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## Surgical interventions for symptomatic mild to moderate knee osteoarthritis (Review)

Palmer JS, Monk AP, Hopewell S, Bayliss LE, Jackson W, Beard DJ, Price AJ

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## TABLE OF CONTENTS

HEADER . . . . .	1
ABSTRACT . . . . .	1
PLAIN LANGUAGE SUMMARY . . . . .	2
SUMMARY OF FINDINGS FOR THE MAIN COMPARISON . . . . .	5
BACKGROUND . . . . .	8
OBJECTIVES . . . . .	10
METHODS . . . . .	10
Figure 1. . . . .	13
RESULTS . . . . .	17
Figure 2. . . . .	20
Figure 3. . . . .	21
Figure 4. . . . .	23
Figure 5. . . . .	24
Figure 6. . . . .	25
Figure 7. . . . .	26
Figure 8. . . . .	27
ADDITIONAL SUMMARY OF FINDINGS . . . . .	28
DISCUSSION . . . . .	35
AUTHORS' CONCLUSIONS . . . . .	37
ACKNOWLEDGEMENTS . . . . .	38
REFERENCES . . . . .	38
CHARACTERISTICS OF STUDIES . . . . .	48
DATA AND ANALYSES . . . . .	72
Analysis 1.1. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 1 Pain. . . . .	73
Analysis 1.2. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 2 Function. . . . .	74
Analysis 1.3. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 3 Adverse events. . . . .	74
Analysis 1.4. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 4 Re-operation rate or TKR (6-12 months). . . . .	75
Analysis 1.5. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 5 Withdrawals due to adverse events (6-12 months). . . . .	75
Analysis 2.1. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 1 Pain. . . . .	76
Analysis 2.2. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 2 Function. . . . .	76
Analysis 2.3. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 3 Quality of life. . . . .	77
Analysis 3.1. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 1 Pain. . . . .	77
Analysis 3.2. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 2 Function. . . . .	78
Analysis 3.3. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 3 Adverse events. . . . .	78
Analysis 3.4. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 4 Re-operation rate or TKR (6-12 months). . . . .	79
Analysis 3.5. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 5 Withdrawals due to adverse events (6-12 months). . . . .	79
Analysis 4.1. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 1 Pain. . . . .	80
Analysis 4.2. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 2 Function. . . . .	80
Analysis 4.3. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 3 Structural progression. . . . .	81
Analysis 4.4. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 4 Quality of life. . . . .	81
Analysis 4.5. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 5 Adverse events. . . . .	82
Analysis 4.6. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 6 Re-operation rate or TKR (6-12 months). . . . .	82
Analysis 4.7. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 7 Withdrawals due to adverse events (6-12 months). . . . .	83
APPENDICES . . . . .	83
CONTRIBUTIONS OF AUTHORS . . . . .	86

DECLARATIONS OF INTEREST . . . . .	86
SOURCES OF SUPPORT . . . . .	86
DIFFERENCES BETWEEN PROTOCOL AND REVIEW . . . . .	87

[Intervention Review]

# Surgical interventions for symptomatic mild to moderate knee osteoarthritis

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## ABSTRACT

### Background

Osteoarthritis affecting the knee is common and represents a continuum of disease from early cartilage thinning to full-thickness cartilage loss, bony erosion, and deformity. Many studies do not stratify their results based on the severity of the disease at baseline or recruitment.

### Objectives

To assess the benefits and harms of surgical intervention for the management of symptomatic mild to moderate knee osteoarthritis defined as knee pain and radiographic evidence of non-end stage osteoarthritis (Kellgren-Lawrence grade 1, 2, 3 or equivalent on MRI/arthroscopy). Outcomes of interest included pain, function, radiographic progression, quality of life, short-term serious adverse events, re-operation rates and withdrawals due to adverse events.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and Embase up to May 2018. We also conducted searches of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform for ongoing trials. Authors of trials were contacted if some but not all their participants appeared to fit our inclusion criteria.

### Selection criteria

We included randomised controlled trials that compared surgery to non-surgical interventions (including sham and placebo control groups, exercise or physiotherapy, and analgesic or other medication), injectable therapies, and trials that compared one type of surgical intervention to another surgical intervention in people with symptomatic mild to moderate knee osteoarthritis.

### Data collection and analysis

Two review authors independently selected trials and extracted data using standardised forms. We analysed the quality of evidence using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach.

## Main results

A total of five studies involving 566 participants were identified as eligible for this review. Single studies compared arthroscopic partial meniscectomy to physical therapy (320 participants), arthroscopic surgery (debridement ± synovectomy ± chondroplasty) to closed needle joint lavage with saline (32 participants) and high tibial osteotomy surgery to knee joint distraction surgery (62 participants). Two studies (152 participants) compared arthroscopic surgery (washout ± debridement; debridement) to a hyaluronic acid injection. Only one study was at low risk of selection bias, and due to the difficulty of blinding participants to their treatment, all studies were at risk of performance and detection bias.

Reporting of results in this summary has been restricted to the primary comparison: surgical intervention versus non-surgical intervention.

A single study, included 320 participants with symptoms consistent with meniscal tear. All subjects had the meniscal tear confirmed on knee MRI and radiographic evidence of mild to moderate osteoarthritis (osteophytes, cartilage defect or joint space narrowing). Patients with severe osteoarthritis (KL grade 4) were excluded. The study compared arthroscopic partial meniscectomy and physical therapy to physical therapy alone (a six-week individualised progressive home exercise program). This study was at low risk of selection bias and outcome reporting biases, but was susceptible to performance and detection biases. A high rate of cross-over (30.2%) occurred from the physical therapy group to the arthroscopic group.

Low-quality evidence suggests there may be little difference in pain and function at 12 months follow-up in people who have arthroscopic partial meniscectomy and those who have physical therapy. Evidence was downgraded to low quality due to risk of bias and imprecision.

Mean pain was 19.3 points on a 0 to 100 point KOOS pain scale with physical therapy at 12 months follow-up and was 0.2 points better with surgery (95% confidence interval (CI) 4.05 better to 3.65 points worse with surgery, an absolute improvement of 0.2% (95% CI 4% better to 4% worse) and relative improvement 0.4% (95% CI 9% better to 8% worse) (low quality evidence). Mean function was 14.5 on a 0 to 100 point KOOS function scale with physical therapy at 12 months follow-up and 0.8 points better with surgery (95% CI 4.3 better to 2.7 worse); 0.8% absolute improvement (95% CI 4% better to 3% worse) and 2.1% relative improvement (95% CI 11% better to 7% worse) (low quality evidence).

Radiographic structural osteoarthritis progression and quality of life outcomes were not reported.

Due to very low quality evidence, we are uncertain if surgery is associated with an increased risk of serious adverse events, incidence of total knee replacement or withdrawal rates. Evidence was downgraded twice due to very low event rates, and once for risk of bias.

At 12 months, the surgery group had a total of three serious adverse events including fatal pulmonary embolism, myocardial infarction and hypoxaemia. The physical therapy alone group had two serious adverse events including sudden death and stroke (Peto OR 1.58, 95% CI 0.27 to 9.21); 1% more events with surgery (95% CI 2% less to 3% more) and 58% relative change (95% CI 73% less to 821% more). One participant in each group withdrew due to adverse events.

Two of 164 participants (1.2%) in the physical therapy group and three of 156 in the surgery group underwent conversion to total knee replacement within 12 months (Peto OR 1.76, 95% CI 0.43 to 7.13); 1% more events with surgery (95% CI 2% less to 5% more); 76% relative change (95% CI 57% less to 613% more).

## Authors' conclusions

The review found no placebo-or sham-controlled trials of surgery in participants with symptomatic mild to moderate knee osteoarthritis. There was low quality evidence that there may be no evidence of a difference between arthroscopic partial meniscectomy surgery and a home exercise program for the treatment of this condition. Similarly, low-quality evidence from a few small trials indicates there may not be any benefit of arthroscopic surgery over other non-surgical treatments including saline irrigation and hyaluronic acid injection, or one type of surgery over another. We are uncertain of the risk of adverse events or of progressing to total knee replacement due to very small event rates. Thus, there is uncertainty around the current evidence to support or oppose the use of surgery in mild to moderate knee osteoarthritis. As no benefit has been demonstrated from the low quality trials included in this review, it is possible that future higher quality trials for these surgical interventions may not contradict these results.

## PLAIN LANGUAGE SUMMARY

### Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Surgical interventions for symptomatic mild to moderate knee osteoarthritis (Review)  
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## Review question

Is surgical intervention safe and beneficial in the management of patients with symptomatic mild to moderate osteoarthritis of the knee?

## Background

Osteoarthritis of the knee affects millions of people worldwide. End-stage osteoarthritis of the knee is successfully treated with a knee replacement. Participants with mild to moderate degenerative changes in the knee can be very symptomatic but are not routinely offered knee replacement surgery as they do less well following this procedure. It is not known whether other types of surgery in this group are beneficial and safe.

## Search date

This systematic review is up to date as of the 24th May 2018.

## Study characteristics

All included studies were randomised controlled trials involving adults (18 years of age and older) with symptomatic mild to moderate knee osteoarthritis. One study, including 320 participants from the USA compared arthroscopic partial meniscectomy (APM) and physical therapy (home-based exercises) to physical therapy (PT) alone. One study, including 32 participants from the USA, compared arthroscopic surgery (debridement ± synovectomy ± chondroplasty) to closed needle joint lavage with saline. Two studies, including 152 participants (120 from Pakistan, 32 from the UK) compared arthroscopic surgery (washout ± debridement, debridement) to a hyaluronic acid injection. One study, including 62 participants from the Netherlands, compared high tibial osteotomy surgery to knee joint distraction surgery.

## Funding sources

One study was supported by grant 9040 from the Robert Wood Johnson Foundation, by the NIH (NIAMS) and by the Percy Surgical Research Trust of Lutheran General Hospital. One study was supported by grants from the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health. One study was funded by ZonMw (The Netherlands Organisation for Health Research and Development). Two studies did not report any funding source.

## Key results

Due to space constraints, reporting of results is restricted to the primary comparison, arthroscopic partial meniscectomy surgery versus a six-week progressive home-based exercise intervention for the knee, at 12 months:

### Pain (lower score means less pain):

Improved by 0.2% with surgery (4% better to 4% worse) on a 0 to 100 point scale

- People who had surgery rated their pain as 19.1 points.
- People who had physical therapy rated their pain as 19.3 points.

