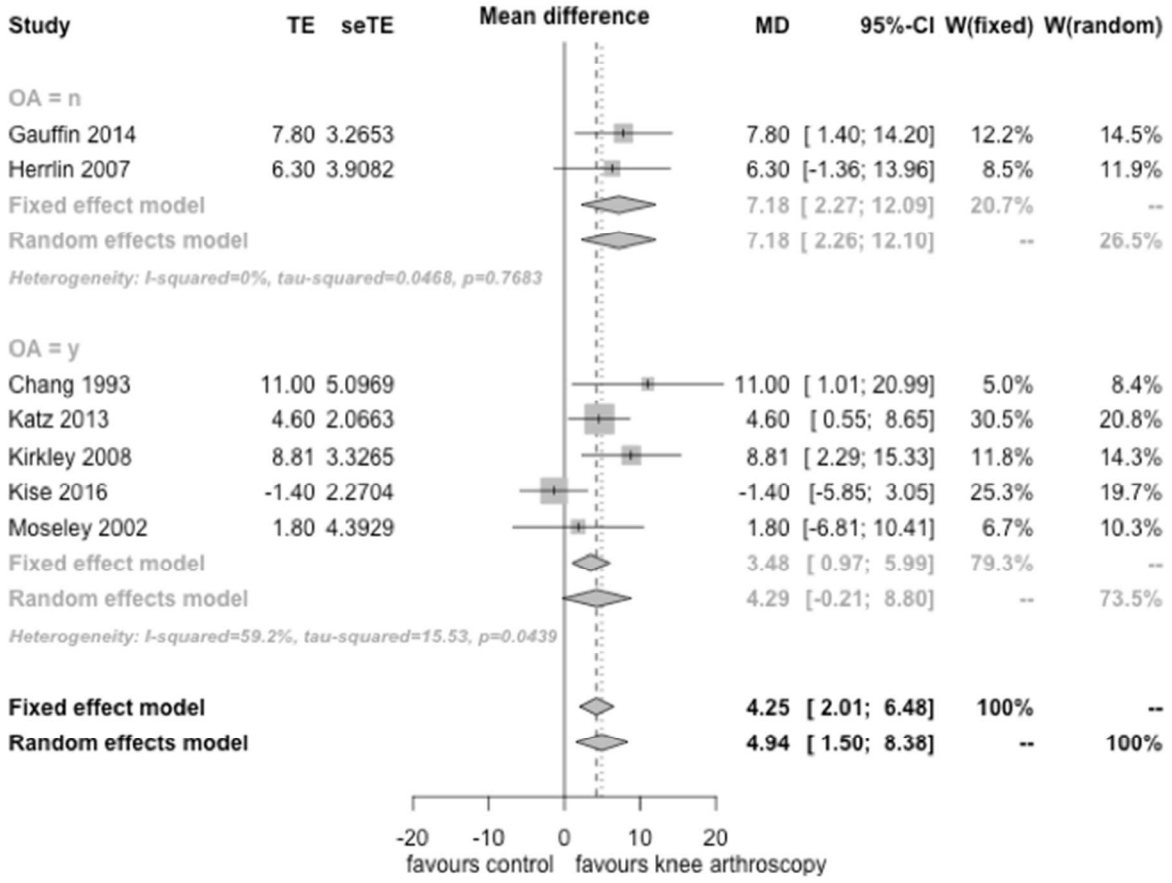
Appendix Figure 8: Subgroup analysis of pain in the long term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.22



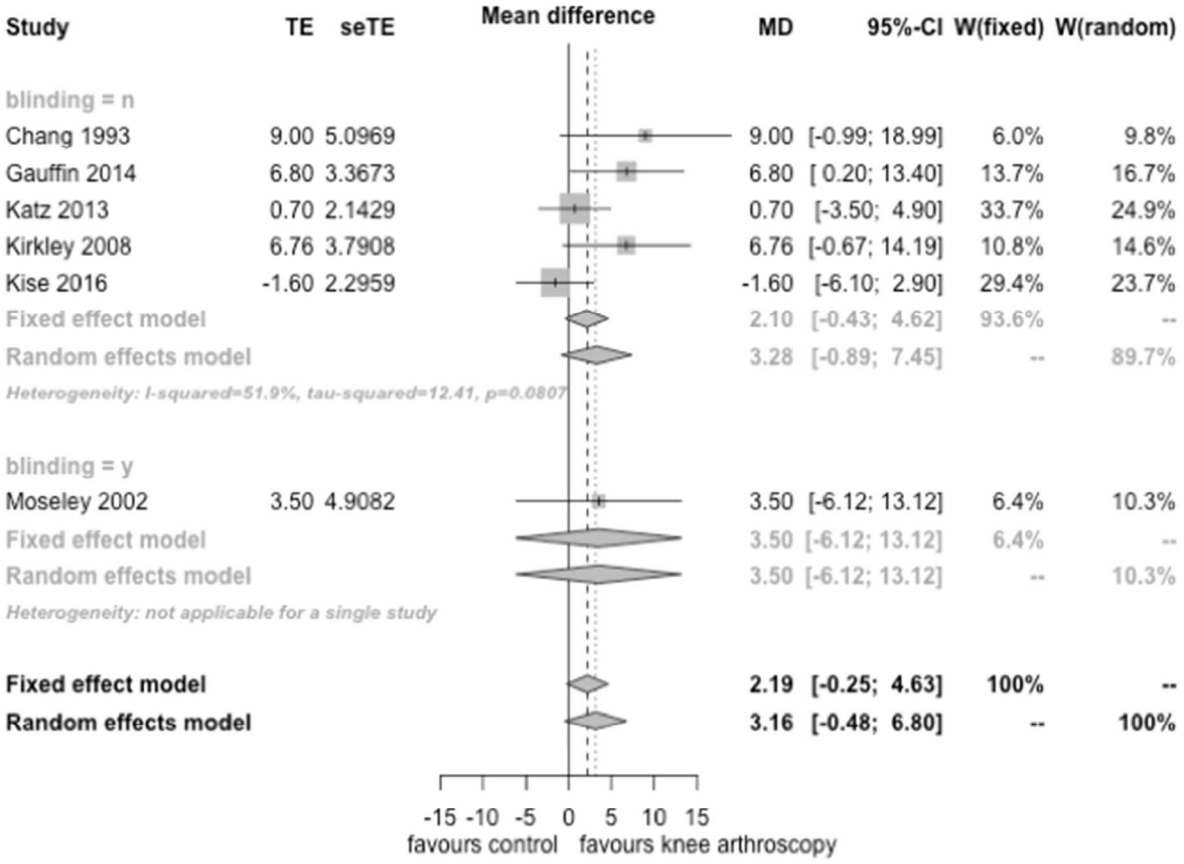
Appendix Figure 9: Subgroup analysis of function in the short term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.46



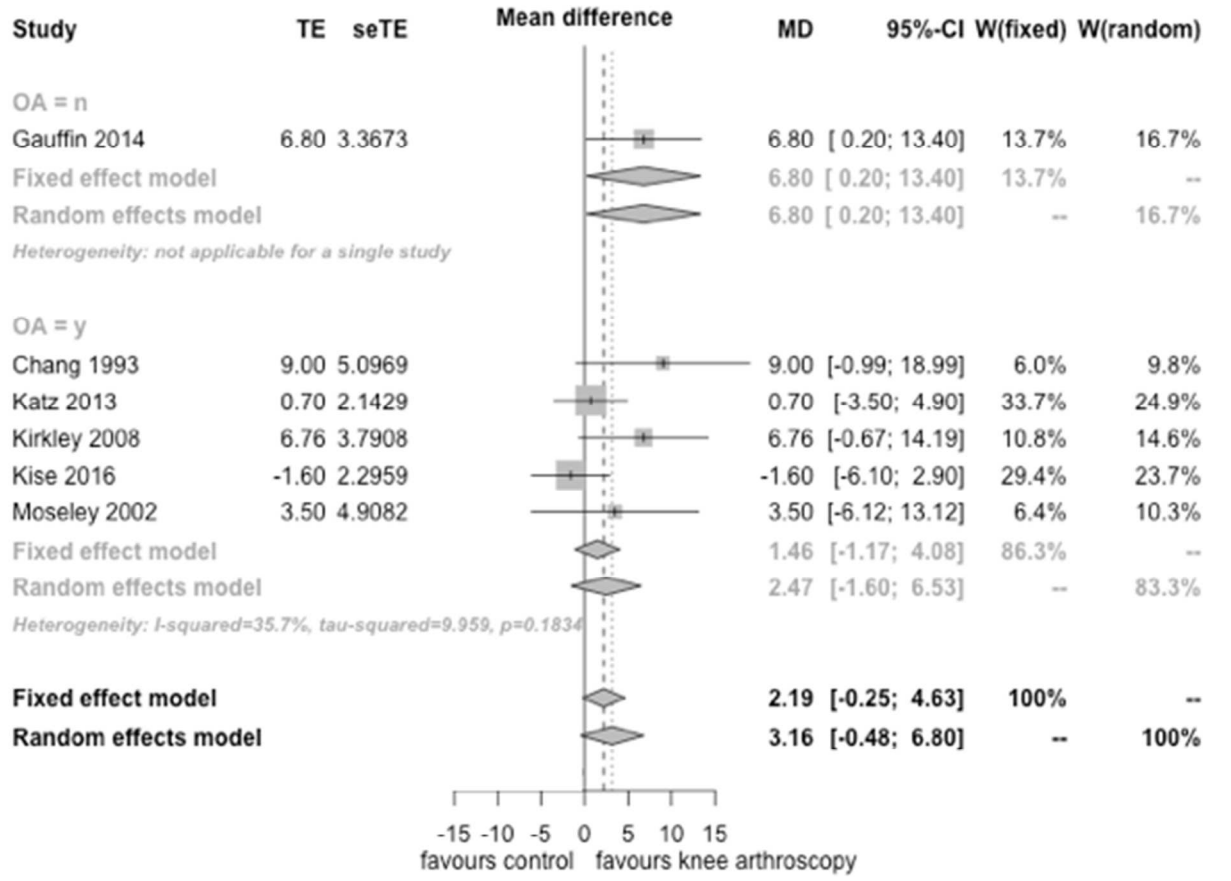
Appendix Figure 10: Subgroup analysis of function in the short term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.40



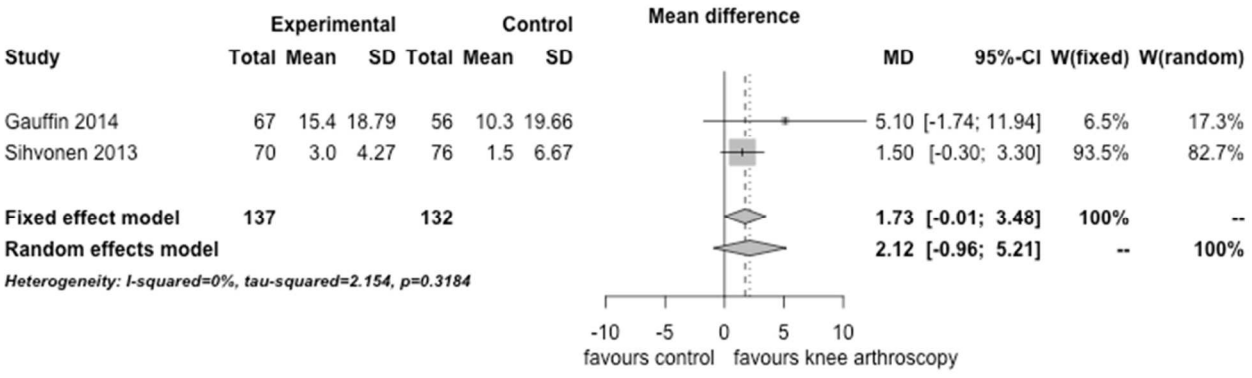
Appendix Figure 11: Subgroup analysis of function in the long term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.97



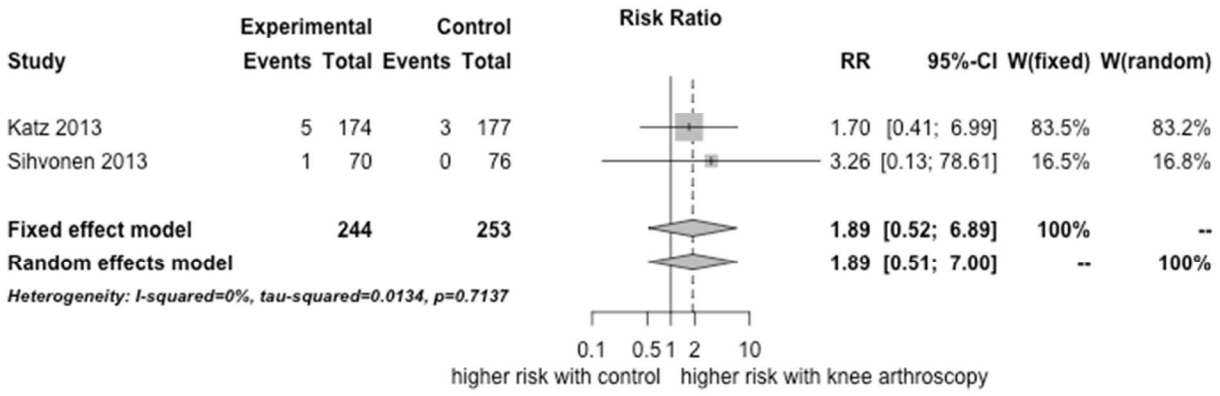
Appendix Figure 12: Subgroup analysis of function in the long term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.27



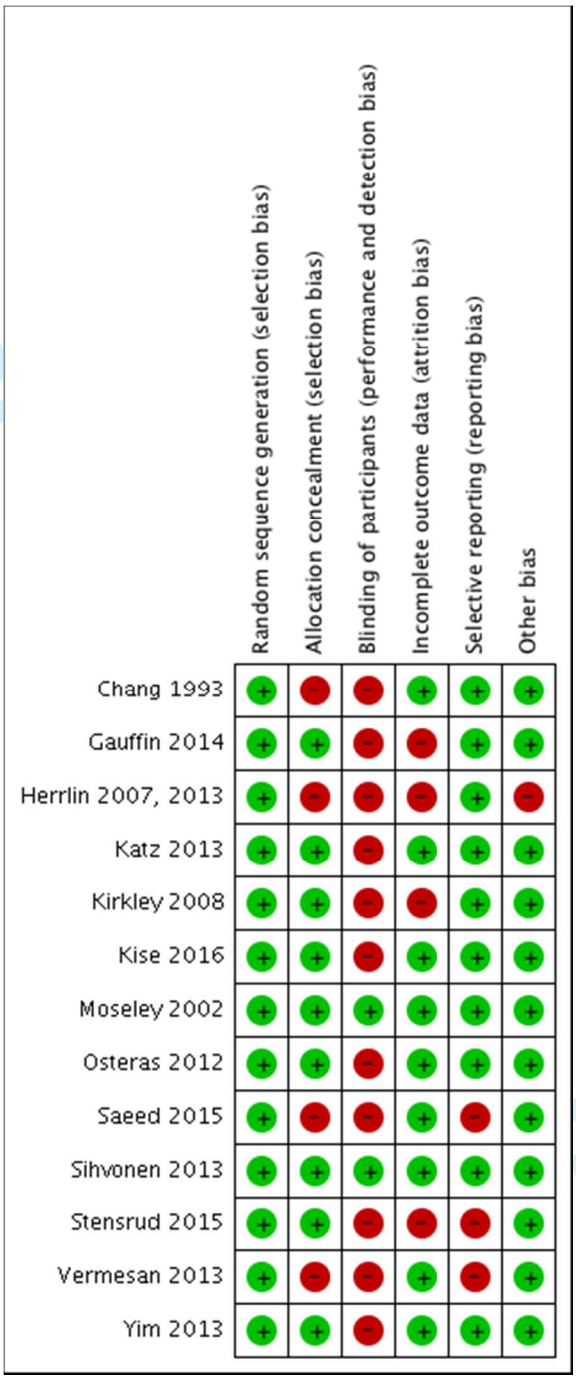
Appendix Figure 13: Meta-analysis of Quality of life in the long-term (difference in change from baseline)



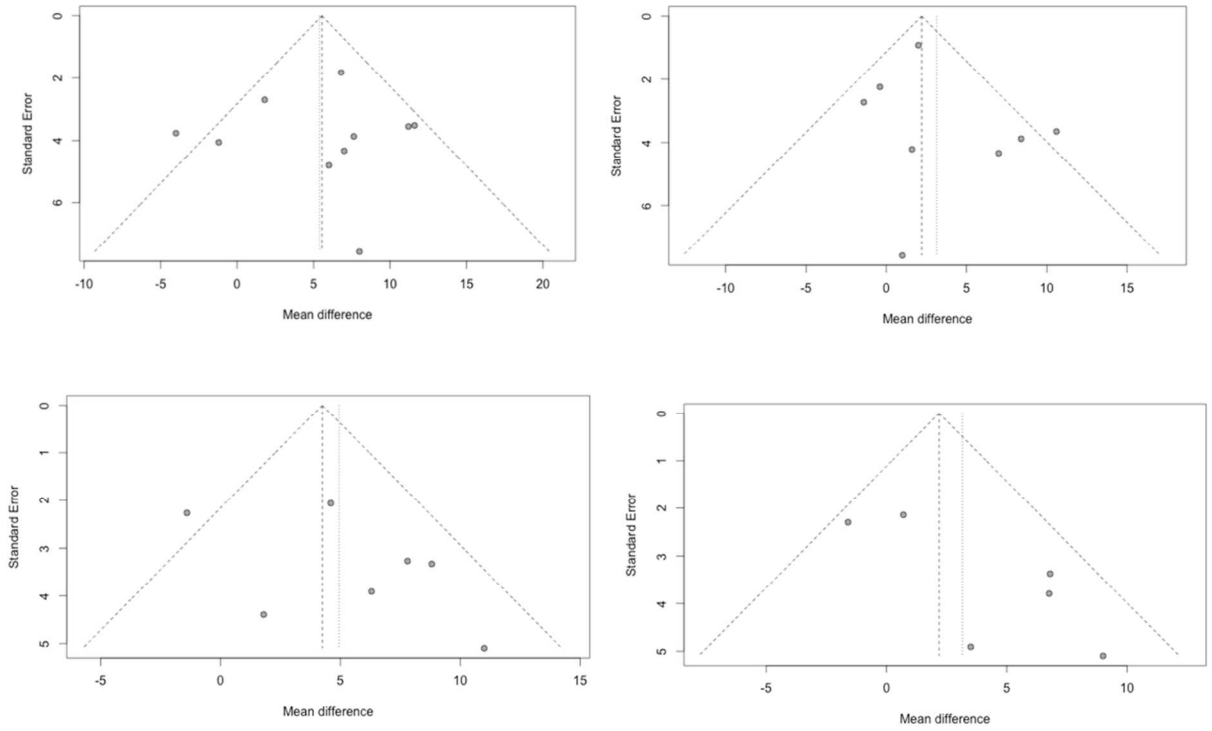
Appendix Figure 14: Meta-analysis of Knee Replacement



Appendix Figure 15: Risk of bias of studies included in the systematic review of effects of knee arthroscopy

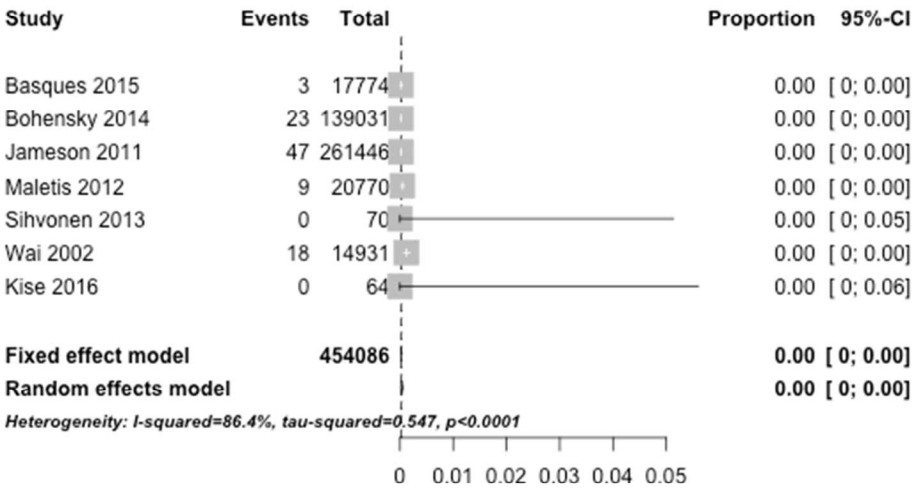


Appendix Figure 16: Funnel plots for publication bias assessments of effects of knee arthroscopy

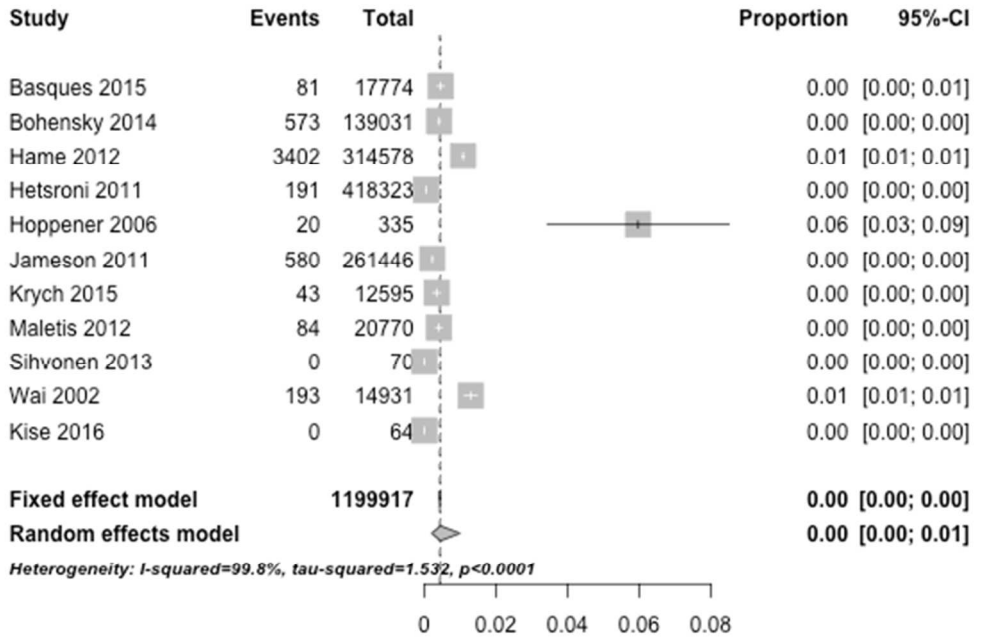


Top left: Short-term pain; Top right: Long-term pain; Bottom left: Short-term function; Bottom right: Long-term function

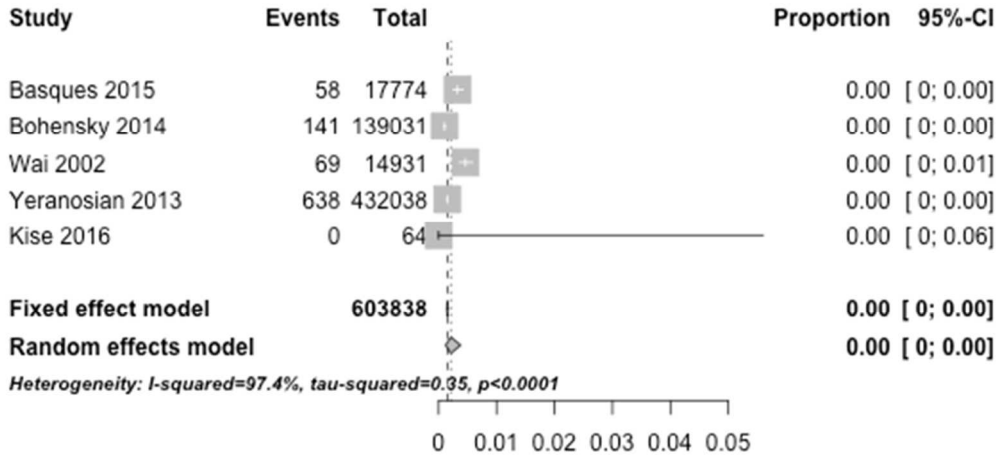
Appendix Figure 17: Meta-analysis of Mortality



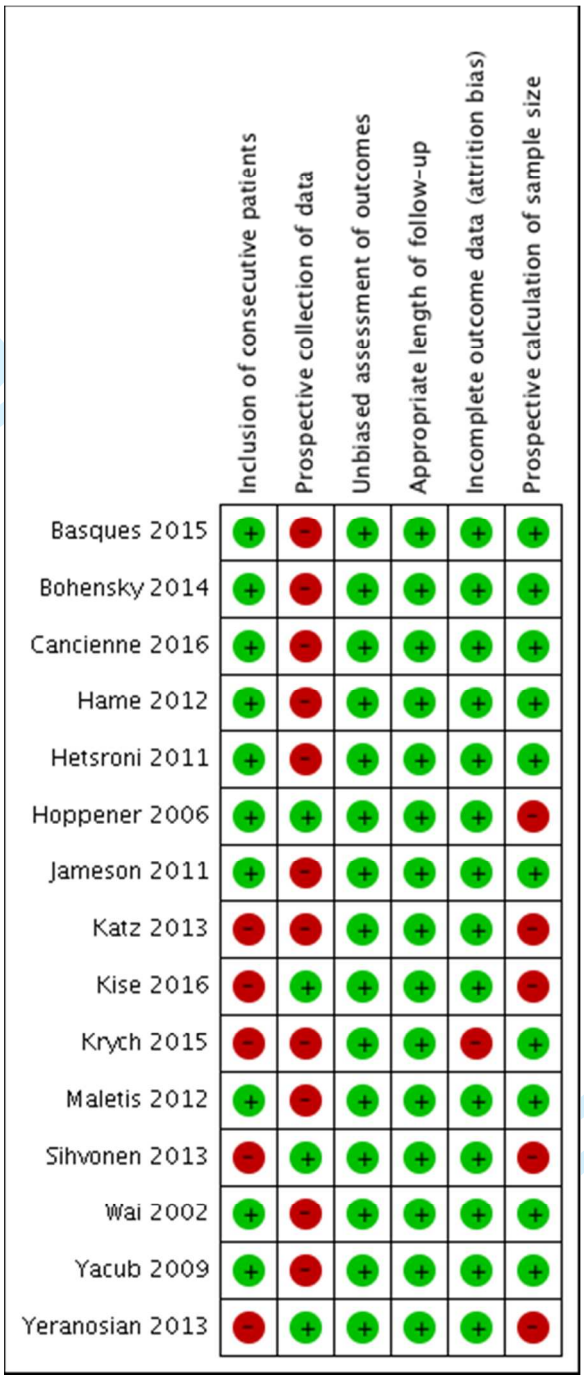
Appendix Figure 18: Meta-analysis of VTE



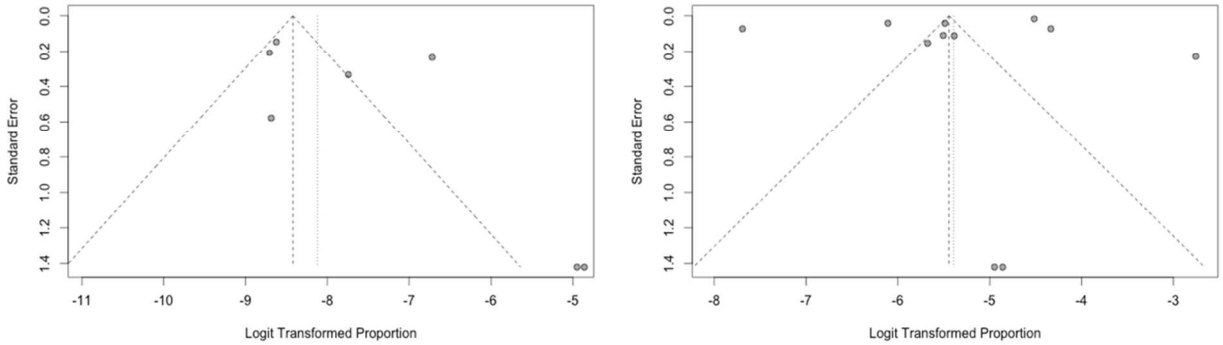
Appendix Figure 19: Meta-analysis of infection



Appendix Figure 20: Risk of bias of the studies included in the systematic review of complications of knee arthroscopy



Appendix Figure 21: Funnel plots for publication bias assessment of complications of knee arthroscopy



Left: Mortality; Right: VTE. Outliers represent the findings of two randomized clinical trials with small sample sizes and 0 events observed.

BMJ Open

Knee arthroscopy versus conservative management in patients with degenerative knee disease: a systematic review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016114.R1
Article Type:	Research
Date Submitted by the Author:	07-Feb-2017
Complete List of Authors:	Brignardello-Petersen, Romina; University of Toronto, Clinical Epidemiology and Health Care Research Siemieniuk, Reed; McMaster University, Clinical Epidemiology & Biostatistics; University of Toronto, Medicine Guyatt, Gordon; McMaster University, Buchbinder, Rachelle; Cabrini Hospital, Monash Department of Clinical Epidemiology Poolman, Rudolf; Onze Lieve Vrouwe Gasthuis, Orthopaedic Surgery Schandelmaier, Stefan; McMaster University Department of Clinical Epidemiology and Biostatistics Chang, Yaping; McMaster University, Department of Clinical Epidemiology and Biostatistics Sadeghirad, Behnam ; Kerman University of Medical Sciences, Research Center for Modeling in Health, Institute for Futures Studies in Health Evaniew, Nathan; McMaster University, Orthopaedic Surgery Vandvik, Per; Innlandet Hospital Trust-divisjon Gjøvik, Department of Medicine
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Evidence based practice, General practice / Family practice, Surgery, Sports and exercise medicine
Keywords:	Knee < ORTHOPAEDIC & TRAUMA SURGERY, arthritis, Osteoarthritis, knee pain, meniscus tear, GRADE

KNEE ARTHROSCOPY VERSUS CONSERVATIVE MANAGEMENT IN PATIENTS WITH DEGENERATIVE KNEE DISEASE: A SYSTEMATIC REVIEW

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ARTICLE SUMMARY

ABSTRACT

Objective: To determine the effects and complications of arthroscopic surgery compared to conservative management strategies in patients with degenerative knee disease

Design: Systematic review

Main Outcome Measures: Pain, function, adverse events

Data sources: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar and Open Grey up to August 2016.

Eligibility criteria: For effects, randomized clinical trials (RCTs) comparing arthroscopic surgery with a conservative management strategy (including sham surgery) in patients with degenerative knee disease. For complications, RCTs and observational studies.

Review methods: Two reviewers independently extracted data and assessed risk of bias for patient-important outcomes. A parallel guideline committee (*BMJ* Rapid Recommendations) provided input on the design and interpretation of the systematic review, including selection of patient-important outcomes. We used the GRADE approach to rate the certainty (quality) of the evidence.

Results: We included 13 RCTs and 12 observational studies. With respect to pain, the review identified high certainty evidence that knee arthroscopy results in a very small reduction in pain up to 3 months (mean difference= 5.4 on a 100-point scale, 95% CI 2.0; 8.8) and very small or no pain reduction up to 2 years (mean difference= 3.1, 95% CI -0.2; 6.4) when compared to conservative management. With respect to function, the review identified moderate certainty evidence that knee arthroscopy results in a very small improvement in the short-term (mean difference= 4.9 on a 100-point scale, 95% CI 1.5; 8.4) and very small or no improved function up to 2 years (3.2, 95% CI -0.5; 6.8). Alternative presentations of magnitude of effect, and associated sensitivity analyses, were consistent with the findings of the primary analysis. Low quality evidence suggested a very low probability of serious complications after knee arthroscopy.