### Function (lower score means better function):

Improved by 0.8 % with surgery (4% better to 3% worse)

- People who had surgery rated their function as 13.7.
- People who had physical therapy rated their function as 14.5.

### Serious adverse events:

Increased by 1% with surgery (2% better to 3% worse)

- 3 people out of 156 had a serious adverse event with surgery including fatal blood clot, heart attack and low blood oxygen levels.
- 2 people out of 164 had a serious adverse event with physical therapy including sudden death and stroke.

### Conversion to total knee replacement:

- Five participants in the APM group (30 per 1,000) and three subjects in the PT group (17 per 1,000) underwent total knee replacement.

### Withdrawals

- One subject died in each group.

### **Quality of the evidence**

Low-quality evidence (downgraded due to biases in the study design and small sample size) indicates there may be little or no benefit of surgery over progressive exercise in terms of pain and function. Arthroscopic surgery may not have any benefits over closed needle joint lavage with saline or hyaluronic acid injection, and surgery to realign non-diseased bone surfaces (osteotomy) may have little or no benefit over surgery to separate diseased bone joint surfaces (knee joint distraction) as there was only low-quality evidence at best from single or two small studies.

Due to the very low adverse event rates, it is not clear if surgery is associated with an increased risk of serious adverse events, incidence of total knee replacement or withdrawal rates.

Osteoarthritis progression and quality of life were not measured.

### **Summary**

There was low-quality evidence that there may be little difference between arthroscopic partial meniscectomy and a home exercise program for the treatment of mild to moderate osteoarthritis. Similarly, surgery may not be better than other interventions to treat this condition, as indicated by low-quality evidence from a few small trials.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Surgical intervention compared to non-surgical intervention for symptomatic mild to moderate knee osteoarthritis						
<b>Patient or population:</b> Adults with symptomatic mild to moderate knee osteoarthritis defined as knee pain and radiographic evidence of non-end stage osteoarthritis (Kellgren-Lawrence grade 1, 2, 3 or equivalent on MRI/arthroscopy). <b>Setting:</b> Seven US tertiary referral centres. <b>Intervention:</b> Arthroscopic partial meniscectomy <b>Comparison:</b> Physical therapy (progressive home-based exercise program)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with physical therapy <sup>1</sup>	Risk with surgery <sup>2</sup>				
<b>Pain</b> assessed with: KOOS Scale from: 0 to 100 (100 = worst) follow-up: mean 12 months	Mean pain score in control groups was <b>19.3</b>	The mean pain was <b>0.20 points better</b> with surgery (4.05 better to 3.65 worse)	-	320 (1 RCT)	⊕⊕○○ LOW <sup>1,2</sup>	0.2% absolute improvement (4% better to 4% worse) <sup>3</sup> 0.4% relative improvement (9% better to 8% worse) <sup>4</sup> NNTB <sup>5</sup>
<b>Physical function</b> assessed with: WOMAC Scale from: 0 to 100 (100 = worst) follow-up: mean 12 months	Mean physical function score <b>14.5</b>	The mean function was <b>0.80 points better</b> with surgery (4.30 better to 2.70 worse)	-	320 (1 RCT)	⊕⊕○○ LOW <sup>1,2</sup>	0.8% absolute improvement (4% better to 3% worse) 2.1% relative improvement (11% better to 7% worse) NNTB <sup>5</sup>
<b>Radiographic structural progression</b>	-	-	-	-	-	Not measured in included studies
<b>Quality of life</b>	-	-	-	-	-	Not measured in included studies

<b>Serious adverse events</b> follow-up: mean 12 months	11 per 1,000	18 per 1,000 (95% CI 3 to 99)	Peto OR 1.58 (0.27 to 9.21) <sup>6</sup>	351 (1 RCT)	⊕○○○ VERY LOW <sup>1,2</sup>	1% absolute change (95% CI 2% less to 3% more) 58% relative change (95% CI 73% less to 821% more) Events: fatal pulmonary embolism, myocardial infarction and hypoxaemia in surgery; sudden death and stroke in exercise group
<b>Re-operation rate or conversion to total knee replacement, or both</b> follow-up: mean 12 months	17 per 1,000	30 per 1,000 (95% CI 7 to 115)	Peto OR 1.76 (0.43 to 7.13)	351 (1 RCT)	⊕○○○ VERY LOW <sup>1,2</sup>	1% absolute change (95% CI 2% less to 5% more) 76% relative change (95% CI 57% less to 613% more) NNTB/NNTB <sup>5</sup>
<b>Withdrawals due to adverse events</b> follow-up: mean 12 months	6 per 1,000	6 per 1,000 (95% CI 0 to 88)	Peto OR 1.05 (0.07 to 16.90)	351 (1 RCT)	⊕○○○ VERY LOW <sup>1,2</sup>	0% absolute change (95% CI 2% less to 2% more) 5% relative improvement (95% CI 93% less to 1590% more) One in each group died

\* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; OR: Odds ratio;

#### **GRADE Working Group grades of evidence**

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

<sup>1</sup> Downgraded due to risk of bias issues

<sup>2</sup> Downgraded for imprecision (only one study contributed data for all outcomes; the study was underpowered to detect any differences for the continuous outcomes. A further downgrade for dichotomous outcomes where the event rates were small.

<sup>3</sup> For dichotomous outcomes, the absolute risk difference was calculated using the risk difference statistic in Review Manager and the result expressed as a percentage. For continuous outcomes, the absolute benefit was calculated as the improvement in the intervention group minus the improvement in the control group.

<sup>4</sup> The relative percent change for dichotomous data was calculated as the risk ratio - 1 and expressed as a percentage. For continuous outcomes, the relative difference in the change from baseline was calculated as the absolute benefit divided by the baseline mean of the control group, expressed as a percentage.

<sup>5</sup> Number needed to treat for an additional beneficial outcome (NNTB) or for an additional harmful outcome (NNTH) not applicable when result is not statistically significant

<sup>6</sup> Reported Peto OR which can be interpreted as an RR due to the low event rate

## BACKGROUND

### Description of the condition

Worldwide musculoskeletal disorders account for 6% to 8% of all disability-adjusted life years, and osteoarthritis accounts for approximately 10% of this disease burden (Murray 2012). Osteoarthritis affecting the knee is common, with a global prevalence of radiographically confirmed symptomatic knee osteoarthritis estimated to be 3.8% (Cross 2014), and a lifetime risk of symptomatic knee osteoarthritis in Western populations estimated to be over 40% (Murphy 2008). In the UK, more people receive disability living allowance as a result of arthritis than for heart disease, stroke, chest disease, and cancer combined (Department for Work and Pensions 2007).

Osteoarthritis of the knee represents a continuum of disease from early cartilage thinning to full-thickness cartilage loss, bony erosion, and deformity. One or more of the three compartments of the knee (patellofemoral, medial tibiofemoral, and lateral tibiofemoral) can be involved, and the disease affects all of the tissues within the joint.

A revised version of the American College of Rheumatologists classification system for osteoarthritis has been validated for clinical use (Altman 1991). This system defines criteria for knee osteoarthritis based on clinical signs or radiological features, or both:

- Clinical: knee pain for most days of the prior month, in addition to three of the following:
  - Crepitus on active joint motion
  - Morning stiffness > 30 minutes duration
  - Age > 38 years
  - Bony enlargement of the knee on examination
  - Bony tenderness of the knee on examination
  - No palpable warmth
- Clinical plus radiographic: knee pain for most days of the prior month, plus radiographic evidence of osteophytes on joint margins in addition to one of the following:
  - Crepitus on active joint motion
  - Morning stiffness > 30 minutes duration
  - Age > 38 years

Whilst this is a useful algorithm for identifying people with knee osteoarthritis, its use cannot reliably be extended to defining the severity or progression of disease.

There are many radiographic descriptions of osteoarthritis that attempt to identify both the presence of osteoarthritis and the severity of the disease. Kellgren and Lawrence described a radiographic classification system that identifies various features of osteoarthritis including osteophytes, joint space narrowing, subchondral sclerosis, subchondral bone cysts and bone deformity (Kellgren 1957). The whole knee is then graded with regards to the severity of these features: none (0), doubtful (1), minimal (2), moderate (3), severe (4).

Magnetic resonance imaging (MRI) is a non-invasive imaging modality that allows for a detailed assessment of structures within the knee. It can be used to establish osteoarthritis diagnosis, assess disease severity, and monitor disease progression. MRI can detect cartilage loss when none is evident on plain film radiographs and can be used to identify structural changes within the knee of a person with osteoarthritic symptoms but without changes on plain film radiographs (Amin 2005; Javaid 2009).

In an effort to synthesise the available information regarding knee osteoarthritis, Luyten and colleagues described early knee osteoarthritis as a combination of clinical (at least two episodes of pain for 10 days or more in the last year) and imaging (radiographic changes of Kellgren-Lawrence 2 or less and MRI or arthroscopic evidence of cartilage change) findings (Luyten 2012). This classification recognises the importance of structural changes within the knee that can precede changes seen on plain film radiographs. The distinctions between the different stages of osteoarthritis are important. End-stage, bone-on-bone osteoarthritis is treated dependably with arthroplasty in the form of total or unicompartmental knee replacement. Arthroplasty surgery is not routinely offered to those with mild to moderate osteoarthritis, as it is associated with a poorer outcome (Dowsey 2012; Niinimäki 2011). People with mild to moderate osteoarthritis are in a 'treatment gap', where symptoms and disability can be significant, and yet surgical options are limited (London 2011). This review will establish whether or not any surgery is safe and or effective for treating people with this condition.

Clearly, a broadly-accepted description of mild to moderate structural knee osteoarthritis does not exist. Definitions of early osteoarthritis include those without radiographic changes and some may consider the presence of radiographic changes in itself as being diagnostic of late disease. The definition of mild to moderate osteoarthritis used in this review (Types of participants) includes both clinical (symptoms) and imaging (structural) criteria. Radiographic criteria include Kellgren-Lawrence grading system (KL grades 1, 2 & 3), arthroscopic criteria include International Cartilage Repair Society grading system (ICRS grades score 1, 2 & 3) and MRI criteria include Boston Leeds Osteoarthritis Knee Score (BLOKS grades 1.0, 1.1, 2.0, 2.1, 3.0, 3.1).