Conclusion: Over the long term, patients who undergo knee arthroscopy versus those who receive conservative management strategies do not have important benefits in pain or function.

Systematic review registration: PROSPERO CRD42016046242

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This in an update of previously published systematic reviews on the topic.
- This review is linked to a BMJ Rapid Recommendations project. We conducted the review directed by a guideline panel that included patient representatives. This guideline panel provided detailed input with regards to the patients, interventions and outcomes, and the interpretation of the results from this review.
- We included 7 new studies, analyzed data focusing on clinical interpretability, and explicitly assessed the certainty in the estimates of effect.
- We performed meta-analyses using different measures of effect, and conducted subgroup and sensitivity analyses that strengthened our conclusions.

WHAT IS ALREADY KNOWN IN THIS TOPIC:

- Although systematic reviews have failed to establish that knee arthroscopy has clear benefits over conservative management strategies, orthopaedic surgeons often offer this procedure to patients with degenerative knee disease
- Current guideline recommendations on managements of knee pain and associated functional limitation provide conflicting guidance and exclude many patients with degenerative knee disease (eg. those with meniscal tears with or without radiographic evidence of osteoarthritis)

WHAT THIS STUDY ADDS

- Moderate to high certainty evidence shows that there are at best only very small differences in pain, function, and quality of life of patients who underwent knee arthroscopy compared to those who received conservative management strategies over the short term, and no benefit over the long term.
- Patients can expect, on average, to achieve small but important improvement over the period of two years, irrespective of what treatment they receive.
- Patients and their health care providers must trade off the marginal short-term benefits against the burden and potential complications of the surgical procedure

INTRODUCTION

As a result of degenerative knee disease (osteoarthritis in the knee which can involve the joint lining and/or menisci), approximately 25% of people over 45 years experience pain and other symptoms that may be severe and negatively impact quality of life.[1 2 3] Total knee arthroplasty is the only definitive therapy available, but is reserved for patients with severe disease who fail conservative management.

In the United States, arthroscopic knee surgery in people with degenerative knee disease is the most common ambulatory orthopaedic procedure, and the ninth most commonly performed ambulatory procedure overall. [4] Such surgery results in transient increase in pain and the necessity for restriction in activities for a period of 2 to 12 weeks.[5 6] Current guidelines recommend against arthroscopic lavage and/or debridement for patients with symptomatic knee osteoarthritis, but do not make specific recommendations for or against partial meniscectomy in those with degenerative meniscal tears (with or without other concomitant degenerative changes).[7 8] Further, many orthopedic surgeons suggest that patients with mechanical symptoms and meniscal tears – typically locking or catching of the knee – may benefit from arthroscopic partial meniscectomy.[9 10]

Our systematic review informs the second *BMJ* Rapid Recommendations,[11] a new *BMJ* series of trustworthy clinical practice recommendations published in response to potentially practice-changing evidence.[12] A trial that compared the outcomes of exercise therapy versus knee arthroscopic partial meniscectomy in 140 middle-aged patients with degenerative meniscal tears, published in July 2016 triggered this systematic review.[13] Previous systematic reviews addressing the impact of arthroscopic knee surgery did not consider all patient-important outcomes; did not consider patient importance when addressing patient-reported outcomes such as pain, function, and quality of life (QoL); and did not include all currently available randomized controlled trials (RCTs).[14 15]

To determine the effects and complications in patients with symptomatic degenerative knee disease, we performed a systematic review and meta-analysis of arthroscopic surgery with debridement, and/or partial meniscectomy compared to conservative management strategies.

METHODS

Readers can access the protocol of this systematic review in PROSPERO (CRD42016046242). According to the *BMJ* Rapid Recommendations process,[12] a guideline panel provided critical oversight to the review and identified populations, subgroups, and outcomes of interest. The panel included eight content experts and front line clinicians (three orthopaedic surgeons, one rheumatologist, one epidemiologist, one general practitioner and two physiotherapists), four methodologists (three of them whom are also front line clinicians and general internists) and three patients with lived experience of degenerative knee disease.

All patients received personal training and support to optimize contributions throughout the guideline development process. The patient panel members led the interpretation of the results based on what they expected the typical patient values and preferences to be, as well as the variation between patients. We also considered patients' values and preferences by using the minimally important difference (MID) to interpret the results obtained in the meta-analyses. These MIDs were obtained from a systematic review of studies in which patients were directly asked about the magnitude of change they had experienced, and whether that change was trivial, small but important, or larger.[16] Clinical experts who were part of the team of that systematic review judged the applicability of such studies to the target population and raised no concerns.

Eligibility criteria

For the effects of arthroscopic surgery, we included RCTs comparing arthroscopic surgery, including any or all of debridement and/or partial meniscectomy to any conservative management strategy (exercise therapy, injections, drugs, sham surgery) in patients with symptomatic degenerative knee disease (defined as persistent knee pain that affects the patient's quality of life and does not respond to conservative treatment), with or without osteoarthritis, of any age. We excluded studies that enrolled patients with acute trauma and those that enrolled fewer than 10 patients. For the complications of arthroscopic surgery, we also included observational studies (cohort studies, registry studies, and case series) in patients with degenerative knee disease undergoing arthroscopic surgery, with or without a comparison group. We excluded studies published before the year 2000 when considering complications (but not effects).

Literature search

We performed an update of a previously published systematic review[15] including MEDLINE (Pubmed), EMBASE (Ovid) and CENTRAL (See Appendix 1) from January 1 2014, to August 16, 2016. In addition, we constructed specific search strategies for these three databases for one outcome not studied in the previous review (nerve damage), with no date limits. We also searched for grey literature using the first 500 hits from Google Scholar and Open Grey. We did not limit any of the searches by language of publication.

Study selection and data abstraction

Teams of two reviewers, working independently, performed all study selection and data abstraction using standardized forms, and reviewed the titles and abstract of all the references resulting from the searches. We retrieved and reviewed the full text of all references identified as potentially eligible by at least one reviewer. We also reviewed the full text of all references excluded at the full text screening stage in the prior review.[17] We included all studies judged as eligible by the two reviewers. Reviewers resolved disagreements by discussion.

Reviewers abstracted characteristics of eligible studies including study design, number of patients enrolled, age and sex distribution, number of patients followed-up, whether partial meniscectomy was performed, co-interventions, and outcomes, including pain, function, quality of life, and knee replacement. When authors reported results from more than one measure of pain or function, we decided a priori to use only the measure ranked highest in a hierarchy of patient-reported outcomes specific to the patients of interest.[18] When studies had more than two arms, we only used the data from the arms relevant

to this study. The review addressed these outcomes at 3 months or less, and at the longest follow-up reported.

The review addressed complication outcomes of mortality, venous thromboembolism (VTE), infection, and nerve damage. Reviewers abstracted the absolute number of patients who experienced the outcomes over the follow-up period. When studies did not report VTE but reported pulmonary embolism and deep-vein thrombosis separately instead, we used these numbers to estimate the number of VTEs, considering the potential overlap due to patients experiencing both.[19] We examined these outcomes over the three months following surgery.

Summary measures and data synthesis

We summarized continuous outcomes (pain, function and quality of life) at the study level using the difference in change from baseline between groups. When baseline mean and standard deviation per group at baseline and follow-up, but not change measures, were available, we assumed a within group correlation of 0.5 to estimate the standard deviation of the change from baseline per study arm. If arm level data were not reported, we abstracted the difference in change from baseline between the groups. When standard deviations at follow up were not reported, we assumed the same standard deviation as at baseline. When no standard deviations were available, we used the weighted average from all the other RCTs measuring the outcome with the same instrument. When studies reported medians and interquartile ranges, we converted to means and standard deviations.[20]

We performed meta-analyses, and present results for patient reported continuous outcomes in two ways. First, we transformed all scores to the scale of an index instrument, the highest in the hierarchy, and pooled results of all studies using the mean difference as the summary measure. This resulted in scores that could range from 0 to 100, in which higher scores signified better outcomes (less pain, better function, better quality of life). Second, we used the minimally important difference (MID) of each of the instruments to determine the proportion of patients who reached a change in the outcome that was larger than a MID. To inform this analysis, a parallel team performed a linked systematic review to establish the most credible MIDs for each of the instruments used to measure pain, function, and QoL. The most credible MID was the median of all the credible MIDs. Details of this review are available in a publication related to this *BMJ* Rapid Recommendation.[16] We then estimated and pooled the difference in the proportion of patients between groups achieving this difference.[17] When no credible MID was found for a particular instrument, we used the MID of the index instrument. Data for time-to-knee replacement was not available, so we summarized the data for knee replacement using the proportion of patients who

had the outcome per group and pooled those data using relative risk as the summary measure. These meta-analyses were performed using random effects models using the Hartung-Knapp-Sidik-Jonkman method.[21 22] All analyses were performed using an intention-to-treat approach. When authors did not report data in a way that allowed incorporation it in the meta-analyses, we summarized the results narratively.

For complications, we used the number of patients having the event and the total number of patients undergoing knee arthroscopy, and pooled these data using a generalized linear mixed effects model that allowed inclusion of studies with no events without a continuity correction.[23]

We planned to perform four subgroup analyses for the outcomes pain and function: trials in which there was more than 50% of patients with radiographic osteoarthritis (defined as Kellgren-Lawrence grades 2 to 4) versus trials with equal or less than 50% of patients with radiographic osteoarthritis; trials in which patients were blinded versus not blinded; trials in which meniscectomy was performed versus those in which it was not; and trials in which a control group received an active intervention (e.g. exercise therapy, injections) versus control groups without such interventions (e.g. waiting list, no treatment). We performed sensitivity analyses for calculating the difference in patients who achieve a change higher than the MID in two ways: 1) using the lowest and highest value of the MID of each instrument, based on the range of the MIDs that were deemed credible, and 2) calculating the standardized mean difference and then transforming the standardized mean difference into a risk difference[17] (this method does not use an MID). All data analyses used the package *meta* in the software R, version 3.3.1.[24]

Certainty of the evidence assessments

We assessed the certainty of the estimates of effect (quality of evidence) using the GRADE approach.[25] We considered potential limitations in risk of bias, inconsistency, imprecision, indirectness, and publication bias. [26-29] We used a modification of the Cochrane Risk of Bias tool[30] to assess the risk of bias of the studies informing on the effects of arthroscopic surgery, and the relevant items of the Methodological Index for Non-Randomized Studies (MINORS) tool[31] to assess the risk of bias of the studies informing on the complications of knee arthroscopy. All authors, in consultation with the parallel *BMJ* Rapid Recommendation guideline panel[32] participated in, and came to consensus regarding, certainty of estimates ratings.

The median of the change in score in the control arm from the studies that reported this information and did not use sham surgery as a control provided estimates of expected outcome in the control group (which

is the equivalent of the baseline risk in dichotomous outcomes), which informed calculation of absolute estimates of effect. Summary of findings tables[33] created using MAGICapp[34] summarized key information for all patient-important outcomes.

RESULTS

Of 710 unique references screened in title and abstract, 149 articles underwent full text screening, of which 13 RCTs informing the effects of knee arthroscopy[13 35-47] and 15 studies informing the complications of knee arthroscopy (12 OS[48-59] and 3 RCTs[13 39 44]) proved eligible (Figure 1).

Effects

Study Characteristics

The 13 eligible RCTs were published between 1993 and 2016, recruited a median of 119 patients, and enrolled patients with mean age from 48.9[45] to 62.8[35] years old, and a sex distribution from 5%[41] to 81.7%[43] women. Two studies performed sham surgery in the control group,[41 44] while most of the other studies used exercise therapy.[13 36 37 39 40 42 45 47] Table 1 presents details of study characteristics.

Table 1: Characteristics of randomised clinical trials included in systematic review of effects

Study	Number of patients enrolled	Comparator	Patients age (mean)	% females	ROA > 50%[1]	Pain measure[2]	Baseline mean intervention (SD)	Baseline mean control (SD)	Function measure[2]	Baseline mean (SD)	Baseline mean control (SD)
Chang, 1993[35]	34	Close needle joint lavage	62.8	71.6	Y	AIMS pain	65 (20)	61 (21)	AIMS physical function	23 (16)	17 (10)
Gauffin, 2014[36]	150	Exercise therapy	54.5	27.3	N	KOOS pain	55 (18)	58 (18)	KOOS ADL	65 (18)	68 (22)
Herrlin, 2007,[37] 2013[38]	96	Exercise therapy	54	38.9	N	KOOS pain	56 (18)	63 (21)	KOOS ADL	68 (21)	73 (20)
Katz, 2013[39]	351	Exercise therapy	58.4	56.7	Y	KOOS pain	54 (16)	53 (16)	WOMAC function	37 (18)	38 (18)
Kirkley, 2008[40]	188	Exercise therapy	59.6	62.9	Y	WOMAC pain	52 (21)	43 (24)	WOMAC function	51 (21)	43 (23)
Kise, 2016[13]	140	Exercise therapy	49.6	39	Y	KOOS pain	68 (15)	63 (21)	KOOS ADL	80 (16)	75 (22)
Moseley, 2002[41]	119	Sham surgery	52.8	5	Y	SF-36 body pain	39 (19)	38 (18)	SF-36 physical function	42 (22)	47 (23)
Osteras, 2012[42]	17	Exercise therapy	49.7	23.6	N	VAS	37 (10)	35 (17)	NM	-	-
Saeed, 2015[43]	120	Hyaluronic acid injection	NR	81.7	NR	Knee society score[3]	NR	NR	Knee society score[3]	NR	NR
Sihvonen, 2013[60]	146	Sham surgery	52	39	N	VAS	58 (20)	61 (20)	Lysholm knee score[3]	NA	NA
Stensrud, 2015[45]	82	Exercise therapy	48.9	35.4	N	Ordinal scale	NR	NR	Ordinal scale	NR	NR
Vermesan, 2013[46]	114	Steroid injection	58.4	79.2	NR	Oxford knee score[3]	NR	NR	Oxford knee score[3]	NR	NR
Yim, 2013[47]	108	Exercise therapy	56.8	79.4	N	VAS	52 (18)	49 (15)	Lysholm score[3]	NA	NA

ROA: Radiographic osteoarthritis, NR: not reported, NM: not measured, NA: not applicable

1. Based on Kellgren-Lawrence classification. Grades 2-4 were considered radiographic OA
2. All measures were converted to 0-100 scale. Higher scores mean less pain and better function
3. Instrument combines pain and function together

Effects of knee arthroscopy

Table 2 presents the GRADE Summary of Findings for effects of knee arthroscopy compared to control. Patients who underwent arthroscopic surgery had a change in pain scores larger on average than patients who received control, both in the short (5.4 points on a 100-point scale, 95% CI 2.0; 8.8, n=10 studies, 1231 patients, Appendix Figure 1), and long-term (3.1 95% CI -0.2; 6.4, n= 8 studies, 1097 patients, Appendix Figure 2). The minimally important difference for this outcome measured with the index instrument (KOOS pain subscale) was 12 points. [61] Using the MIDs specific to each instrument,[16] 12.4% more patients receiving arthroscopy achieved an improvement in pain greater than the MID (n=11 studies, 1102 patients) in the short-term.

Over the first three months of follow-up, the median average of improvement in pain was 15 points in patients who received conservative management versus 20 points in patients who underwent knee arthroscopy; over the long term, the median average improvement 19 points in patients who received conservative management, versus 22 points in patients who underwent knee arthroscopy.

Patients who underwent arthroscopic surgery had an improvement in function score that was, on average, 4.9 points larger on a 100-point scale than patients who received control in the short-term (95% CI 1.5; 8.4, n= 7 studies, 964 patients, Appendix Figure 3), and 3.2 points larger (95% CI -0.5; 6.8, n= 6 studies, 843 patients Appendix Figure 4) in the long term. The minimally important difference for this outcome measured with the index instrument (KOOS ADL subscale) was 8 points.[61] The probability of achieving a change in function higher than the MID was 13.4% higher in patients receiving arthroscopy (n= 6 studies, 835 patients) in the short-term.

In the short term, patients who received conservative management achieved a median average improvement in function of 9 points, versus 14 points in patients who underwent knee arthroscopy; over the long term, the median average improvement was 10 points in patients who received conservative management, versus 13 points in patients who underwent knee arthroscopy.

We were able to perform subgroup analyses according to blinding of patients and proportion of patients with radiographic osteoarthritis >50% for both of these outcomes. None of the analyses showed differences in results between groups (Appendix Figures 5-12). All RCTs performed partial meniscectomy as part of the intervention when needed, and all used active comparators. Therefore, we did not perform subgroup analyses for these variables.

Sensitivity analyses showed that for both short-term pain and short-term function, results using the upper and lower limit of the MID estimate, and the approach using the standardized mean difference, in all cases yielded lower estimates of the numbers with important benefit from arthroscopy than did our primary analysis (Appendix 2).

Changes in QoL scores were similar between patients undergoing knee arthroscopy and patients receiving control. In the short-term, the difference in change from baseline scores was 6.0 points greater for knee arthroscopy (95% CI -1.5; 13.5, n= 1 study, 120 patients). In the long-term, the difference in change from baseline was 2.1 points (95% CI -1.0; 5.2, n= 2 studies, 269 patients, Appendix Figure 13). The MID for the index instrument (EQ5D) is 15 points.[62] The median average of improvement in QoL was 8.0 points in patients who received conservative management versus 14.0 points in patients who underwent knee arthroscopy in the short term; and 10.3 points in patients who received conservative management, versus 12.4 points in patients who underwent knee arthroscopy.

The risk of undergoing knee replacement up to 1 year after the intervention was 1.89 times higher in patients undergoing knee arthroscopy (95% CI 0.51; 7, n= 2 studies, 497 patients, Appendix Figure 14).

Table 2: Summary of findings for the effects of knee arthroscopy versus control in patients with degenerative knee disease

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conservative management	Arthroscopy	**Certainty in effect estimates** (Quality of evidence)	**Summary**
Short term					
Pain (difference in change from baseline) 3 months	Measured by: Different instruments converted to scale of index instrument (KOOS pain sub scale) Scale: 0-100 High better, Minimally important difference 12) Data from 1231 patients in 10 studies Follow up 3 months	**15.0 points (Mean)**	**20.0 points (Mean)** **Difference: Mean Difference 5.4 more** (CI 95% 1.9 more - 8.8 more)	**High**	On average, knee arthroscopy results in very small extra reduction in pain scores when compared to control
Pain (difference in patients who achieve a change higher than the MID) 3 months	Data from 1102 patients in 9 studies Follow up 3 months	**669 per 1000**	**793 per 1000** **Difference: 124 more per 1000**	**High**	Knee arthroscopy increases the number of patients with an important reduction in short-term pain by approximately 12 in 100
Function (difference in change from baseline) 3 months	Measured by: Different instruments converted to scale of index instrument (KOOS ADL sub scale, Scale: 0-100, High better Minimally important difference 8) Based on data from 964 patients in 7 studies Follow up 3 months	**9.0 points (Mean)**	**14.0 points (Mean)** **Difference: Mean Difference 4.9 more** (CI 95% 1.5 more - 8.4 more)	**Moderate** Due to serious risk of bias, borderline inconsistency, and borderline imprecision	Knee arthroscopy may increase function change slightly more than control
Function (difference in patients who achieve a change higher than the MID) 3 months	Based on data from 835 patients in 6 studies Follow up 3 months	**519 per 1000**	**653 per 1000** **Difference: 134 more per 1000**	**Moderate** Due to serious risk of bias	Knee arthroscopy probably increases the number of patients with an important improvement in short-term function approximately 13 in 100.
Quality of life (difference in change from baseline) 3 months	Measured by: EQ5D VAS- Scale: 0-100 High better Minimally important difference 15 Based on data from 120 patients in 1 studies Follow up 3 months	**8.0 points (Mean)**	**14.0 points (Mean)** **Difference: Mean difference 6.0 greater** (CI 95% 1.5 fewer - 13.5 more)	**Low** Due to serious risk of bias, Due to serious imprecision	Knee arthroscopy may have, on average, little or no difference on QoL change, compared to control.
Pain and function up to 3 months	Based on data from 316 patients in 3 studies Follow up up to 3 months	Three studies evaluated the effects of knee arthroscopy in pain and function using measures that combined these two outcomes together or that could not be pooled. One study reported a difference in change from baseline in the Oxford knee score that favoured arthroscopy by 4.9 points (95% CI 3.61; 6.20, 114 patients) over steroids		**Moderate** Due to serious risk of bias	Knee arthroscopy probably has little or no difference in pain and function when compared to control

		injections. A second study reported no differences in the median in an overall self- assessment based on a 7-point ordinal scale (82 patients) when comparing knee arthroscopy to exercise therapy. The third study reported that patients who received intra-articular hyaluronic acid injections reported less pain than patients who received knee arthroscopy (120 patients)		
Long term				
Pain (difference in change from baseline) 1-2 years	Measured by: Different instruments converted to scale of index instrument (KOOS pain sub scale- Minimally Important Difference 12) Scale: 0-100 High better Based on data from 1097 patients in 8 studies Follow up 2 years	**19.0 points (Mean)** **22.0 points (Mean)** **Difference: Mean Difference 3.13 more** (CI 95% 0.17 fewer - 6.43 more)	**High**	On average, knee arthroscopy results in no difference, or a very small reduction, in pain
Function (difference in change from baseline) 1-2 years	Measured by: Different instruments converted to scale of index instrument (KOOS ADL sub scale- Minimally Important Difference 8) Scale: 0-100 High better Based on data from 843 patients in 6 studies Follow up 2 years	**10.0 points (Mean)** **13.0 points (Mean)** **Difference: Mean Difference 3.16 more** (CI 95% 0.48 less - 6.8 more)	**Moderate** Due to serious risk of bias and bordeline imprecision	On average, knee arthroscopy probably does results in no improvement, or a very small improvement, in function
Quality of life (difference in change from baseline) 1-2 years	Measured by: EQ5D VAS, 15D (converted to EQ5D scale- MID 15) Scale: 0-100 High better Based on data from 269 patients in 2 studies Follow up 1 year	**10.3 points (Mean)** **12.4 points (Mean)** **Difference: Mean Difference 2.12 more** (CI 95% 0.96 fewer - 5.21 more)	**High**	On average, knee arthroscopy does not result in an important improvement in quality of life
Knee replacement 1-2 years	Relative risk: 1.89 (CI 95% 0.51 - 7.0) Based on data from 497 patients in 2 studies Follow up 1 year	**12 per 1000** **23 per 1000** **Difference: 11 more per 1000** (CI 95% 107 more - 6 fewer)	**Moderate** Due to serious imprecision	On average, knee arthroscopy does not result in an increase in the risk of knee replacement
Pain and function 1-2 years	Based on data from 114 patients in 1 studies Follow up 1 year	One study measured pain and function using a composite score. The study showed that patients who receive arthroscopy have a change in Oxford knee score 2.6 points higher than patients receiving steroids injections (95% CI 1.14; 4.06)	**Moderate** Due to serious risk of bias	Knee arthroscopy probably has little or no difference on pain and function

Certainty of the evidence

There was high certainty in the estimates of effects for the outcome pain and moderate certainty in the estimates of effect for the outcome function. Although risk of bias due to lack of blinding that could affect the patient-reported outcomes was a concern in most of the trials, and the proportion of losses to follow-up was higher than desirable (Appendix Figure 15), for pain, trials with a low risk of bias reported similar

results to those in which there were risk of bias concerns (Appendix Figures 5 and 7). For function, there was less evidence from trials at low risk of bias, so we rated down our certainty in evidence for risk of bias (Appendix Figures 9 and 11)). In addition, the estimates for this outcome were imprecise. There was no evidence of publication bias (Appendix Figure 16)

The certainty of the estimates of quality of life was low in the short term due to risk of bias and imprecision, but high in the long term. The certainty of the estimates for knee replacement was moderate due to imprecision. Table 2 presents the details of the assessments per outcome.

Complications

Study Characteristics

The studies included in the complications systematic review reported data from a median of 20,770 patients. Average patient age ranged from 42[53] to 62.4[57] years, and the proportion of females from 39%[13] to 64.6%.[50] Table 3 presents detailed study characteristics.

Table 3: Characteristics of studies included in systematic review of complications

Study	Design	Number of patients	Age (mean)	% females
Basques, 2015[48]	Retrospective cohort (registry)	17774	53	46.9
Bohensky, 2014[49]	Retrospective cohort (registry)	139031	NR	42.5
Cancienne, 2016[50]	Prospective cohort	173216	NR	64.6
Hame, 2012[51]	Retrospective cohort (registry)	314578	NR	62
Hetsroni, 2011[52]	Retrospective cohort (registry)	418323	45.5	46.8
Hoppener, 2006[53]	Retrospective cohort (registry)	335	42	43.3
Jameson, 2011[54]	Retrospective cohort (registry)	261446	46	40.7
Katz, 2013[39]	RCT	174	59	55.9
Kise, 2016[13]	RCT	70	48.9	39
Krych, 2015[55]	Retrospective cohort (registry)	12595	NR	NR
Maletis, 2012[56]	Retrospective cohort (registry)	20770	44	42.8
Sihvonen, 2013[60]	RCT	70	52	58
Wai, 2002[57]	Retrospective cohort (registry)	14391	62.4	49.9
Yacub, 2009[58]	Retrospective cohort (registry)	12426	NR	57.3
Yeranosian, 2013[59]	Retrospective cohort (registry)	432038	NR	NR

Complications of knee arthroscopy

Table 4 provides a GRADE Summary of Findings for the complications of knee arthroscopy. Patients who underwent knee arthroscopy have an extremely small risk of death that is (<1 in 1000 95% CI 0; 1, n= 7 studies, 454,086 patients, Appendix Figure 17); a risk of VTE of 5 in 1000 (95% CI 2; 10, n= 11 studies, 1 119 920 patients, Appendix Figure 18); a risk of infection of 2 in 1000 (95% CI 1; 4, n= 5 studies, 603 838 patients, Appendix Figure 19); and an extremely small risk of nerve damage (<1 in 1000 95% CI 0; 1, n=1 study, 12 426 patients).

Table 4: Summary of findings for the complications of knee arthroscopy versus control in patients with degenerative knee disease

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conservative management / Arthroscopy	**Certainty in effect estimates** (Quality of evidence)	**Summary**
Mortality 3 months	Based on data from 454086 patients in 7 studies Follow up 3 months	**0 per 1000** / **0 per 1000** **Difference: <1 more per 1000** (CI 95% 0 more - 1 more)	**Low** Due to serious risk of bias and serious inconsistency	Arthroscopy may have an extremely small risk of mortality
Venous thromboembolism 3 months	Based on data from 1119920 patients in 11 studies Follow up 3 months	**0 per 1000** / **5 per 1000** **Difference: 5 more per 1000** (CI 95% 2 more - 10 more)	**Low** Due to serious risk of bias, Due to serious inconsistency	Arthroscopy may have a small risk for venous thromboembolism
Infection 3 months	Based on data from 603838 patients in 5 studies Follow up 3 months	**0 per 1000** / **2 per 1000** **Difference: 2 more per 1000** (CI 95% 1 more - 4 more)	**Low** Due to serious risk of bias, Due to serious inconsistency	Arthroscopy may have a very small risk for infection
Nerve damage 3 months	Based on data from 12426 patients in 1 studies Follow up 3 months	**0 per 1000** / **0 per 1000** **Difference: <1 more per 1000** (CI 95% 0 more - 1 more)	**Low** Due to serious risk of bias, Due to serious indirectness	Arthroscopy may have an extremely small risk of nerve damage

Certainty of the evidence

The estimates of complications of knee arthroscopy had low certainty. All studies suffered from risk of bias concerns, mainly due to the retrospective nature of the data collection (using data that had not been collected for the purposes of the study) (Appendix Figure 20). The studies informing mortality, VTE and infection showed inconsistent results from both a clinical and statistical perspective, which resulted in rating down the certainty for the pooled estimate. Finally, the only study informing nerve damage included patients with arthroscopy of the shoulder as well,[58] and therefore warranted rating down this estimate for indirectness. There was no evidence of publication bias (Appendix Figure 21). Table 4 presents details regarding the assessments of the certainty of the complications of knee arthroscopy per outcome.

DISCUSSION

This systematic review provides high quality evidence that patients with degenerative knee disease who undergo arthroscopy experience, on average, very small benefits in pain, function, and quality of life over

periods of up to three months when compared to patients who receive a conservative management strategy (Table 2). Results up to two years failed to show benefits in pain or function, and excluded any but very small benefits (Table 2). The median of the average pain change in patients receiving conservative management was 15 points in the short-term and 19 points in the long term (MID 12 points). Patients receiving arthroscopy had an average change 5.4 points higher in the short-term, and 3.1 points higher in the long term. These differences were not patient important. Thus, whether patients receive arthroscopy or not, the clinical trial experience suggests, on average, a small benefit in pain reduction over both the short and long term.

The results for function proved similar, with very small average differences in the short term, and no convincing evidence of benefit in the long term (Table 2). Patients who received a conservative management strategy had a median average change of 9 points in the short term and 10 points in the long term, corresponding (MID 8 points). Risk of bias limitations leave this evidence less secure (moderate quality) than for pain.

Study results provide high quality evidence that the benefits of arthroscopic surgery on quality of life over the long term are minimal, if they exist at all (Table 2). Low quality evidence raises the possibility of a higher risk of knee replacement with arthroscopic surgery.

We found a low risk of serious adverse effects in patients undergoing knee arthroscopy. The risk of mortality and nerve damage may be close to 0, while the risk of VTE and infection may be 5 and 2 in 1000 patients, respectively. We have low certainty in this evidence, however, because the studies included were likely to be biased and showed results that were inconsistent.

Our systematic review has particular strengths. First, it provides the most comprehensive and trustworthy body of evidence up to date, including 10 studies not included in the most recent prior review.[15] While the conclusions of our systematic review may not be qualitatively different from the conclusions of previous reviews addressing the same question, we believe that all the additions in terms of studies included and methods for summarizing, presenting, and appraising the evidence strengthen the conclusions derived from this body of evidence considerably. Second, this systematic review was developed in parallel with a BMJ Rapid Recommendation according to predefined standards, methods and processes.[12] Extensive input from content experts and patients in the guideline panel throughout the process secured appropriate selection of outcomes and analyses as well as appropriate interpretation of the results from the systematic review. The Rapid Recommendations published together with our linked systematic review should

provide clinicians and their patients with optimal guidance in practice and will also allow other guideline organizations to re-use or adapt content to their contexts, if needed. Third, by converting all the instruments to the scale of an index instrument we do not only overcome the potential limitations of using the standardized mean difference (namely, the analysis depending on a similar standard deviation across studies, and the resulting measure of effect being difficult to interpret), but also provide an estimate of the proportion of patients who would achieve a minimally important change per arm, and the difference between these proportions. This allows incorporating patients' values and preferences explicitly when interpreting the results. A rigorous linked systematic review of studies addressing the issue informed our estimates of the minimally important change[16] and our results were robust to accounting for the uncertainty in the MID, as well as to calculating the proportion who might benefit using an approach relying on the standardized mean difference. Fourth, we provide an explicit and transparent assessment of the certainty in the absolute estimates of effect, which considers limitations of the evidence with regards to risk of bias, inconsistency, imprecision, indirectness, and publication bias.[63]

Our review is limited by suboptimal reporting in many of the original studies, requiring imputing standard deviations and, in a number of studies, estimating correlations between baseline and follow-up. It is possible that there is a subgroup of patients – for instance, those with locking symptoms – who do achieve substantial benefit from arthroscopic knee surgery. The available studies do not, however, provide evidence of any such subgroup. The burden of proof now rests with those who claim that such a subpopulation exists, with compelling RCT evidence required to substantiate the claim.

In summary, our results provide low quality evidence that knee arthroscopy is a safe procedure with a low risk of complications and moderate to high quality evidence that the procedure provides very small benefits in pain and function over conservative therapy in the short term. The evidence fails to support a persistence of these benefits over the long term. Patients and their health care providers must trade off the marginal short term benefits against the burden of the surgical procedure (pain, swelling, limited mobility, restriction of activities, over a period of 2 to 6 weeks).