The selection criteria have been proposed in order to identify those patients with symptomatic knee osteoarthritis who are not suitable for knee replacement. The role of surgery in such individuals is the central focus of this review.

### Description of the intervention

This systematic review will take a disease-based approach in order to assess the effectiveness of any surgical intervention that may be employed in the management of mild to moderate knee osteoarthritis. This broad approach will enable the full scope of surgical interventions available for this condition to be considered

simultaneously. Surgical interventions for the treatment of mild to moderate knee osteoarthritis include the following.

### **Arthroscopic procedures**

Arthroscopy is a minimally invasive procedure that is offered to people with osteoarthritis of the knee. Generally, two small incisions are made in the front of the knee enabling the passage of a fiberoptic camera through one incision and surgical instruments through the other. Many surgical procedures can be performed using this technique.

Arthroscopic irrigation, also termed joint lavage, involves flushing the joint through with a sterile solution. Arthroscopic debridement is a surgical intervention that enables resection of damaged tissue within the knee joint. This may involve a variety of different procedures, including excision of inflammatory soft tissues, burring down of obstructive osteophytes, and removal of loose bodies. A meniscectomy involving excision of all (total meniscectomy) or part (partial meniscectomy) of a degenerate meniscus (a disc of fibrocartilage within the knee joint) can be performed arthroscopically. Alternatively, a meniscal repair using sutures or anchors to repair a degenerate tear whilst preserving the remaining meniscus is possible. Partial or total meniscal substitutes with a synthetic or donor meniscus (meniscal allograft) can be used to restore a de-functioned meniscus.

Cartilage repair can be performed using a variety of techniques. Chondroplasty involves the trimming down of loose or damaged cartilage. Subchondral bone marrow stimulation encompasses a variety of techniques that perforate the subchondral bone and expose a cartilage-deficient region to the underlying bone marrow. Autologous chondrocyte implantation and matrix-assisted autologous chondrocyte implantation involve the application of cultured chondrocytes (cartilage-producing cells) to regenerate cartilage in areas where it is deficient.

### **Load-modifying procedures**

An osteotomy for osteoarthritis of the knee joint is a re-alignment procedure aimed at transferring the weight-bearing region of the knee joint from the diseased region to a disease-free region. This is achieved by cutting and reshaping the bone in the upper tibia (high tibial osteotomy) or lower femur (distal femoral osteotomy). Chronic medial compartment joint-loading can be modified using a device that is inserted outside the knee joint. Devices such as the KineSpring® (Moximed Inc, Hayward, CA, USA) have been developed to partially absorb the load passing through the medial compartment without compromising the joint surface (Clifford 2011).

Metallic interpositional devices are designed to remedy medial joint space narrowing caused by osteoarthritis; in so doing, a varus (bow-legged) knee can be placed into a more neutral alignment (Clarius 2010). Such devices can be inserted using minimally in-

vasive techniques and without the need for resection of underlying bone.

Knee joint distraction is a surgical technique that uses an external fixation device to separate the knee joint surfaces for a defined period of time. Joint distraction aims to reduce mechanical stresses on the joint surface, prevent further wear and tear of the cartilage, and allow chondrocytes to initiate repair (Lafeber 2006).

### **Knee replacement surgery**

Total knee replacement involves replacing the surfaces of the knee joint with artificial implants. The implants are usually made from a combination of metal alloy and high-density plastic, and require bone to be resected in order to accommodate them. Unicompartmental knee replacement only involves replacing the surfaces of a single diseased compartment (medial, lateral, or patellofemoral), rather than the whole joint surface.

## **How the intervention might work**

### **Arthroscopic procedures**

Arthroscopic procedures for osteoarthritis of the knee are generally intended to promote a smooth excursion of the knee joint surface. This may be achieved by washing debris out of the knee joint (irrigation), removing torn or irregular cartilage (debridement or chondroplasty), reconstituting a degenerate meniscus (meniscal repair/replacement), or promoting cartilage growth in areas of deficiency (subchondral bone marrow stimulation or autologous chondrocyte implantation). The exact mechanism by which a smooth joint surface relates to pain-free movement is unclear.

Cartilage repair techniques aim to restore a smooth articular surface. Loss of cartilage and exposure of the subchondral bone leads to pain (Buckwalter 1998), therefore any efforts to reduce friction or cover the subchondral bone may improve this. Trials in this area have involved isolated full-thickness cartilage lesions outside the context of osteoarthritis.

The meniscus is responsible for increasing surface area of the knee and dissipating load through the knee joint. Meniscal injury causes symptoms by promoting inflammation and pain. Meniscal resection, either total or partial, has been used where the meniscus is irreparably damaged. However, there is growing concern over the effect of this operation, as it may in fact accelerate progression of osteoarthritis (Roos 2001). Meniscal repair is usually performed in the context of isolated injuries. Meniscal replacement in the form of cadaveric (allograft) or synthetic grafts is appealing in that it aims to restore the function of the meniscus.

### **Load-modifying procedures**

Longitudinal cohort studies have demonstrated that malalignment at the knee is associated with both incidence and progression of

knee osteoarthritis (Hayashi 2012; Sharma 2001; Sharma 2013; Tanamas 2009). The effect of malalignment on osteoarthritis is attributed to its unequal influence on loading of the knee joint. In cases of bow-legged deformity, more load crosses the medial compartment, and in valgus (knock-knee) alignment, more load crosses the lateral compartment. Load-modifying procedures aim to lessen the load passing through the compartment in order to both relieve symptoms and slow disease progression.

KineSpring® is a relatively new device that is both extra-articular and extra-capsular. It is specifically indicated for medial compartment osteoarthritis and consists of a load absorber that can absorb a maximal load of 30 pounds in weight, with promising results in the short and medium term (Clifford 2011; London 2013).

Interpositional arthroplasty is indicated for unicompartmental osteoarthritis. The result is a protection to the underlying subchondral bone exposed due to damaged cartilage and intra-articular correction of varus deformity (Koeck 2009). Reports of high revision rates and unpredictable outcomes have raised concerns over these implants (Bailie 2008).

The principle of joint distraction is to offload the knee joint and reduce the mechanical stresses that contribute to the degeneration of cartilage. One study has demonstrated both symptom improvement and cartilage repair using this technique (Wiegant 2013), however the exact mechanism by which cartilage regenerates under these conditions remains unclear.

### **Knee replacement surgery**

Knee replacement surgery is an established technique for end-stage osteoarthritis, with good clinical outcomes described for both total knee replacement and partial knee replacement. However, the use of arthroplasty surgery is not routinely extended to those with less severe osteoarthritis, as it is associated with a poorer outcome (Dowsey 2012; Niinimäki 2011). The inclusion of knee replacement surgery in this review reflects the need to establish the level of evidence supporting or opposing its use in the management of early to moderate osteoarthritis.

### **Why it is important to do this review**

The current literature concerning osteoarthritis of the knee frequently takes an intervention-based approach. Many of these studies have not stratified their results based on the severity of the disease at baseline or recruitment. Where mild to moderate osteoarthritis of the knee is considered, there is often a focus on non-surgical or pharmacological treatments (Brahmachari 2009; Jang 2013; Nelson 2013).

Evidence for arthroscopic irrigation is poor, with a previous Cochrane review concluding no benefit for joint lavage when compared to sham surgery or no intervention (Reichenbach 2010). The trials included in this review did not stratify results based on stage of osteoarthritis. A further Cochrane review found no sig-

nificant benefit for arthroscopic debridement compared to sham surgery or arthroscopic irrigation (Laupattarakasem 2008). Interestingly, the one trial in this review that reported improved outcomes in the arthroscopic debridement group involved people with single degenerative lesions, suggesting less extensive disease (Hubbard 1996).

With regard to load-modifying procedures, the results for osteotomy are good. However, patient selection, operative technique, and degree of correction have all been demonstrated to influence outcome (Briem 2007; Coventry 1993; Duivenvoorden 2014). A previous Cochrane review concluded that although there was good evidence to support the fact that high tibial osteotomy (HTO) improves function and pain in people with osteoarthritis, there is significant heterogeneity of the clinical trials to date (Brouwer 2014).

Many people who present with features of mild to moderate knee osteoarthritis will have pain and functional profiles that are similar to people with end-stage disease undergoing arthroplasty (Jones 2014). People with symptomatic knee osteoarthritis who are not suitable for arthroplasty surgery may dwell in the 'treatment gap' for over 20 years, with significant clinical and economic implications (London 2011). The James Lind Alliance, a patient-driven enterprise that works to prioritise unanswered questions about the effects of treatments, has highlighted the outcome of arthroplasty and non-arthroplasty surgery in this patient group as an important area for research (JLA 2015).

This systematic review will drive the direction of future research in this hard-to-treat patient group and will be conducted according to the guidelines recommended by the Cochrane Musculoskeletal Group Editorial Board (Ghogomu 2014).

## **OBJECTIVES**

To assess the benefits and harms of surgical intervention for the management of symptomatic mild to moderate knee osteoarthritis.

## **METHODS**

### **Criteria for considering studies for this review**

#### **Types of studies**

We included randomised controlled trials and quasi-randomised controlled trials only. We included studies reported as full text, those published as abstract only, and unpublished data. There was no language restriction.

## Types of participants

We included adults (18 years of age and older) with diagnosis of mild to moderate knee osteoarthritis, defined as the presence of pain and one of the following features:

### Radiographic

Kellgren-Lawrence grade 1, 2, 3 or equivalent.

### MRI

Cartilage degradation but minimal full-thickness loss (< 10% of surface area or < 1 cm)

e.g. Boston Leeds Osteoarthritis Knee Score (BLOKS) cartilage morphology (Hunter 2008)

Percent of sub-region surface area affected by cartilage loss (any loss score):

- grade 1: < 10%
- grade 2: 10% to 75%
- grade 3: > 75%

Extent of full-thickness loss (full-thickness loss score):

- grade 0: none
- grade 1: < 10%

OR

Whole Organ Magnetic Resonance Imaging Score (WORMS) cartilage morphology (Peterfy 2004)

- grade 1: increased signal from normal-thickness cartilage
- grade 2: partial-thickness focal defect < 1 cm
- grade 2.5: full-thickness focal defect < 1 cm
- grade 3: multiple areas of partial-thickness defect within areas of normal thickness
- grade 4: diffuse partial-thickness loss

OR

MRI Osteoarthritis Knee Score (MOAKS) cartilage morphology (Hunter 2011)

Size of any cartilage loss as a % of surface area

- grade 1: < 10%
- grade 2: 10% to 75%
- grade 2: > 75%

Extent of full-thickness cartilage loss in a region

- grade 0: 0%
- grade 1: < 10%

or any equivalent MRI scoring system.