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assessments. RBP performed the data analysis. RBP, RB and GHG interpreted the data analysis. RBP and GHG interpreted the data performed certainty of evidence assessments. RBP wrote the first draft of the manuscript. GHG, POV, RB, and RP critically revised the manuscript. All authors approved the final version of the manuscript. RBP had full access to all of the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. RBP is guarantor.

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ETHICAL APPROVAL: Not required.

TRANSPARENCY DECLARATION: RBP affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

DATA SHARING STATEMENT: Extra data is available in the publication of the BMJ Rapid Recommendation in MAGICapp.

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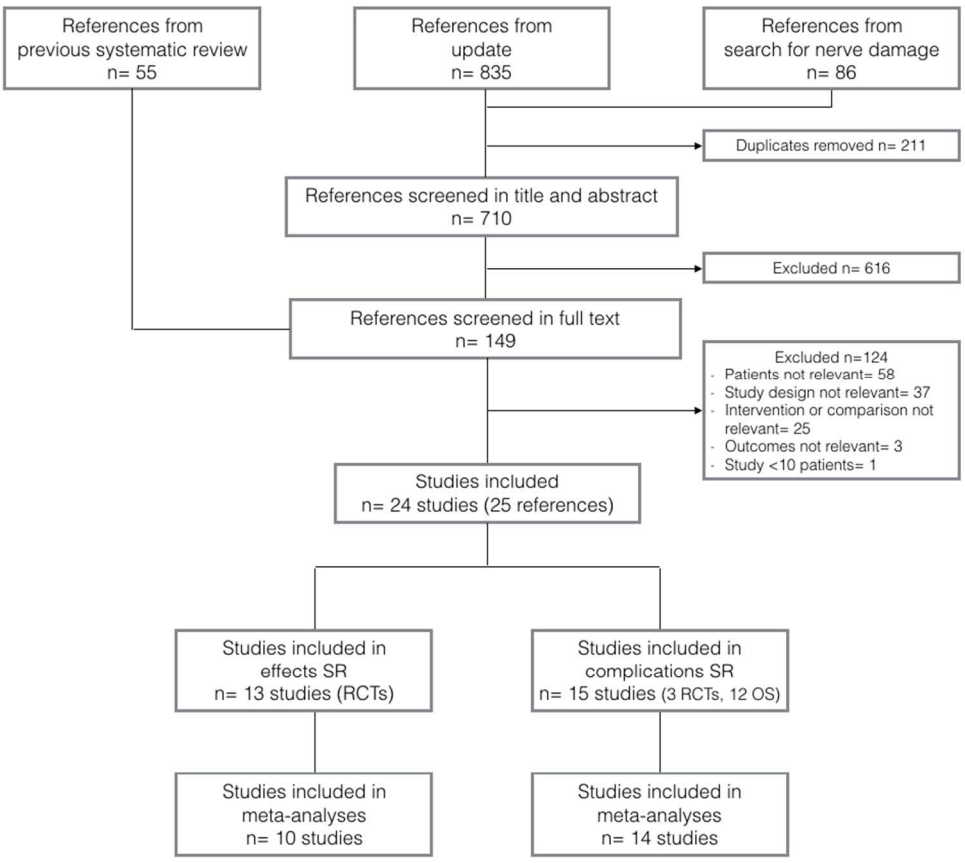
FIGURES LEGENDS

Figure 1: Study selection process



Study selection process
Figure 1
346x306mm (72 x 72 DPI)

Appendix 1: Search strategies

Update of effects and complications of knee arthroscopy

MEDLINE (Pubmed)

1. (((((("Menisci, Tibial/surgery"[MeSH Major Topic]) OR ("Menisci, Tibial/injuries"[MeSH Major Topic]) OR ("Degenerative meniscal tear"[Title/Abstract]) OR ("Arthroscopic lavage"[Title/Abstract]) OR ("Arthroscopic debridement"[Title/Abstract]) OR ("arthroscopic meniscectomy"[Title/Abstract]) OR ((arthroscopy[Title/Abstract]) AND knee[Title/Abstract]))
2. (("Randomized"[Title/Abstract]) OR ("Randomized controlled trial"[Publication Type]) OR ("randomized controlled trials as topic"[MeSH Major Topic]) OR ("Random allocation"[MeSH Major Topic]) OR ("Control group"[Title/Abstract]) OR ("Control groups"[MeSH Terms]) OR ("Cross-over studies"[Title/Abstract]) OR ("Cross-over study"[Title/Abstract])))
3. ((("Menisci, Tibial/surgery"[MeSH Major Topic]) OR ("Menisci, Tibial/injuries"[MeSH Major Topic]) OR ("Degenerative meniscal tear"[Title/Abstract]) OR ("Arthroscopic lavage"[Title/Abstract]) OR ("Arthroscopic debridement"[Title/Abstract]) OR ("arthroscopic meniscectomy"[Title/Abstract]) OR ((arthroscopy[Title/Abstract]) AND knee[Title/Abstract]))
4. (("adverse events"[Title/Abstract]) OR ("side effects"[Title/Abstract]) OR ("adverse effects"[Title/Abstract]) OR (complication*[Title/Abstract]) OR ("adverse effects"[MeSH Subheading])))))
5. 1 AND 2
6. 3 AND 4
7. 5 OR 6

EMBASE (Ovid)

1. Arthroscopic meniscectomy.ti,ab,kw.

2. Arthroscopic debridement.ti,ab,kw.

3. Arthroscopic lavage.ti,ab,kw.

4. Degenerative meniscal tear.ti,ab,kw.

5. knee meniscus/ or meniscus tibial.mp.

6. exp knee arthroscopy/

7. 1 or 2 or 3 or 4 or 5 or 6

8. randomized controlled trial/

9. randomized.ti,ab,kw.

10. randomised.ti,ab,kw.

11. Random allocation.mp.

12. randomised.mp.

13. "randomized controlled trial (topic)"/

14. Control group.mp.

15. control group/

16. crossover procedure/

17. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16

18. adverse events.mp.

19. side effects.mp.

20. adverse effects.mp.

21. complications.mp.

22. 18 or 19 or 20 or 21

23. 7 and 17

24. 7 and 22

25. 23 or 24

26. limit 25 to yr="2014-2016"

Cochrane Central Register of Controlled Trials

#1 MeSH descriptor: [Menisci, Tibial] explode all trees and with qualifier(s): [Injuries - IN, Surgery - SU]
#2 MeSH descriptor: [Arthroscopy] explode all trees
#3 MeSH descriptor: [Knee] explode all trees
#4 #2 and #3
#5 Degenerative meniscal tear:ti,ab,kw (Word variations have been searched)
#6 Arthroscopic lavage:ti,ab,kw (Word variations have been searched)
#7 Arthroscopic debridement:ti,ab,kw (Word variations have been searched)
#8 arthroscopic meniscectomy:ti,ab,kw (Word variations have been searched)
#9 #1 or #4 or #5 or #6 or #7 or #8 Publication Year from 2014 to 2016, in Trials

New search of outcome nerve damage

Medline Pubmed

("Peripheral Nerve Injuries"[Mesh]) AND ("Arthroplasty, Replacement, Knee/adverse effects"[Mesh] OR "knee arthroscopy" OR ("arthroscop*" AND "knee"))

Embase (Ovid)

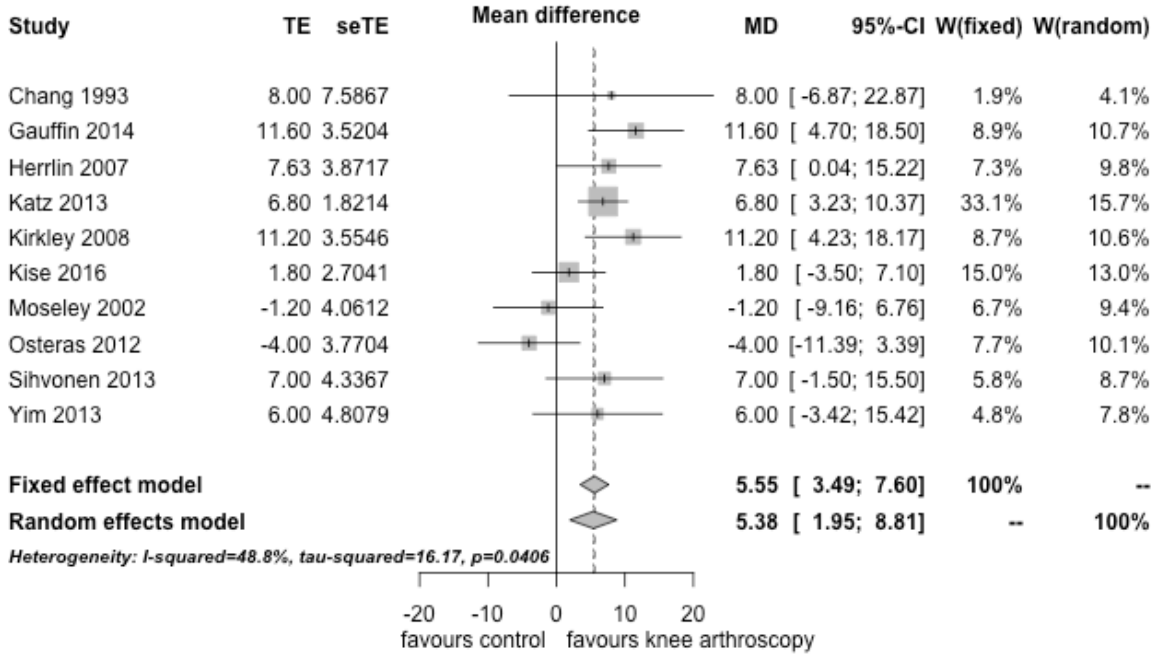
1. exp nerve injury/
2. exp knee arthroscopy/
3. 1 AND 2

Appendix 2: Results of sensitivity analyses to assess the robustness of the difference in the proportion of patients who reach a change higher than the MID

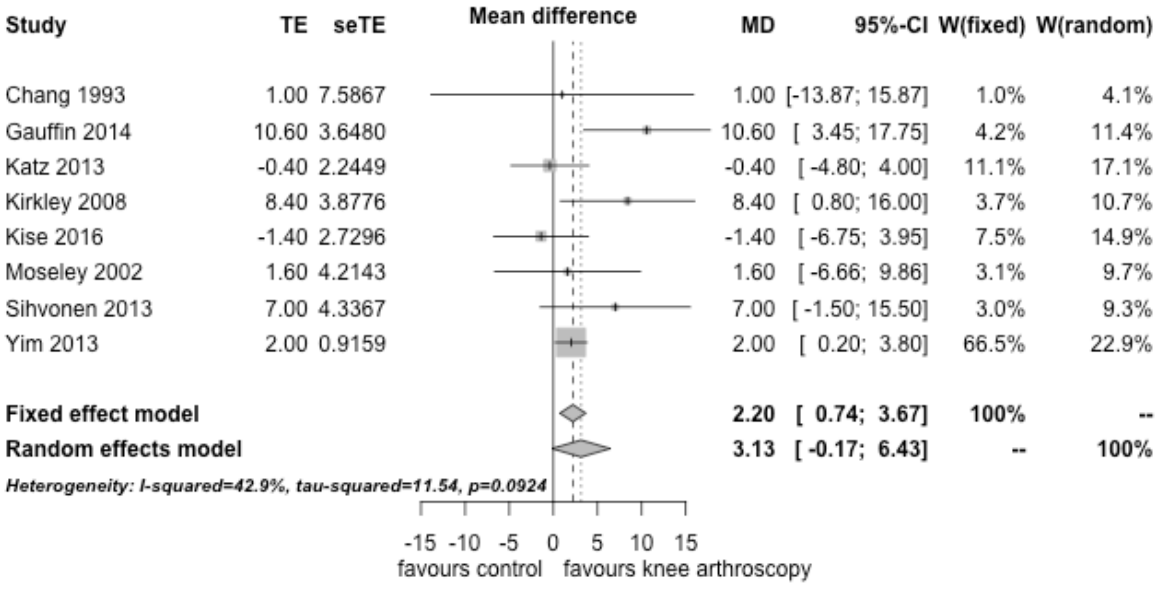
Outcome	MID (range)	Risk difference (95% CI))	Risk difference when using lowest value of the range (95% CI)	Risk difference when using highest value of the range (95% CI)	Risk difference based on the standardized mean difference* (95% CI)
Pain in the short term	KOOS pain[58] 12 (4; 20) WOMAC pain[61] 12 (2; 30)	12.4% (4.4; 20.4)	10.5% (4.3; 16.7))	11.3% (2.9; 19.7)	9% (1.7; 15.7)
Function in the short term	KOOS ADL[58] 8 (3; 9) WOMAC function[61 62] 13 (3; 34)	13.4% (4.4; 22.3)	11.3% (3; 19.5)	11% (2; 19.9)	7.3% (-0.06; 15.1)

*This method relies on the standardized mean difference. It does not use any specific threshold to calculate the risk difference.

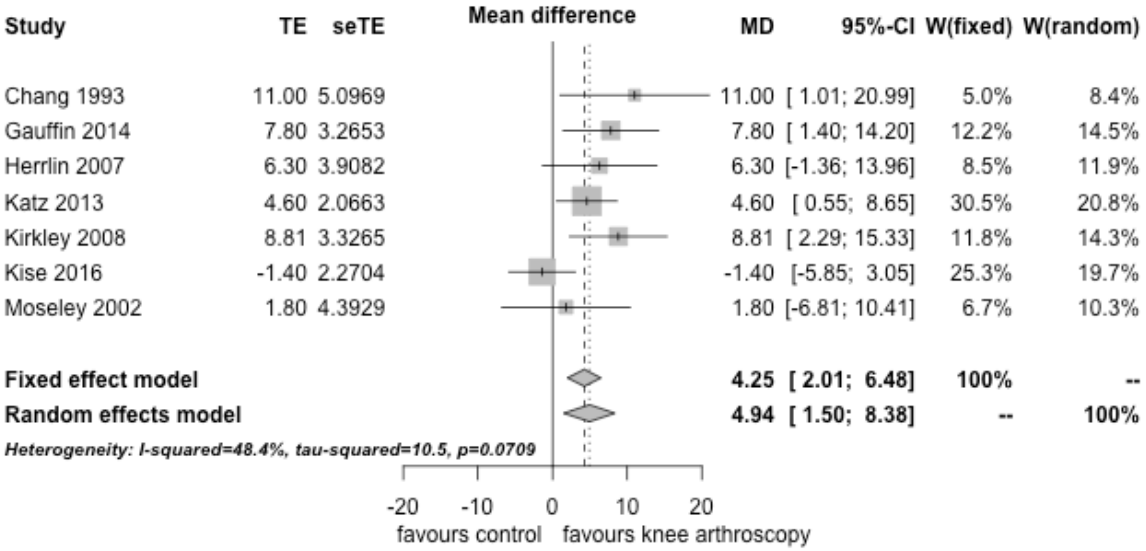
Appendix Figure 1: Meta-analysis of pain in the short-term (difference in change from baseline)



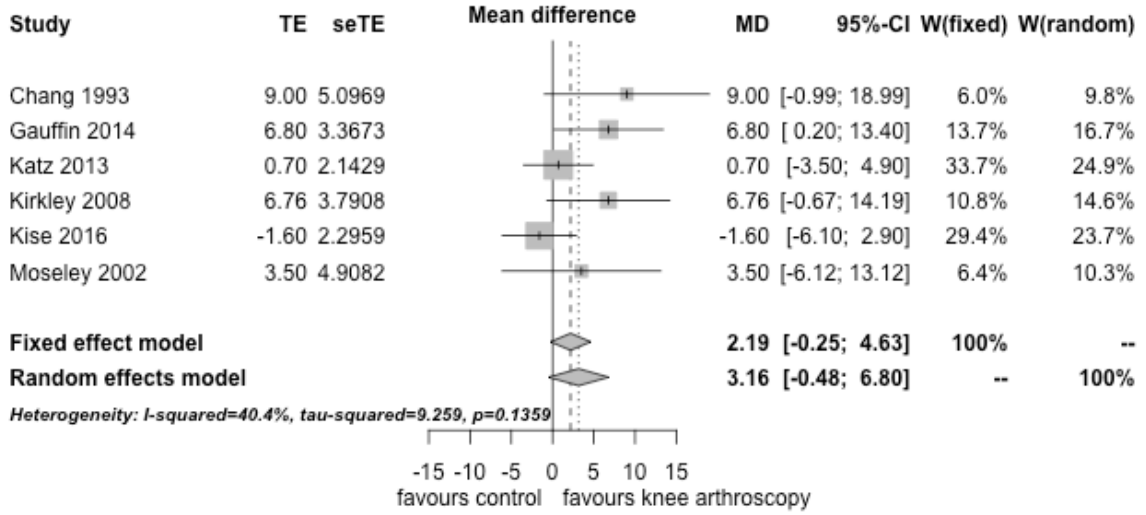
Appendix Figure 2: Meta-analysis of pain in the long-term (difference in change from baseline)



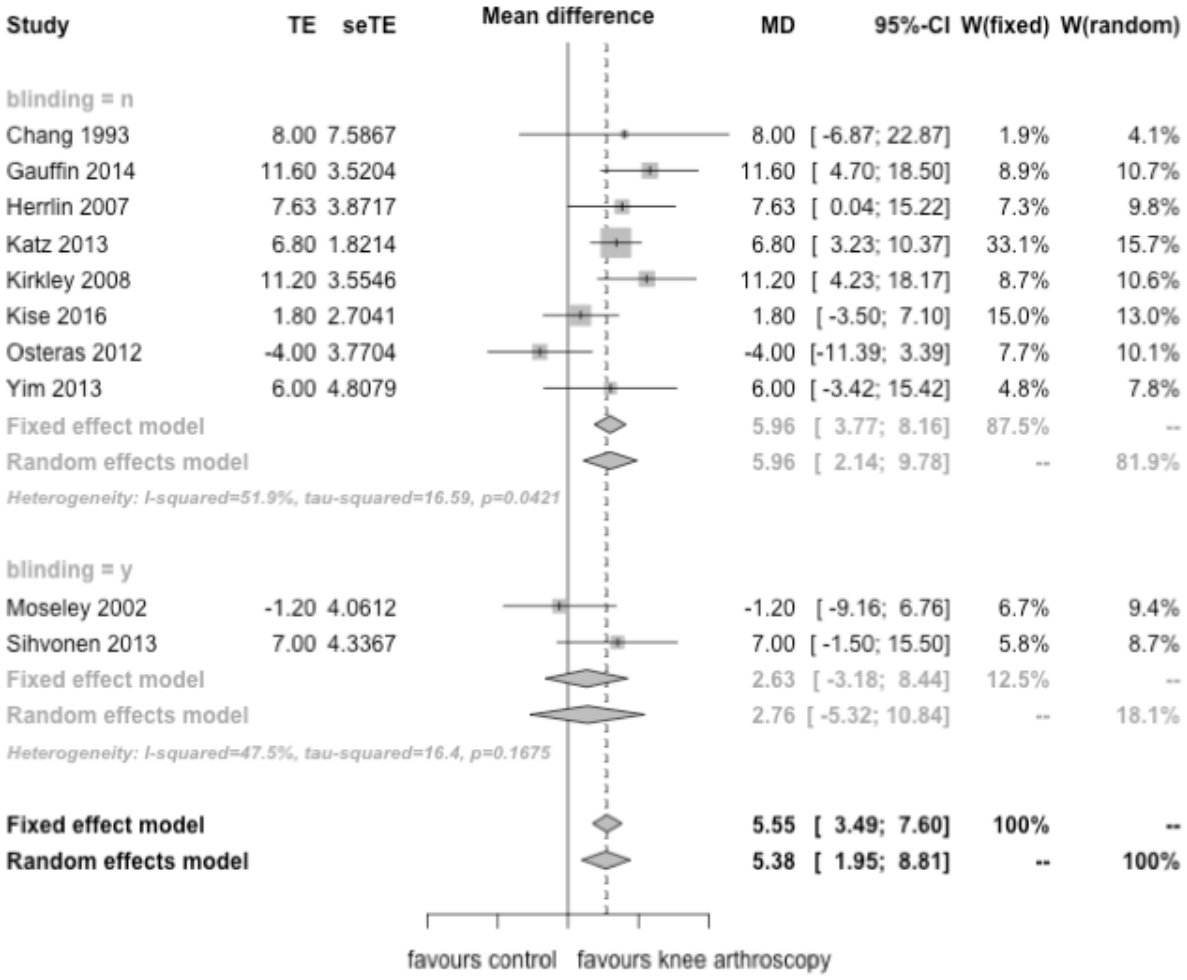
Appendix Figure 3: Meta-analysis of function in the short-term (difference in change from baseline)



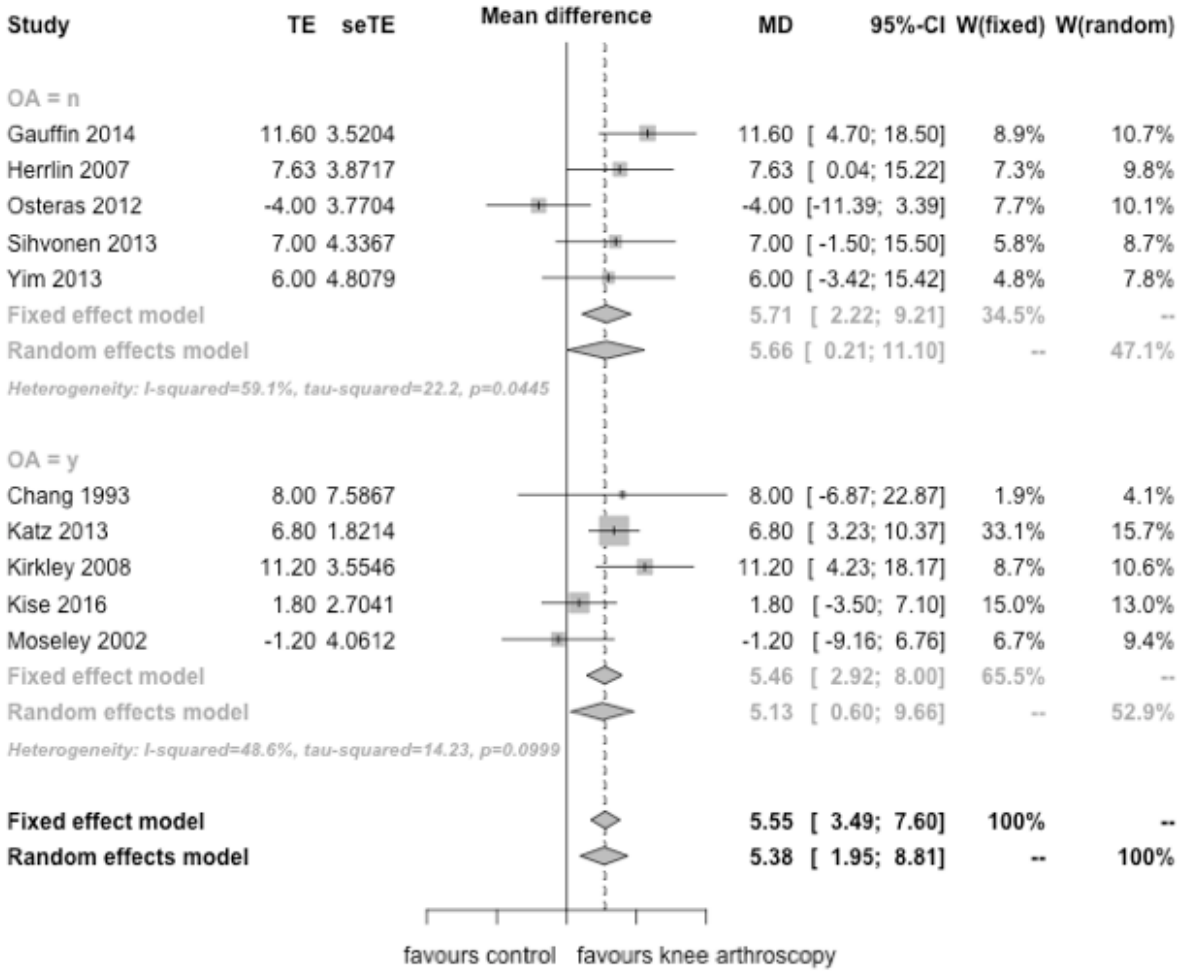
Appendix Figure 4: Meta-analysis of function in the long-term (difference in change from baseline)



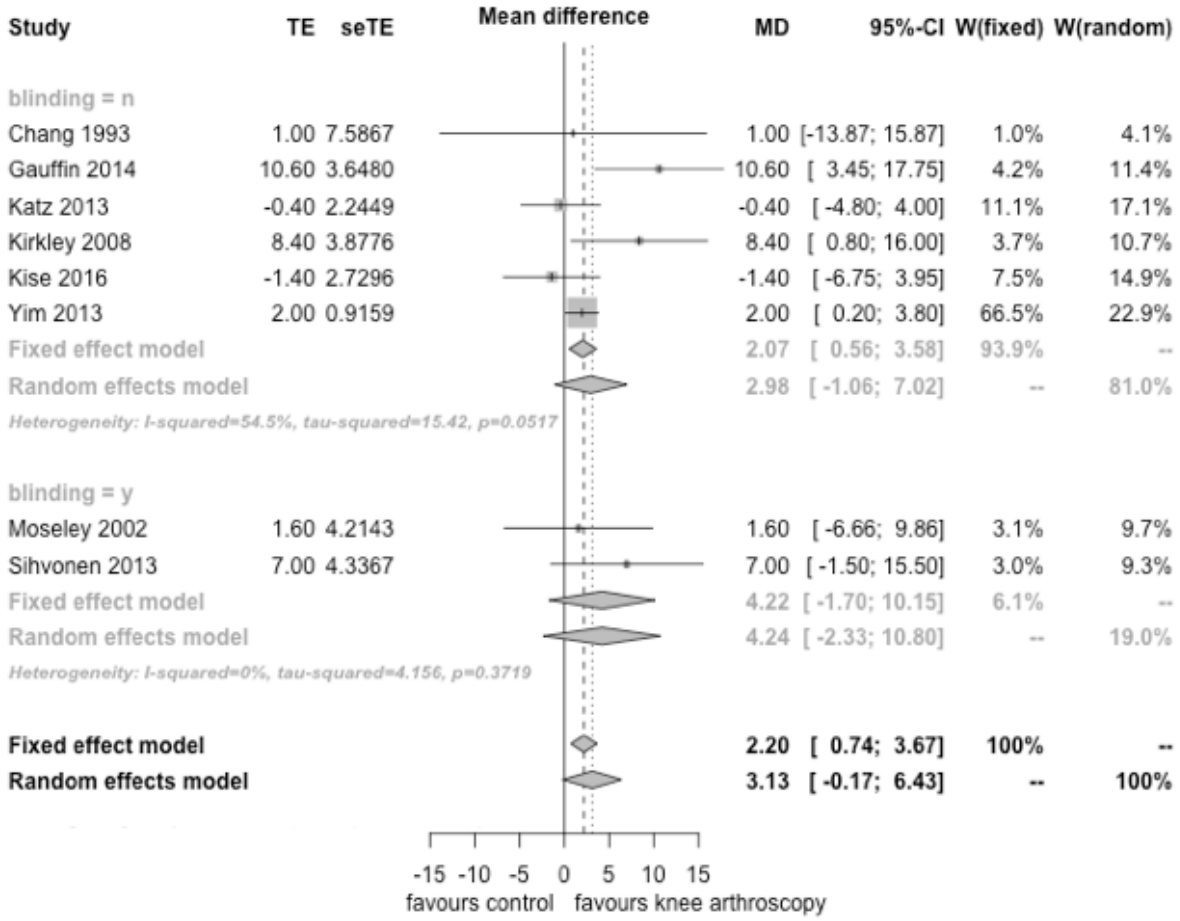
Appendix Figure 5: Subgroup analysis of pain in the short term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.48



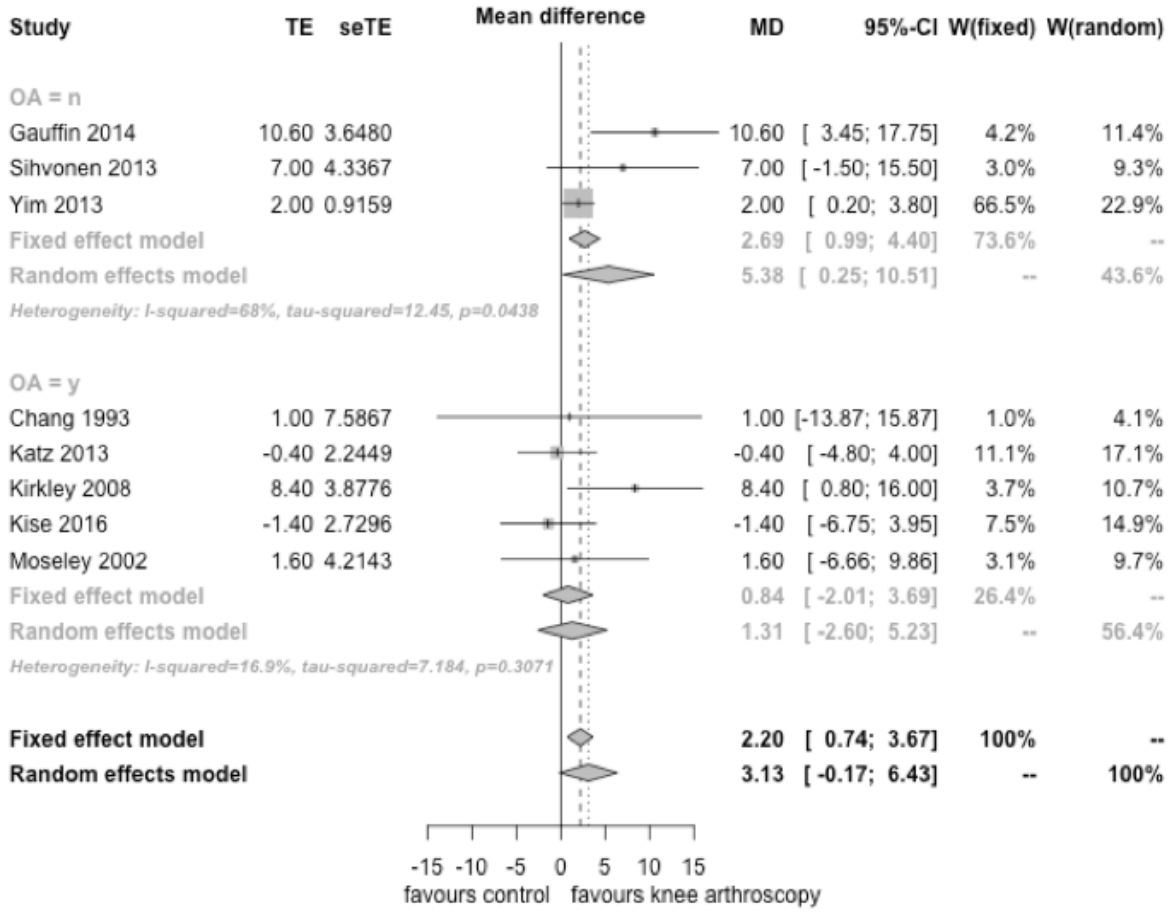
Appendix Figure 6: Subgroup analysis of pain in the short term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.88