### Arthroscopy

Cartilage degradation but no more than one isolated full-thickness defect

e.g. International Cartilage Repair Society (ICRS) score (ICRS 2000)

- grade 1: soft indentation (A) and/or superficial fissures and cracks (B)
- grade 2: lesions extending down to < 50% of cartilage depth
- grade 3: cartilage defects extending down > 50% of cartilage depth (A) as well as down to calcified layer (B)

or any equivalent arthroscopic scoring system.

We excluded trials which included participants with the following comorbidities/characteristics:

- asymptomatic individuals
- end-stage osteoarthritis full-thickness cartilage loss (> 1 cm) or bony deformity (Kellgren-Lawrence grade 4), or both
- degenerate meniscal tears but no radiographic or MRI evidence of osteoarthritis
- history of trauma
- inflammatory arthropathy, metabolic bone disease, rheumatoid arthritis

If a trial included a subgroup of participants with mild to moderate knee osteoarthritis (as defined above), and these results were reported separately from those with more or less structural osteoarthritis, we planned to include the data that related to mild to moderate knee osteoarthritis only. However, this scenario did not arise. If a trial appeared to have a subgroup of participants with mild to moderate knee osteoarthritis but did not report their results separately, then we contacted the authors of the trial to ask them to provide the data for the mild to moderate knee osteoarthritis subgroup.

## Types of interventions

We assessed trials that included any type of surgical intervention (see [Description of the intervention](#)), for example:

- arthroscopic procedures including but not limited to debridement, meniscectomy, cartilage repair techniques or any combination of these procedures
- load-modifying procedures including but not limited to osteotomy, knee distraction, KineSpring® and interpositional arthroplasty
- knee replacement surgery including total knee replacement and partial knee replacement

These could be compared with:

- any non-surgical intervention including but not limited to sham surgery, placebo, physiotherapy, bracing, nonsteroidal anti-inflammatory drugs, orthotics
- any injectable therapy including but not limited to steroid, hyaluronic acid, and regenerative therapies: stem cell therapy, platelet-rich plasma, platelet lysates, prolotherapy
- any other type of surgical intervention
- any surgery plus additional surgical intervention (e.g. arthroscopy versus arthroscopy + osteotomy)

No interventions were excluded.

## Types of outcome measures

### Major outcomes

1. Pain with a hierarchy of 11 levels (when more than one was reported, the highest on the list was used):
  - i) Pain overall
  - ii) Pain on walking
  - iii) Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale
    - iv) Pain on activities other than walking
    - v) WOMAC global scale
    - vi) Lequesne osteoarthritis index global score
    - vii) Other algofunctional scale
    - viii) Patient's global assessment
    - ix) Physician's global assessment
    - x) Other outcome
    - xi) No continuous outcome reported
2. Physical function with a hierarchy of eight levels (when more than one was reported, the highest on the list was used):
  - i) Global disability score
  - ii) Walking disability
  - iii) WOMAC disability subscore
  - iv) Composite disability scores other than WOMAC
  - v) Disability other than walking
  - vi) WOMAC global scale
  - vii) Lequesne osteoarthritis index global score
  - viii) Other algofunctional scale
3. Radiographic joint structure changes according to the given hierarchy (the first two outcomes, minimum joint-space width and median joint-space width, are used most often):
  - i) Minimum joint-space width
  - ii) Median joint-space width
  - iii) Semi-quantitative measurement
4. Health-related quality of life: generic and overall or disease-specific tools. For SF-36, mental component score would be used.
5. Short-term serious adverse events from trials
6. Re-operation rate or conversion to/revision of total knee replacement (indicating failure of the primary intervention)
7. Withdrawals due to adverse events

Where multiple time points were reported, we planned to group them into early- (up to and including one year), intermediate- (one to three years), and long-term (greater than three years) follow-up.

## Search methods for identification of studies

### Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and Embase.

We conducted searches of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform ([www.who.int/ictrp/en/](http://www.who.int/ictrp/en/)).

We searched all databases from their inception to the 24th May 2018 and imposed no restriction on language of publication.

See [Appendix 1](#); [Appendix 2](#); [Appendix 3](#) for the search strategy.

### Searching other resources

We checked reference lists of all primary studies and review articles for additional references. We searched relevant manufacturers' websites for trial information and contacted individuals or organisations, where appropriate.

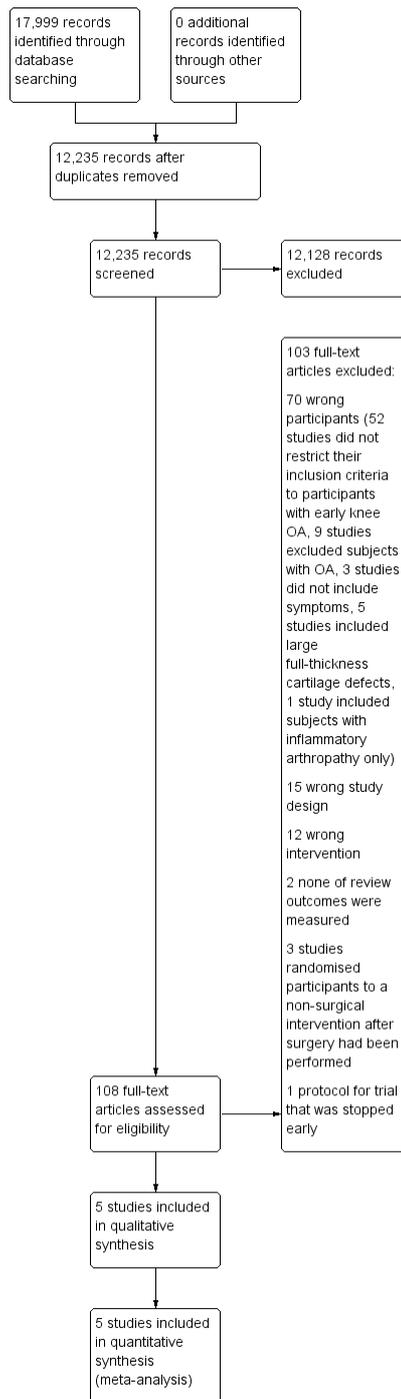
We searched for errata or retractions from included studies published in full text on PubMed ([www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed)).

## Data collection and analysis

### Selection of studies

All review authors independently screened titles and abstracts of all the potential studies we identified as a result of the search for inclusion and coded them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We retrieved the full-text study reports/publications, and all review authors independently screened the full text and identified studies for inclusion, and identified and recorded reasons for exclusion of the ineligible studies. We resolved any disagreements through discussion. If an agreement could not be reached within the group, all seven authors would have been given an 'in' or 'out' vote to decide whether or not to include the study. This was not necessary. We identified and excluded duplicates and collated multiple reports of the same study so that each study, rather than each report, was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram ([Figure 1](#)) and 'Characteristics of excluded studies' table ([Excluded studies](#)).

**Figure 1. Study flow diagram.**



## Data extraction and management

We used a data collection form for study characteristics (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) and outcome data was piloted on a single study in the review. One review author (JSP) extracted study characteristics from the included studies. A second review author (SH) spot-checked study characteristics for accuracy against the trial report. We extracted the following study characteristics:

1. Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and location, study setting, withdrawals, and date of study.
2. Participants: N, mean age, age range, sex, body mass index, disease duration, severity of condition, comorbidities, sociodemographics, ethnicity, diagnostic criteria, important baseline data, inclusion criteria, and exclusion criteria.
3. Interventions: total number of intervention groups within each trial, specific details of each intervention and comparator, e.g. who provided the intervention, materials used, standardisation of the surgical intervention and adherence to the standardised technique, any modifications or tailoring of the intervention during the trial period.
4. Outcomes: major outcomes specified and collected, and time points reported.
5. Characteristics of the design of the trial as outlined below in the [Assessment of risk of bias in included studies](#) section.
6. Notes: funding for trial, and notable declarations of interest of trial authors.

Two review authors (JSP, LEB) independently extracted outcome data from included studies. Where available, we extracted the number of events and number of participants per treatment group for dichotomous outcomes, and means and standard deviations and number of participants per treatment group for continuous outcomes. We noted in the '[Characteristics of included studies](#)' table if outcome data were not reported in a usable way and when data were transformed or estimated from a graph. We resolved disagreements by consensus or by involving a third review author (AJP). One review author (JSP) transferred data into the Review Manager file ([RevMan 2012](#)). We double-checked that data were entered correctly by comparing the data presented in the systematic review with the study reports.

If more than one outcome measure was reported in a trial, we prioritised outcomes based on the hierarchy of major outcomes listed above.

Where both final values and change from baseline values were reported for a given outcome, we extracted the final value; if both unadjusted and adjusted values for the same outcome were reported, we extracted the unadjusted value.

## Main planned comparisons

1. Any type of surgical intervention versus any non-surgical intervention. This was the primary comparison of the study. We planned to present data separately according to the type of non-surgical comparator (e.g. sham surgery, physiotherapy, bracing, nonsteroidal anti-inflammatory drugs, orthotics). However, there were insufficient data for this.
2. Any type of surgical intervention versus any injectable therapy.
3. Any type of surgical intervention versus any other surgical intervention.

## Assessment of risk of bias in included studies

Two review authors (APM, JSP) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We resolved any disagreements by discussion or by involving another review author (SH). We assessed the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Major baseline imbalance.
8. Differences in rehabilitation.

We graded each potential source of bias as high, low, or unclear risk of bias and provided a quote from the study report together with a justification for our judgement in the 'Risk of bias' table. We summarised the 'Risk of bias' judgements across different studies for each of the domains listed. We considered blinding separately for different key outcomes, where necessary (for example, for unblinded outcome assessment, risk of bias for all-cause mortality may be different than for a patient-reported pain scale). We considered the impact of missing data by key outcomes. Where information on risk of bias related to unpublished data or correspondence with a trialist, we noted this in the 'Risk of bias' table.

When considering treatment effects, we took into account the risk of bias for the studies that contributed to that outcome.

We presented the figures generated by the 'Risk of bias' tool to provide summary assessments of the risk of bias.

## Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol and reported any deviations from it in the 'Differences between protocol and review' section of the systematic review.

### Measures of treatment effect

We analysed dichotomous data as risk ratios or Mantel-Haenszel Peto odds ratio when the outcome was a rare event (approximately less than 10%), and used 95% confidence intervals. We analysed continuous data as mean difference or standardised mean difference (SMD), depending on whether the same scale was used to measure an outcome, and 95% confidence intervals. We entered data presented as a scale with a consistent direction of effect across studies.

When different scales were used to measure the same conceptual outcome (e.g. disability), SMDs were calculated instead, with the corresponding 95% confidence intervals. SMDs were back-translated to a typical scale (e.g. 0 to 10 for pain) by multiplying the SMD by a typical among-person standard deviation (e.g. the standard deviation of the control group at baseline from the most representative trial) as per Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011b).

In the 'Effects of interventions' results section and the 'Comments' column of the 'Summary of findings' table, we provided the absolute per cent difference, the relative change from baseline, the number needed to treat for an additional harmful outcome (NNTH) and the number needed to treat for an additional beneficial outcome (NNTB).

For dichotomous outcomes such as serious adverse events, we calculated the NNTH and NNTB from the control group event rate and the relative risk using the Visual Rx calculator (Cates 2008). We calculated the NNTH and NNTB for continuous measures using the Wells calculator (available at the Cochrane Musculoskeletal Group Editorial office, <http://musculoskeletal.cochrane.org/>). We input the minimal clinically important difference (MCID) into the calculator. We assumed an MCID of 1.5 points on a 0 to 10 point pain scale and 10 points on a 0 to 100 point function scale. For dichotomous outcomes, the absolute risk difference was calculated using the risk difference statistic in Review Manager and the result expressed as a percentage. For continuous outcomes, the absolute benefit was calculated as the improvement in the intervention group minus the improvement in the control group, in the original units.

The relative percent change for dichotomous data was calculated as the risk ratio -1 and expressed as a percentage. For continuous outcomes, we calculated the relative difference in the change from baseline as the absolute benefit divided by the baseline mean of the control group, expressed as a percentage.

### Unit of analysis issues

Where multiple trial arms were reported in a single trial, we planned to include only the relevant arms. If two comparisons (for

example, surgical intervention A versus non-surgical intervention and surgical intervention B versus non-surgical intervention) were combined in the same meta-analysis, we planned to halve the control group to avoid double counting. This was not necessary for any of the included studies.

If multiple time points were reported, we grouped them into short- (less than one year), intermediate- (one to three years), and long-term (greater than three years) follow-up. If a single trial reported multiple time points within one of these groups, then we extracted the data that related to the later time point (for example, if one trial reported outcomes at six months and one year, we extracted the one-year results only).

### Dealing with missing data

We contacted investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data (for example, when a study was identified as abstract only or when data were not available for all participants). Where possible, and the missing data were thought to introduce serious bias, we planned to explore the impact of including such studies in the overall assessment of results by a sensitivity analysis. This was not necessary for any of the included studies. We clearly described any assumptions and imputations to handle missing data and explored the effect of imputation by sensitivity analyses.

For dichotomous outcomes (for example, number of withdrawals due to adverse events), we planned to calculate the withdrawal rate using the number of participants randomised in the group as the denominator. This was not possible as withdrawal rates were poorly reported and the participant numbers from included studies were too small.

For continuous outcomes (for example mean change in pain score), we calculated the standardised mean difference based on the number of participants analysed at that time point. If the number of participants analysed was not presented for each time point, we planned to use the number of randomised participants in each group at baseline, however, this was not necessary.

Where possible, we computed missing standard deviations from other statistics such as standard errors, confidence intervals, or P values, according to the methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). If standard deviations could not be calculated, they were imputed (for example, from other studies in the meta-analysis).

### Assessment of heterogeneity

We assessed clinical and methodological diversity in terms of participants, interventions, outcomes, and study characteristics for the included studies in order to determine whether a meta-analysis was appropriate. We conducted this by observing the data from the data extraction tables. We assessed statistical heterogeneity by visual inspection of the forest plot for obvious differences in results between the studies, and by using the  $I^2$  and  $\text{Chi}^2$  statistical tests.

As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011), the interpretation of an  $I^2$  value of 0% to 40% might 'not be important'; 30% to 60% may represent 'moderate' heterogeneity; 50% to 90% may represent 'substantial' heterogeneity; and 75% to 100% may represent 'considerable' heterogeneity. As noted in the *Cochrane Handbook*, we kept in mind that the importance of  $I^2$  depends on (i) magnitude and direction of effects and (ii) strength of evidence for heterogeneity. We planned to interpret the  $\text{Chi}^2$  test where a P value less than or equal to 0.10 indicated evidence of statistical heterogeneity. This was not indicated for any of the included studies.

If we identified substantial heterogeneity, we reported it and investigated possible causes by following the recommendations in Section 9.6 of the *Cochrane Handbook* (Deeks 2011).

### Assessment of reporting biases

We created and examined a funnel plot to explore possible small-study biases. In interpreting funnel plots, we examined the different possible reasons for funnel plot asymmetry as outlined in Section 10.4 of the *Cochrane Handbook* (Sterne 2011) and related this to the results of the review. If we were able to pool more than 10 trials, we planned to undertake formal statistical tests to investigate funnel plot asymmetry, and follow the recommendations in Section 10.4 of the *Cochrane Handbook* (Sterne 2011). This was not necessary.

We checked trial protocols against published reports to assess outcome reporting bias. For studies published after 1 July 2005, we screened the WHO International Clinical Trials Registry Platform ([www.who.int/ictrp/en/](http://www.who.int/ictrp/en/)) for the a priori trial protocol. We evaluated whether selective reporting of outcomes was present.

### Data synthesis

We undertook meta-analyses only where it was meaningful, that is, if the treatments, participants, and the underlying clinical questions were similar enough for pooling to make sense.

We analysed the data separately for each of the three main comparisons: surgical intervention versus non-surgical intervention, surgical intervention versus injectable therapy, and surgical intervention versus other surgical intervention. Where possible, we analysed data separately according to the type of non-surgical comparator (for example sham surgery, physiotherapy, bracing, non-steroidal anti-inflammatory drugs, orthotics). If sufficient data were available, we planned to identify subgroups within each of the main analyses based on type of surgical intervention (for example arthroscopic, load-modifying, and knee replacement procedures). This was not possible as the number of included studies was too small. We only performed further analysis within each subgroup based on surgical procedure (for example, arthroscopic irrigation, arthroscopic debridement, cartilage repair) if sufficient data were collated from our search.

We recognised that there was likely to be significant clinical heterogeneity between participants across different trials. As such, we used a random-effects model and performed a sensitivity analysis with a fixed-effect model.

### Summary of findings table

We included 'Summary of findings' tables based on the following three main comparisons:

1. Arthroscopic partial meniscectomy versus physical therapy;
2. Arthroscopic surgery versus injectable therapy;
3. High tibial osteotomy versus knee distraction therapy.

We planned to present data separately according to the type of surgical intervention (for example arthroscopic, load-modifying, and knee replacement procedures) and type of non-surgical comparator (for example sham surgery, physiotherapy, bracing, non-steroidal anti-inflammatory drugs, orthotics). This was not possible due to insufficient data from the included studies.

We have included the following outcomes in each of the 'Summary of findings' tables:

1. Pain;
2. Physical function;
3. Radiographic joint structure changes;
4. Quality of life;
5. Short-term serious adverse effects from trials;
6. Re-operation rate or conversion to/revision of total knee replacement, or both (indicating failure of the primary intervention);
7. Withdrawals due to adverse events.

Two review authors (JSP, APM) independently assessed the quality of the evidence. We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it related to the studies that contributed data to the meta-analyses for the prespecified outcomes. We used methods and recommendations described in Sections 8.5 and 8.7, Chapter 11, and Chapter 13, Section 13.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* using GRADEpro software (Higgins 2011; Schünemann 2011a; GRADEpro 2015). We justified all decisions to downgrade the quality of studies using footnotes, and made comments to aid the reader's understanding of the review, where necessary.

### Subgroup analysis and investigation of heterogeneity

If sufficient data were available, we planned to carry out the following subgroup analyses for outcomes related to patient-reported pain and function.

1. Age 18 to 40 years, 40 to 65 years, > 65 years
2. Gender
3. Type of surgical intervention (e.g. arthroscopic, load-modifying, and knee replacement procedures)

4. Type of surgical procedure (e.g. arthroscopic irrigation, arthroscopic debridement, osteotomy)

There were insufficient data for this to be done and, as such, it was not necessary to use the formal test for subgroup interactions in Review Manager (RevMan 2012) or use caution in the interpretation of subgroup analyses as advised in Section 9.6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). The magnitude of the effects would have been compared between the subgroups by means of assessing the overlap of the confidence intervals of the summary estimated. Non-overlap of the confidence intervals would have indicated statistical significance.

### Sensitivity analysis

We planned to carry out sensitivity analyses on pain and function by examining the effects of:

1. including missing or inappropriately analysed data;
  2. including trials with unclear allocation concealment (at risk of selection bias);
  3. including trials with an incomplete description of mild to moderate knee osteoarthritis;
  4. the choice of statistical model for pooling (fixed-effect versus random-effects);
  5. including trials at risk of detection bias (i.e. unclear or no blinding of participant for participant-reported outcomes).
- Insufficient data from the included studies meant such sensitivity analysis was not possible.

## RESULTS

### Description of studies

A total of five studies involving 568 subjects were selected for this review.

### Results of the search

The search strategy retrieved 17,999 citations from the following databases: Cochrane Central Register of Controlled Trials, CENTRAL (4,380 citations), OVID MEDLINE (7,688 citations) and OVID Embase (5,931 citations).

A total of 5,764 duplicate studies were identified, leaving 12,235 potentially eligible citations. After title and abstract screening, a total of 108 full reports were retrieved. After full-text screening, five reports were included and 103 reports were excluded from this review. (see Figure 1, PRISMA diagram).