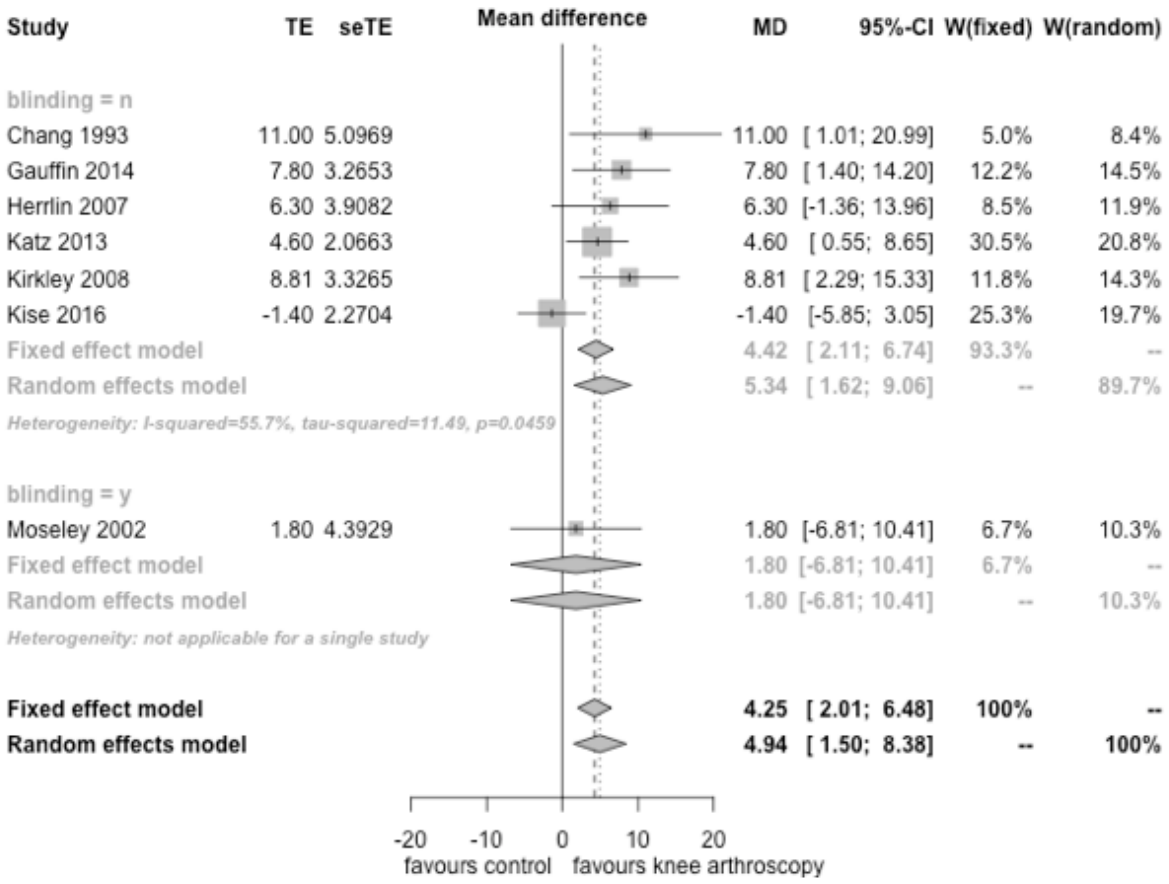
Appendix Figure 7: Subgroup analysis of pain in the long term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.75



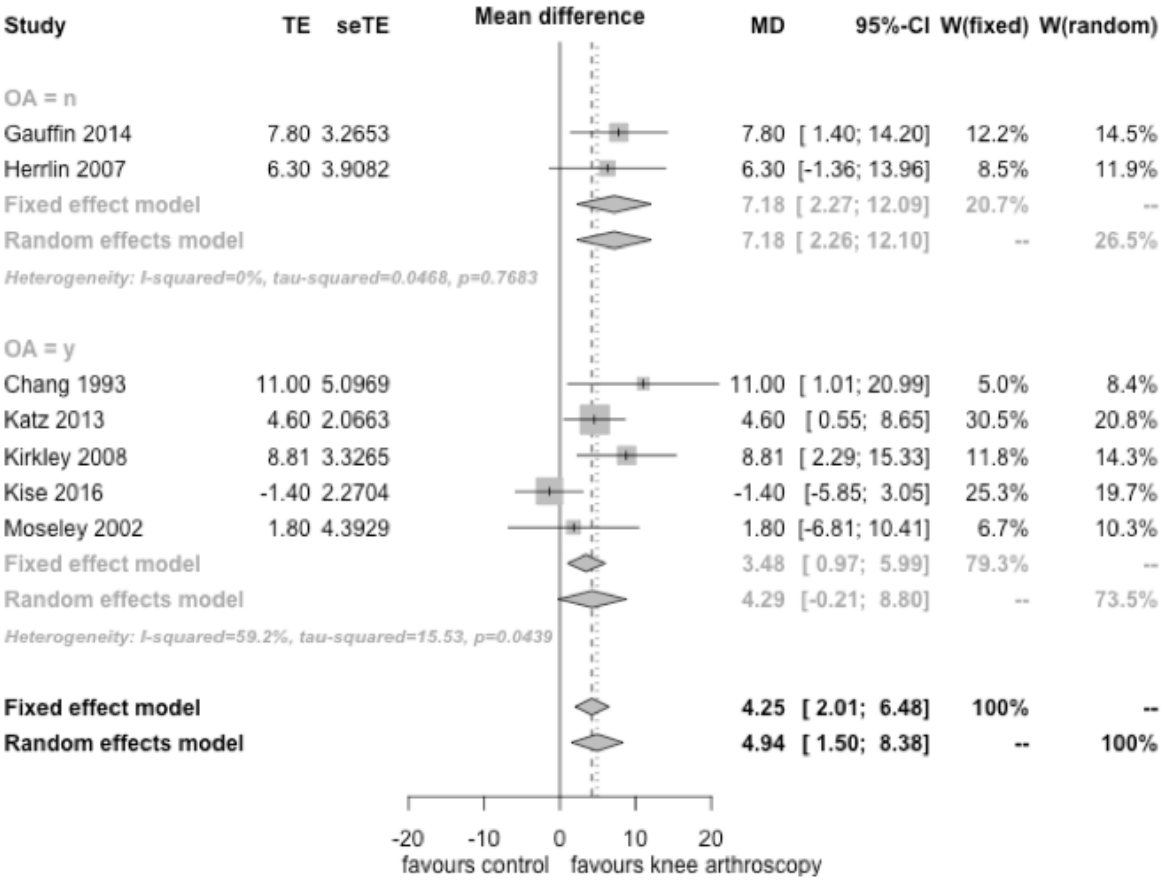
Appendix Figure 8: Subgroup analysis of pain in the long term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.22



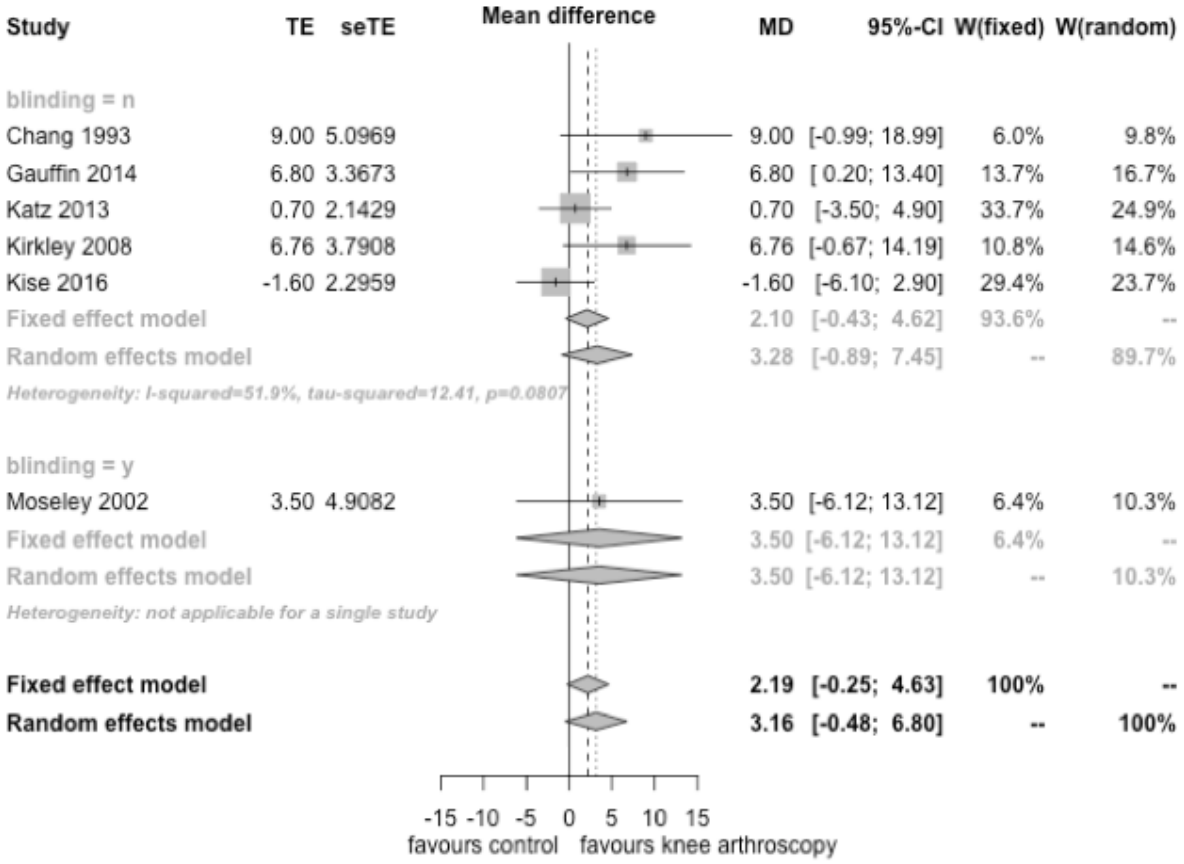
Appendix Figure 9: Subgroup analysis of function in the short term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.46



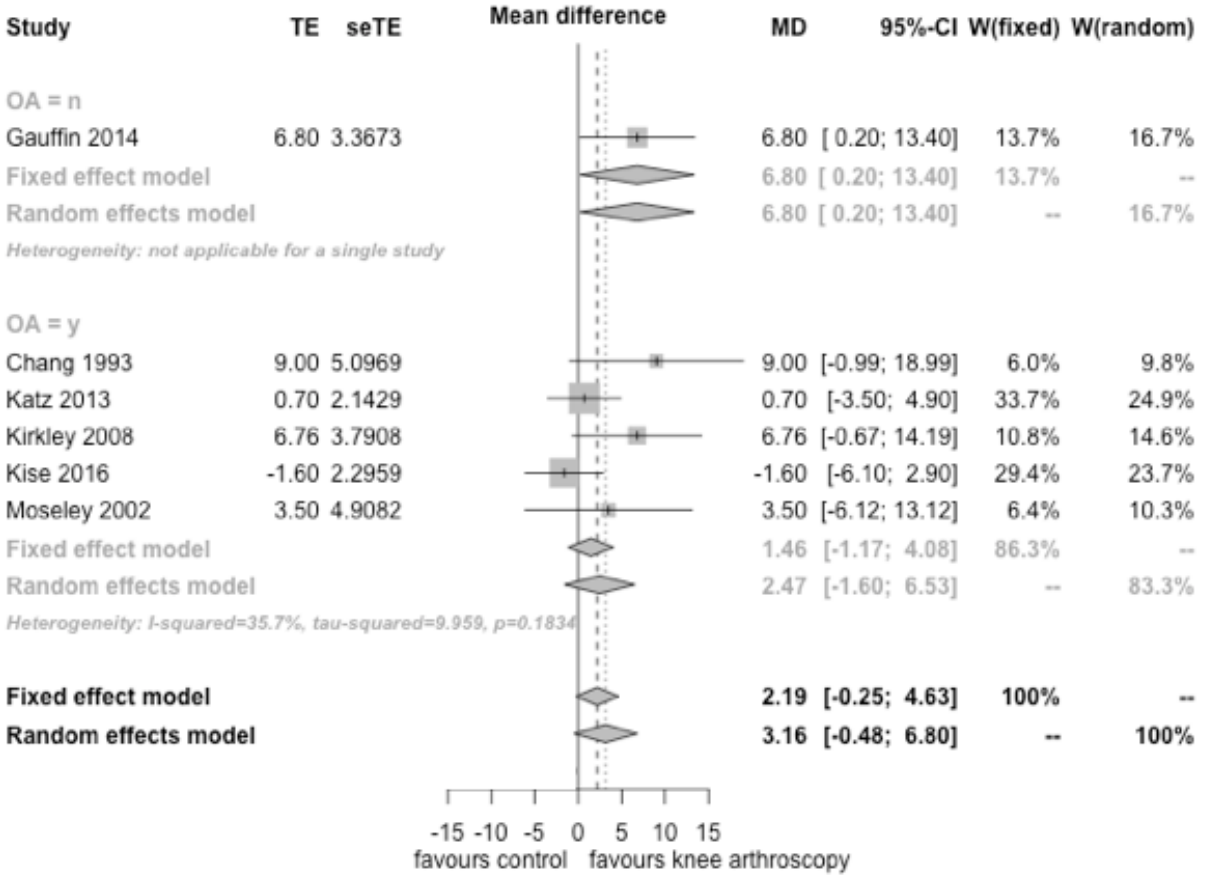
Appendix Figure 10: Subgroup analysis of function in the short term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.40



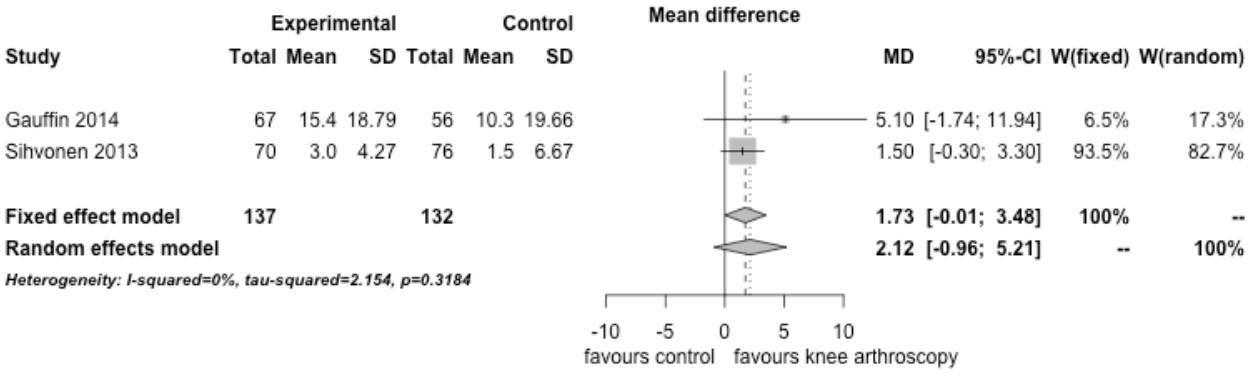
Appendix Figure 11: Subgroup analysis of function in the long term (difference on change from baseline) according to blinding of the studies. P value of test for subgroup effect= 0.97



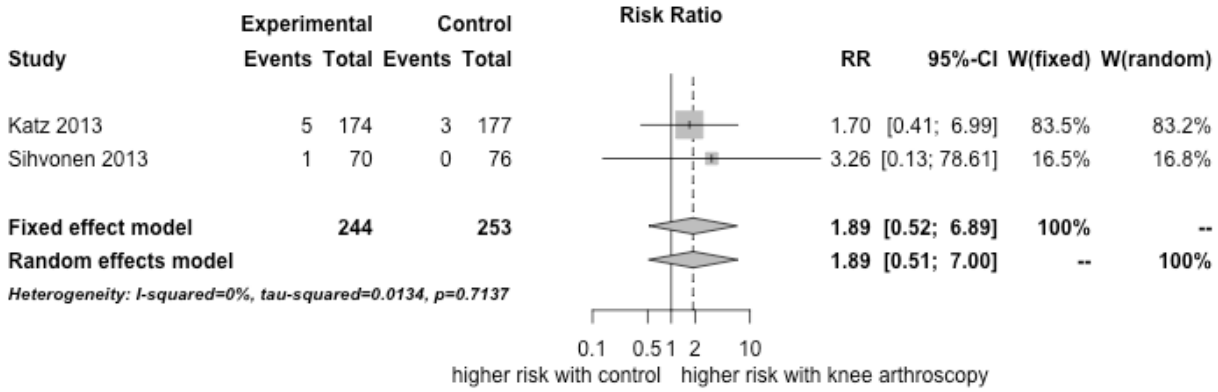
Appendix Figure 12: Subgroup analysis of function in the long term (difference on change from baseline) according to percentage of patients with radiographic knee osteoarthritis (>50% patients). P value of test for subgroup effect= 0.27