One ongoing trial was identified from clinicaltrial.gov but it is still actively recruiting and not due for completion until 2019. Details of the trial are given in [Characteristics of ongoing studies](#) table. No studies await classification.

Full details of the search strategy and results are given in [Appendix 1](#); [Appendix 2](#) and [Appendix 3](#).

### Included studies

A detailed description of the five included studies is given in [Characteristics of included studies](#) table. All available data were extracted from published reports. No errata or retractions were identified. Following communication with the contact author, one study provided data that were refined to meet our inclusion criteria (Van der Woude 2017). Details of this adjustment are given in the notes section of the [Characteristics of included studies](#) table. All studies were published in English.

### Design

The five included studies were randomised parallel-group controlled trials. Pre-published protocols were available for two of the trials (Van der Woude 2017; Katz 2013).

### Sample sizes

The studies reported results on a total of 566 participants. Chang 1993 randomised 34 participants to two groups and reported results for 32. Forster 2003 randomised 38 participants to two groups and reported results for 32. Katz 2013 randomised 351 participants, in blocks of varying sizes, to two groups and reported results on 320 participants. Saeed 2015 randomised 120 participants and reported results for all. Van der Woude 2017 randomised 69 patients in blocks of 6 at a ratio of (control 2:1 intervention) and provided results for the 62 participants that were relevant to this review.

### Setting

One single-centre study was conducted in Pakistan (Saeed 2015). Three studies were conducted across two sites in the USA, UK and the Netherlands (Chang 1993, Forster 2003 and Van der Woude 2017, respectively). Katz 2013 was a multicentre trial conducted in seven separate tertiary referral centres in the USA.

### Participants

Chang 1993 had a study population that was largely older females with moderate symptomatic osteoarthritis (mean age 62.7 years; 72% female). All subjects had persistent knee pain for longer than 3 months, despite conservative medical and rehabilitation management and radiographic changes consistent with Kellgren Lawrence grade 1, 2 or 3. Subjects with Kellgren-Lawrence (KL) grade 4 were excluded.

Forster 2003 had a study population with a mean age of 61.4 years. The authors did not report the distribution of gender. All subjects

had symptomatic osteoarthritis with some residual joint space on weight-bearing radiographs (equivalent to KL grade < 4).

[Katz 2013](#) had a study population that was largely older males (mean age 58.2 years; 28.5% female) with MRI-confirmed meniscal tear. All subjects had symptoms consistent with meniscal tear for more than a month and evidence on knee MRI of osteophytes or full-thickness cartilage defect; or plain radiographic evidence of osteophytes or joint space narrowing. Patients with KL grade 4 were excluded.

[Saeed 2015](#) had a study population that was largely older females (all subjects > 40 years; 81.7% female). Only subjects with KL grade 2 or 3 were included.

[Van der Woude 2017](#) had a study population that was largely older males (mean age 50 years; 35.8% female) with symptomatic knee osteoarthritis. The published report included participants with severe osteoarthritis (KL grade 4). In order to meet the inclusion criteria for this review, a refined dataset was procured from the corresponding author. The remaining participants had KL grade 1, 2 or 3.

## Intervention

Interventions for the eligible studies included arthroscopic partial meniscectomy, arthroscopic debridement and or irrigation, high tibial osteotomy, and knee joint distraction. None of the included studies involved cartilage repair techniques, interpositional arthroplasty, KineSpring® (Moximed Inc, Hayward, CA, USA), or knee replacement surgery.

### Any type of surgical intervention versus any non-surgical intervention

[Katz 2013](#) compared a surgical intervention (arthroscopic partial meniscectomy) with a non-surgical intervention (physical therapy).

### Any type of surgical intervention versus any injectable therapy

Three trials compared a surgical intervention against injectable therapy ([Chang 1993](#), [Forster 2003](#); [Saeed 2015](#)).

### Saline irrigation

[Chang 1993](#) compared arthroscopic surgery (debridement ± synovectomy ± chondroplasty) to closed-needle joint lavage with normal saline.

### Hyaluronic acid

[Forster 2003](#) compared arthroscopic surgery (washout ± debridement) to hyaluronic acid injection (five intra-articular injections of

20mg Hyalgan at 1-week intervals). [Saeed 2015](#) compared arthroscopic surgery (debridement) to hyaluronic acid injection (five intra-articular injections of hyaluronic acid at 1-week intervals). Dose of hyaluronic acid was not described.

### Any type of surgical intervention versus any other surgical intervention

[Van der Woude 2017](#) compared a surgical intervention (high tibial osteotomy) with another surgical intervention (knee joint distraction).

## Outcomes

All studies reported at least one major outcome described in our protocol. All outcomes that related to knee pain or physical function, or both, used at least one validated instrument. When a study provided data on more than one pain or physical function scale, we used the hierarchy described in our protocol to select a single outcome from each domain [Types of outcome measures](#).

### Any type of surgical intervention versus any non-surgical intervention

[Katz 2013](#) assessed pain using the pain section within the Knee Injury and Osteoarthritis Outcome Score (KOOS) and function using the physical function scale of the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC). Serious adverse events, conversion to total knee replacement, and withdrawals from the study were also reported. Radiographic structural progression was not reported. This study did not report a quality of life outcome. Whilst the SF-36 was reported, only the physical activity component of the questionnaire was included.

### Any type of surgical intervention versus any injectable therapy

All three studies included a pain outcome. In no study was radiographic structural progression reported.

### Saline irrigation

[Chang 1993](#) reported the pain and function domains of the Arthritis Impact Measurement Scales (AIMS). A Visual Analogue Scale of Well-being was used to assess the quality of life outcome at 12 months. Serious adverse events, conversion to total knee replacement, and withdrawals from the study due to adverse events were not reported.

## Hyaluronic acid

Forster 2003 used the Visual Analogue Scale (VAS) to assess pain outcomes. They reported the Lequesne Index (LI) and the functional component of the Knee Society Scoring (KSS) system to assess functional outcomes. The control and intervention groups were not matched at baseline for the KSS function score with the intervention group having poorer function. As such the LI, for which the groups were matched, was selected as the functional outcome for the study. Conversion to total knee replacement was reported. Serious adverse events and withdrawals from the study due to adverse events were not reported.

Saeed 2015 used the pain component of the Knee Society Scoring System as their primary outcome. The study also reported no loss to follow-up from the point of randomisation and no significant adverse events. Outcomes related to function, quality of life, and conversion to total knee replacement (TKR) were not included.

## Any type of surgical intervention versus any other surgical intervention

Van der Woude 2017 provided our review with an amended dataset which contained results for participants relevant to our study. Several outcomes were reported that related to pain and function. According to our hierarchy of outcomes, the Visual Analogue Scale and WOMAC were selected for pain and function, respectively. A radiographic structural progression outcome was included (minimum joint space width). The EQ-5D index (0 to 1, 1 being the best) was used to assess improvement in quality of life. Serious adverse events, withdrawals due to adverse events, and re-operation rates were reported.

## Timing of outcome assessment

None of the included studies reported outcomes beyond 12 months. In accordance with the published protocol, all outcomes were considered at the longest time point reported within this early outcome period (see [Unit of analysis issues](#)). Four studies reported outcomes at 12 months (Chang 1993; Forster 2003; Katz 2013; Van der Woude 2017) and a single study reported outcomes at six months (Saeed 2015).

## Excluded studies

A full list of the excluded studies is reported in the [Characteristics of excluded studies](#) table.

A total of 103 full-text articles were reviewed and excluded, including the following notable studies:

Kalunian 2000 studied the effect of visually guided irrigation on patients with mild to moderate knee osteoarthritis. This study included individuals without radiographic features of knee osteoarthritis who did not meet the inclusion criteria for this review.

The corresponding author was contacted to provide an amended dataset without these individuals. No response was received.

Bradley 2002 compared the effect of tidal irrigation to sham irrigation for the treatment of knee osteoarthritis. Tidal irrigation was considered to be an injectable therapy and as such represented a valid comparator for our study but not a valid intervention. As such it was excluded from the review.

Moseley 2002 randomised study participants to arthroscopic debridement, lavage, or placebo surgery. This blinded study measured severity of knee osteoarthritis (OA) by combining the KL grade for each compartment. The results were not stratified by severity of OA and it was not possible using this combined grade to identify which subjects would have been appropriate for inclusion in our review. As such, the study was excluded. The pilot study for this trial was also excluded as it did not give a radiographic description of OA severity (Moseley 1996).

Sihvonen 2013 randomised subjects with degenerative meniscal tears to arthroscopic partial meniscectomy or sham surgery. This study actively excluded individuals with knee osteoarthritis and as such was not eligible for inclusion in this review.

Seventy studies did not include participants that met the inclusion criteria for participants in this review. Fifty two studies were excluded as they did not restrict their inclusion criteria to participants with mild to moderate knee OA:

- Twelve studies included subjects with a spectrum of radiographic knee OA and described the range of osteoarthritis using a validated radiographic or arthroscopic grading system (Bisson 2017; Brouwer 2006; Duivenvoorden 2014a; Gauffin 2014; Gauffin 2017; Herrlin 2007; Herrlin 2013; Kalunian 2000; Kirkley 2008; Marsh 2016; Roos 2018; Stukenborg Colman 2001). The corresponding authors were contacted to provide an amended dataset including only those individuals relevant to this study. No response was received.

- Twenty-six studies did not define the severity of radiographic OA within their included subjects (Dallari 2007; Duivenvoorden 2014; Fu 2015; Gaasbeek 2010; Gouin 2010; Han 2010; Heir 2013; Hubbard 1996; Huizinga 2014; Linke 2007; Luchikhina 2014; Luites 2009; Merchan 1993; Moseley 1996; Moseley 2002; Myrner 1980; Narkbunnam 2012; Nerhus 2017b; Osman 2014; Osteras 2011; Rodkey 2009a; Russell 2003; Smith 2003; Smith 2018; Vermesan 2013; Zhang 2018).

- Eight studies included subjects with severe osteoarthritis (Duif 2015; Ferruzzi 2012; Hempfling 2007; Kulshrestha 2016; Liu 2004; Magyar 1999; Ward 1998; Zorzi 2011).

- Four studies included subjects with no radiographic, arthroscopic, or MRI description of OA (Bloembergen 2017; Hede 1992; Rodkey 2009; Stensrud 2015).

- Two studies included subjects with no radiographic evidence of knee osteoarthritis (Ou 2008; Yim 2013).

Nine studies included subjects with articular cartilage defects or degenerate meniscal tears but excluded subjects with associated knee

osteoarthritis (Aae 2017; Gudas 2012; Jarvinen 2014; Knutsen 2004; Knutsen 2007; Spahn 2010; Spahn 2016; Sihvonen 2013; Volz 2017).

Five studies included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria (Brittberg 2013; Lee 2013; Pascale 2011; Saris 2008; Shive 2015).

Three studies did not include symptoms as part of their inclusion criteria (Kang 2005; Kim 2017; Shaofei 2017).

Van Oosterhout 2006 included subjects with inflammatory arthropathy only.

Fifteen studies were excluded because they were not randomised controlled trials. Eight studies were prospective but non-randomised (Adeyemi 2017; Akizuki 1997; Börjesson 2005; Gudas 2002; Marmotti 2013; Schultz 1999; Van Egmond 2016; Zhao 2018). Four studies were retrospective (Benedetto 1993; Brouwer 2005a; Cho 2013; Ferruzzi 2014). Two studies included retrospective analyses of prospectively gathered data (Besselink 2017; Collins 2017). Campbell 2010 was a mixed-methods study aimed at evaluating the feasibility of performing a further placebo-controlled trial for knee osteoarthritis.

Twelve studies were excluded as they included no surgical intervention (Adler 1970; Bradley 2002; Alpayci 2011; Alpayci 2013; Arden 2008; Aslan 2012; Dawes 1987; Frias 2004; Frias 2009;

Parmigiani 2010; Ravaud 1999; Raynauld 2002).

Two studies were excluded as none of the review's outcome measures were measured (Nakamura 2001; Nerhus 2017a).

One study was the protocol for a trial which was terminated early due to recruitment difficulties (Freitag 2015).

In three studies, subjects were randomised to receive or not receive a non-surgical intervention after the surgical procedure had been performed (Atay 2008, Hiemstra 2012, Jung 2014).

### Ongoing studies

Searches of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform revealed one trial which met the inclusion criteria for our review (see Characteristics of ongoing studies table). This trial is still actively recruiting and not due for completion until 2019.

### Risk of bias in included studies

Further information regarding risk of bias for each individual study is available in Figure 2; Figure 3 and the 'Risk of bias' tables within the Characteristics of included studies section.

**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**

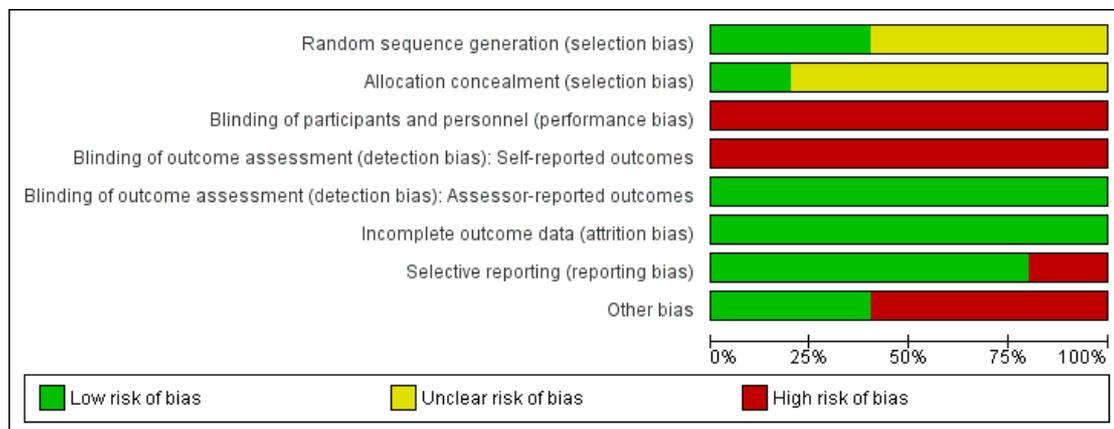


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias): Self-reported outcomes	Blinding of outcome assessment (detection bias): Assessor-reported outcomes	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chang 1993	?	?	-	-	+	+	+	+
Forster 2003	?	?	-	-	+	+	+	-
Katz 2013	+	+	-	-	+	+	+	-
Saeed 2015	?	?	-	-	+	+	-	+
Van der Woude 2017	+	?	-	-	+	+	+	-

## Allocation

Three studies mentioned a randomisation element to the study but did not describe the randomisation process leading to an unclear risk of selection bias (Chang 1993; Forster 2003; Saeed 2015). Both Katz 2013 and Van der Woude 2017 used computer-generated randomisation methods (low risk of bias).

One study (Katz 2013) reported that randomisation was performed by a research coordinator in real time using a secure website, thus ensuring concealment until the time of allocation to treatment (low risk). Sealed envelopes were used in two studies (Chang 1993; Forster 2003), however, neither of these studies gave sufficient description of the safeguards employed to ensure allocation concealment was maintained (unclear risk). The remaining studies (Saeed 2015; Van der Woude 2017) did not report a method of allocation concealment (unclear risk).

## Blinding

All studies were considered at high risk of performance bias as in all cases participants and personnel were not blinded to the treatment allocation.

In order to accurately describe the risk of detection bias, we grouped outcomes, where necessary, according to whether the patient reported the outcome (self-reported outcome) or an independent assessor recorded the outcome (assessor-reported outcome). Self-reported outcomes were reported by all studies and they were considered to be at high risk of bias in all cases as the participants reporting the outcome were likely aware of their treatment allocation (Chang 1993; Forster 2003; Katz 2013; Saeed 2015; Van der Woude 2017).

Chang 1993 included assessor-reported outcomes such as knee swelling, knee range of motion, and knee tenderness. The assessors were unaware of treatment allocation (low-risk of detection bias). These outcomes did not meet the criteria for this review and were not included.

Forster 2003 reported conversion to TKR. Katz 2013 reported serious and non-serious adverse events and conversion to TKR. Saeed 2015 reported significant adverse events. Van der Woude 2017 reported serious adverse events, re-operation and conversion to TKR. Knowledge of treatment allocation should not have influenced the interpretation of these assessor-reported outcomes (low risk of detection bias).

Van der Woude 2017 also reported structural progression using an assessor “blinded to the order of acquisition”. The presence or absence of a metal plate from those that underwent osteotomy would have made it clear to which group the participant had been randomised. However, private correspondence with the authors of this study confirmed that the radiographic assessments were made by non-clinical staff who were unaware of the relevance of

the metal plate (low risk) and performed in accordance with their previously published KIDA protocol (Marijnissen 2008).

## Incomplete outcome data

All studies were considered to be at low risk for attrition bias. One study reported no loss to follow-up following randomisation (Saeed 2015). The remaining studies experienced losses to follow-up that were small and similarly sized in each treatment arm (Chang 1993; Forster 2003; Katz 2013; Van der Woude 2017).

## Selective reporting

Two studies demonstrated outcomes that were consistent with pre-published protocols (Katz 2013; Van der Woude 2017) and therefore at low risk of reporting bias. Both Chang 1993; Forster 2003 described acceptable and expected outcomes using validated instruments to assess both knee pain and function (low risk of bias). Saeed 2015 reported the Knee Society Pain Score as the single outcome of interest. However, in their methodology, they discussed the use of the Knee Society Score to assess range of motion, function, and stability. These were not included in the analyses, suggesting a high risk of reporting bias. The Knee Society Pain Score data had to be reshaped in order to be included in the review. The authors concluded that the group receiving injectable therapy improved more than the arthroscopy group at six months, however, they failed to identify or report if this difference was significant. The outcome of this study was markedly different to the other two studies comparing surgical intervention versus injectable therapy. The results of this study should be interpreted with caution.

## Other potential sources of bias

No other sources of bias were identified in two studies (Chang 1993; Saeed 2015).

Bias due to differences in important baseline prognostic indicators were present in two studies (Forster 2003; Van der Woude 2017). The functional scores in the arthroscopy were significantly worse pre-intervention in the study by Forster 2003. A significant difference in female gender between the HTO group and the knee joint distraction group (41% versus 29%) was observed in the study by Van der Woude 2017.

The study by Katz 2013 was at further risk of bias as 30.2% of those assigned to physical therapy crossed over to arthroscopy within six months of the study start time. Outcomes were, however, reported on an intention-to-treat basis meaning that almost a third of the outcomes in the physical therapy had actually undergone arthroscopic surgery, possibly underestimating any benefit of surgery.

## Effects of interventions

See: [Summary of findings for the main comparison Surgical intervention compared to non-surgical intervention for symptomatic mild to moderate knee osteoarthritis](#); [Summary of findings 2 Surgical intervention compared to injectable saline therapy for symptomatic mild to moderate knee osteoarthritis](#); [Summary of findings 3 Surgical intervention compared to other surgical intervention for symptomatic mild to moderate knee osteoarthritis](#)

Quality assessments were performed using [GRADEpro 2015](#) ([Summary of findings for the main comparison](#); [Summary of findings 2](#); [Summary of findings 3](#)). The study by [Chang 1993](#) was chosen to demonstrate the effect of any surgical intervention versus any injectable therapy ([Summary of findings 2](#)) as the quality of the outcomes for this study were marginally superior to those provided by the other two included studies ([Forster 2003](#); [Saeed 2015](#)). The outcomes for each study are reported in the [Data and analyses](#) section.

### Any type of surgical intervention versus any non-surgical intervention

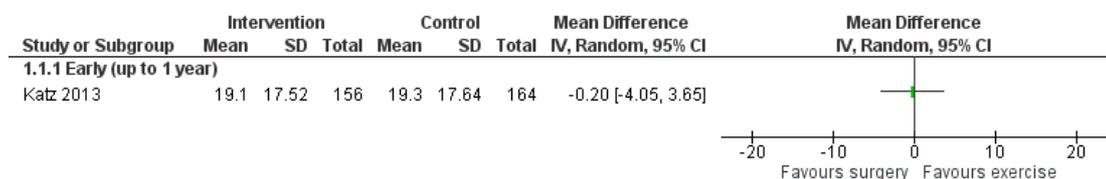
[Katz 2013](#) compared arthroscopic partial meniscectomy (APM) to

physical therapy (PT). The quality of evidence for this study was considered to be low for outcomes related to pain and function; with one downgrade due to risk of bias issues and one downgrade for imprecision. Outcomes related to short-term serious adverse events, re-operation rates, and withdrawals due to serious adverse events were graded very low quality; with one downgrade due to risk of bias issues and two downgrades for serious imprecision (see [Summary of findings for the main comparison](#)). No studies were found comparing surgery to a placebo or sham surgical procedure.