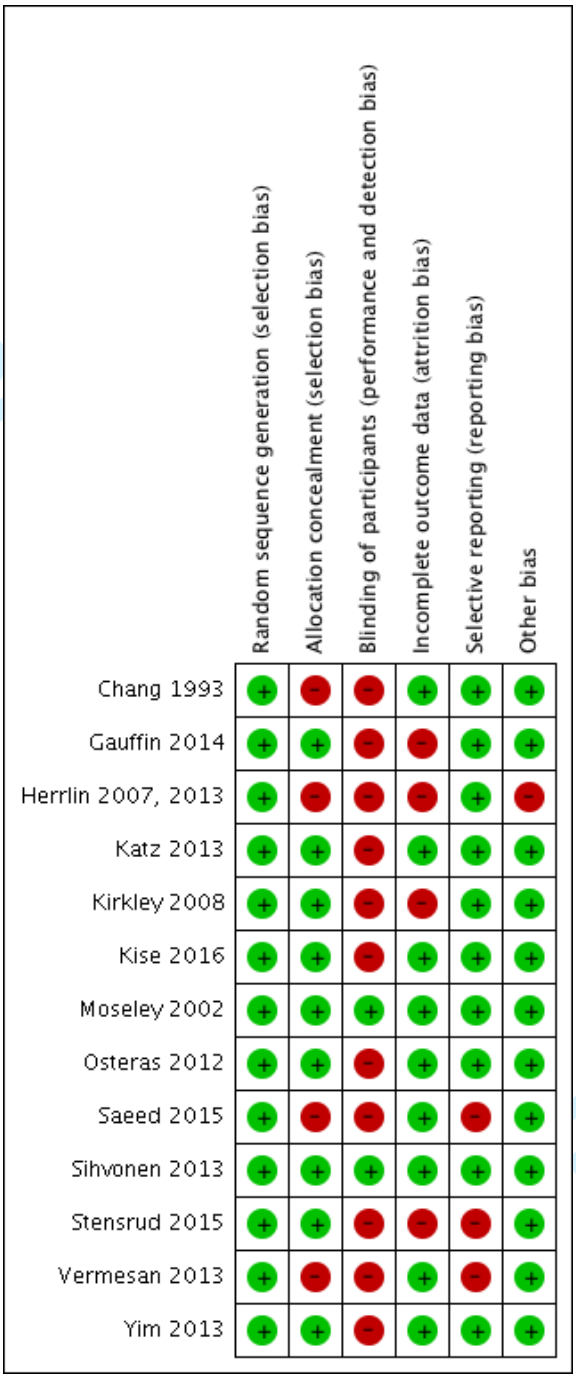
Appendix Figure 13: Meta-analysis of Quality of life in the long-term (difference in change from baseline)



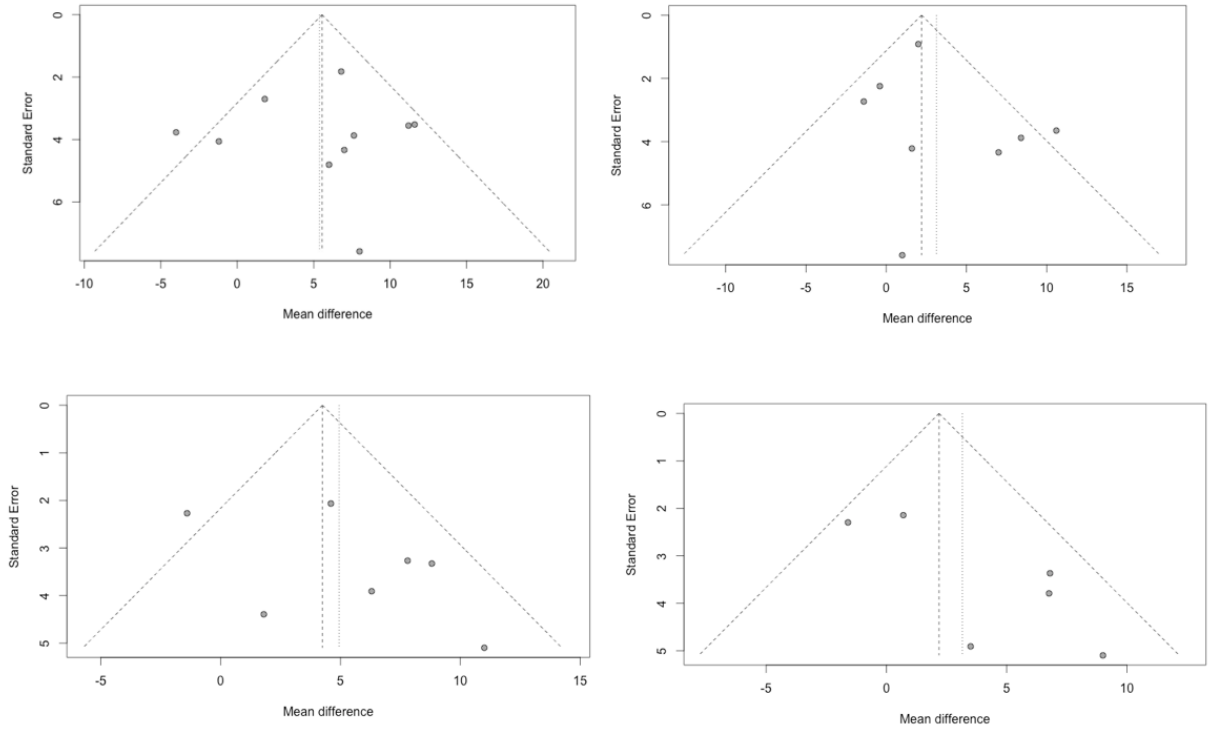
Appendix Figure 14: Meta-analysis of Knee Replacement



Appendix Figure 15: Risk of bias of studies included in the systematic review of effects of knee arthroscopy

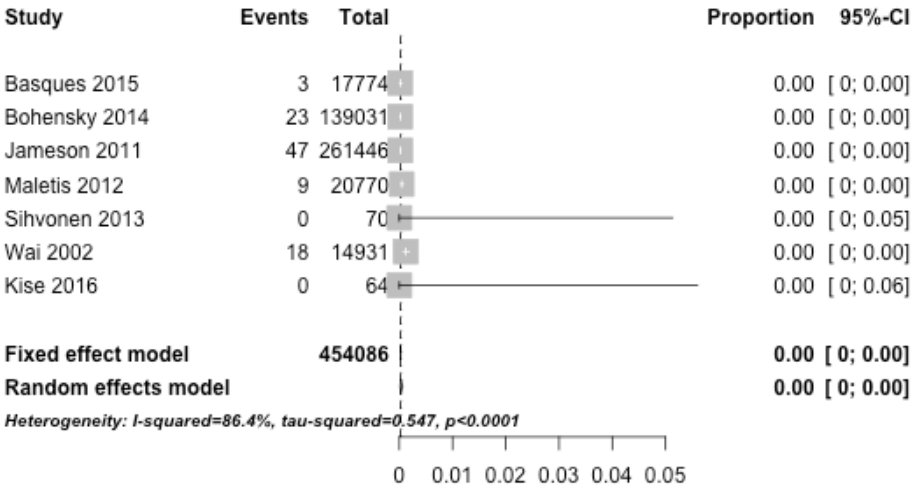


Appendix Figure 16: Funnel plots for publication bias assessments of effects of knee arthroscopy

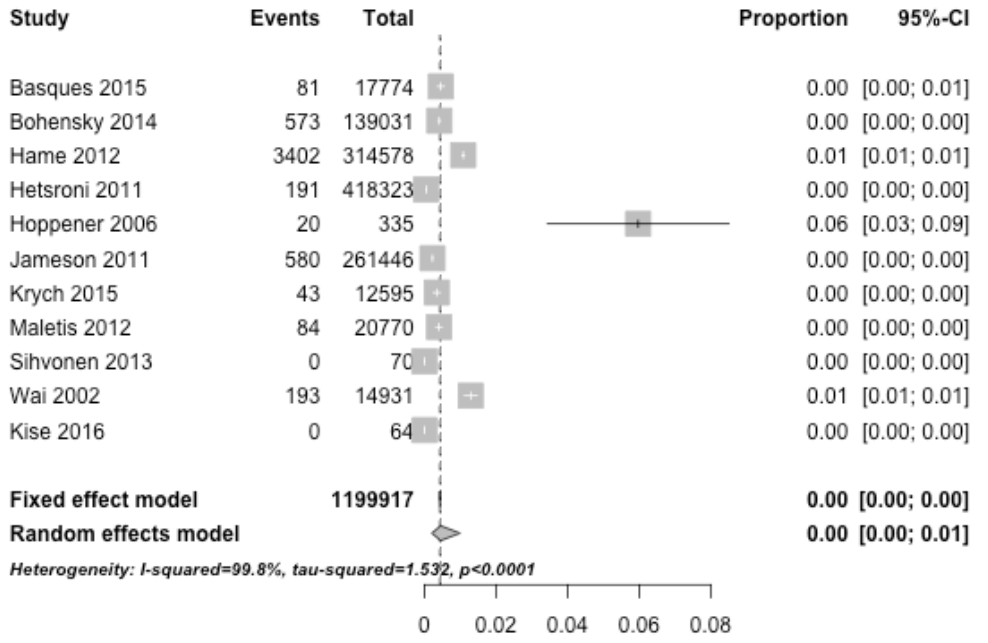


Top left: Short-term pain; Top right: Long-term pain; Bottom left: Short-term function; Bottom right: Long-term function

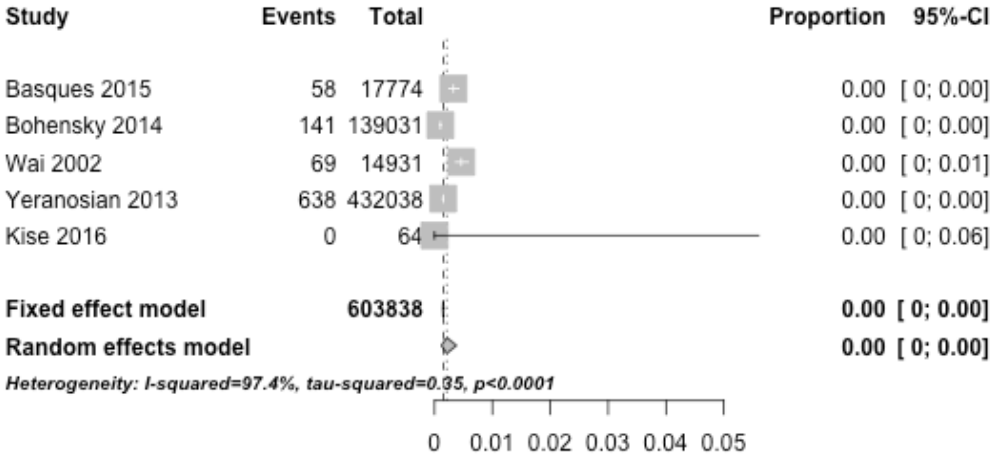
Appendix Figure 17: Meta-analysis of Mortality



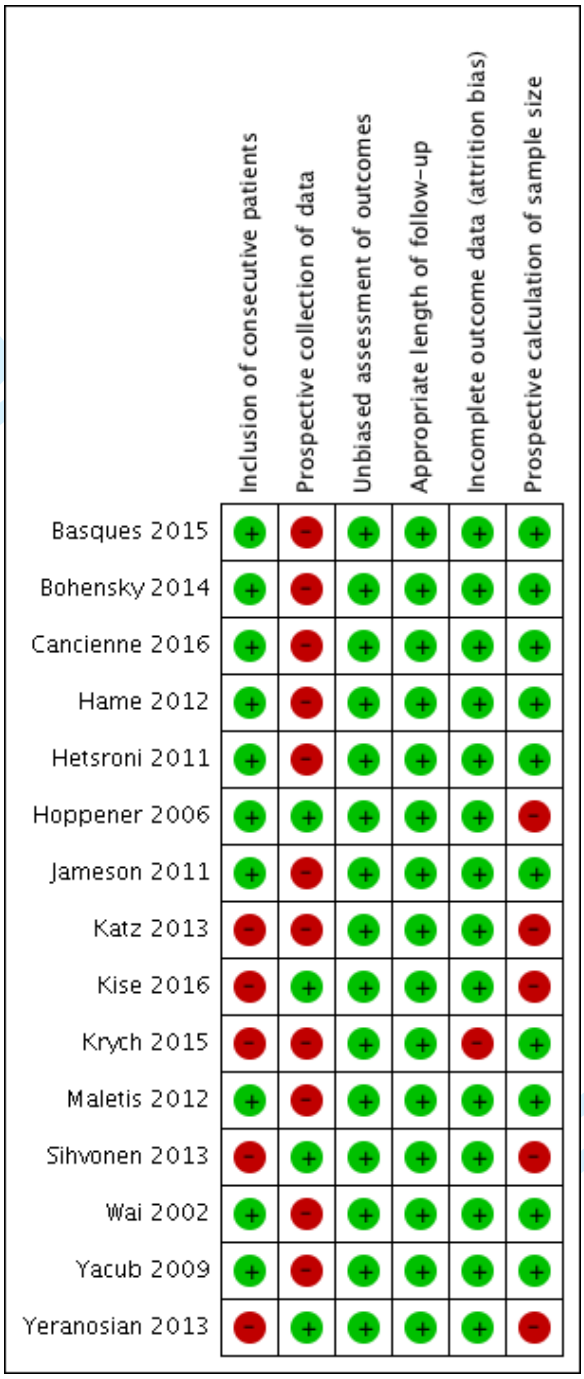
Appendix Figure 18: Meta-analysis of VTE



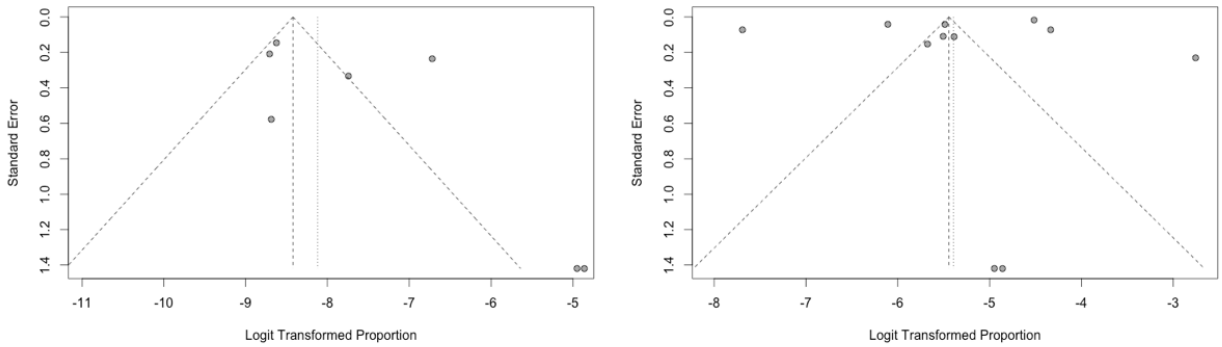
Appendix Figure 19: Meta-analysis of infection



Appendix Figure 20: Risk of bias of the studies included in the systematic review of complications of knee arthroscopy



Appendix Figure 21: Funnel plots for publication bias assessment of complications of knee arthroscopy



Left: Mortality; Right: VTE. Outliers represent the findings of two randomized clinical trials with small sample sizes and 0 events observed.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3,5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5,6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	26-28
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9,25
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-10, 15-16
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15, 17, 41, 44
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	30-31, 39-40, 42-43
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-13, 16-17, 30-31, 39-40, 44-43
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15, 17
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-12, 29, 32-39
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17, 18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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