### Pain

Both groups demonstrated improved KOOS pain scores at 12 months (mean change score, APM = 26.8 (95% CI 23.7 to 30.0); PT = 27.3 (95% CI 24.1 to 2.0)) compared to baseline scores. However, there was no observed between-group difference in the 12-month pain score (one study; 320 participants; MD at 12 months -0.2 (95% CI -4.05 to 3.65); 0.2% absolute improvement (95% CI 4% better to 4% worse); 0.4% relative improvement (95% CI 9% better to 8% worse); low-quality evidence; [Analysis 1.1](#); [Figure 4](#); [Summary of findings for the main comparison](#)). No further time points were reported.

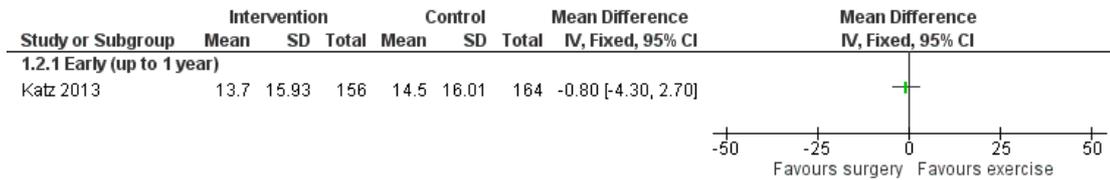
**Figure 4. Forest plot of comparison: 1 Surgical intervention vs non-surgical intervention, outcome: 1.1 Pain.**



### Function

Both groups demonstrated improved WOMAC physical function scores at 12 months (mean change score APM = 23.5 (95% CI 20.5 to 26.5); PT = 22.8 (95% CI 19.8 to 25.8)) compared to baseline scores. There was no observed between-group difference in function score (one study; 320 participants; MD at 12 months = 0.8 points better (95% CI 4.3 better to 2.7 worse); 0.8% absolute improvement (95% CI 4% better to 3% worse); 2.1% relative improvement (95% CI 11% better to 7% worse); low-quality evidence; [Analysis 1.1](#); [Figure 5](#); [Summary of findings for the main comparison](#)).

**Figure 5. Forest plot of comparison: I Surgical intervention vs non-surgical intervention, outcome: 1.2 Function.**



### **Radiographic structural progression**

Radiographic assessments were recorded at baseline but no measurement of radiographic structural progression was performed at follow-up.

### **Quality of life**

This study did not report a quality of life outcome. Whilst the SF-36 was measured, only the physical activity component of the questionnaire was included.

### **Serious adverse events**

The APM group had a total of three serious adverse events, including fatal pulmonary embolism, myocardial infarction, and hypoxaemia. The PT group had two serious adverse events, including sudden death and stroke. No significant between-group differences in the frequency of serious adverse events at 12 months was noted (one study; 320 participants; APM n = 3; PT n = 2; 1% absolute change (95% CI 2% less to 3% more), 58% relative change (95% CI 73% less to 821% more); very low-quality evidence; [Analysis 1.3; Summary of findings for the main comparison](#)).

Non-serious adverse events were also reported. The APM group had a total of 15 non-serious adverse events; pain from fall or other trauma (n = 2), tendonitis (n = 3), rupture of baker's cyst (n = 1), knee pain (n = 1), pain in back, hip, or foot (n = 2), deep vein thrombosis (n = 2), syncope (n = 1), skin (n = 2), other (n = 1). The PT group had a total of 13 non-serious adverse events; pain from fall or other trauma (n = 4), knee bursitis (n = 1), knee pain (n = 1), pain in back, hip, or foot (n = 4), atrial fibrillation (n = 1), skin (n = 1), other (n = 1).

### **Re-operation rate or conversion to total knee replacement**

No significant differences were observed in the number of individuals who underwent conversion to total knee replacement

within 12 months (one study; 320 participants; APM n = 5; PT n = 3; 1% absolute change (95% CI 2% less to 5% more); 76% relative change (95% CI 57% less to 613% more); very low-quality evidence; [Analysis 1.4; Summary of findings for the main comparison](#)).

### **Withdrawals due to adverse events**

Two subjects died and were withdrawn from the study (one study; 320 participants; APM n = 1; PT n = 1; 0% absolute change (95% CI 2% less to 2% more); 5% relative improvement (95% CI 93% less to 1590% more); very low-quality evidence; [Analysis 1.5; Summary of findings for the main comparison](#)).

### **Any type of surgical intervention versus any injectable therapy**

Three studies compared a surgical (arthroscopic) intervention to an injectable therapy ([Chang 1993](#); [Forster 2003](#); [Saeed 2015](#)). These studies have been grouped according to the type of injectable therapy.

### **Saline irrigation**

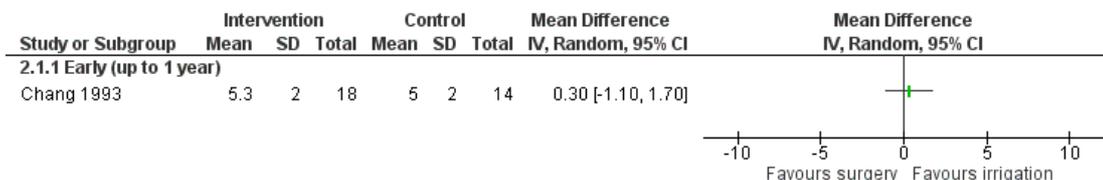
[Chang 1993](#) compared arthroscopic surgery (debridement ± synovectomy ± chondroplasty) to closed-needle joint lavage with normal saline. The quality of evidence for this study was considered to be low for outcomes related to pain, function, and quality of life; with one downgrade for risk of bias issues and one downgrade for imprecision (see [Summary of findings 2](#)). No other outcomes were reported.

### **Pain**

Using the pain subscale of the AIMS, [Chang 1993](#) observed no improvement in either group at 12 months compared to baseline. No between-group difference was observed at 12 months (one study; 32 participants; MD at 12 months = 0.3 points higher

(95% CI 1.1 lower to 1.7 higher); 0% absolute change (95% CI 10% less to 17% more); 5% relative change (95% CI 18% less to 28% more); low-quality evidence; [Analysis 2.1](#); [Summary of findings 2](#); [Figure 6](#)).

**Figure 6. Forest plot of comparison: 2 Surgical intervention vs injectable therapy (saline irrigation), outcome: 2.1 Pain.**



### Function

Using the physical function subscale of the AIMS, [Chang 1993](#) observed an improvement in function at 12 months. There was, however, no between-group difference in the 12 month functional score (one study; 32 participants; MD at 12 months = 0.30 points lower (95% CI 1.10 lower to 0.50 higher); 0% absolute change (95% CI 11% less to 5% more); 18% relative change (95% CI 65% less to 29% more); low-quality evidence; [Analysis 2.2](#); [Summary of findings 2](#)).

### Radiographic structural progression

This outcome was not reported by the included studies.

### Quality of life

No between-group differences were reported for the single study that reported a quality of life outcome ([Chang 1993](#)) (one study; 32 participant; MD at 12 months = 0.80 (95%CI 5.30 lower to 6.90 higher), 8% absolute change (95% CI 53% less to 69% more); 17% relative change (95% CI 115% less to 150% more); low-quality evidence; [Analysis 2.3](#); [Summary of findings 2](#)).

### Serious adverse events

This outcome was not reported by the included studies.

### Re-operation rate or conversion to total knee replacement

This outcome was not reported by the included studies.

### Withdrawals due to adverse events

This outcome was not reported by the included studies.

### Hyaluronic acid

[Forster 2003](#) compared arthroscopic surgery (washout ± debridement) to hyaluronic acid injection (five intra-articular injections of 20 mg Hyalgan at 1-week intervals). [Saeed 2015](#) compared arthroscopic surgery (debridement) to hyaluronic acid injection (five intra-articular injections of hyaluronic acid at 1-week intervals). Dose of hyaluronic acid was not described. The quality of evidence was very low for outcomes related to pain (two downgrades for risk of bias issues and one downgrade for inconsistency) and low for outcomes related to function (one downgrade for risk of bias issues and one downgrade for imprecision). Outcomes related to short-term serious adverse events, re-operation rates, and withdrawals due to serious adverse events were graded very low-quality (one downgrade for risk of bias issues and two downgrades for imprecision).

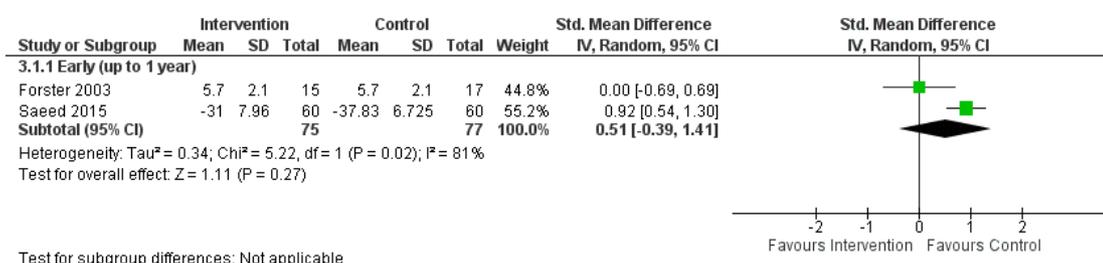
### Pain

[Forster 2003](#) used VAS to assess pain outcomes. The standard deviation (SD) was not reported and could not be provided by the authors. As such, the SD was imputed from another study included in this review ([Van der Woude 2017](#)).

The data presented in the study by [Saeed 2015](#) had to be reshaped in order to obtain a mean and standard deviation for each group. The study used the Knee Society pain score and reported clinical improvement in both groups at 12 months.

No between-group difference was observed in patient-reported pain at 12 months (two studies; 152 participants; SMD at 12 months = 0.41 (95% CI -0.23 to 1.05); [Analysis 3.1](#); [Figure 7](#)). The SMD was back-translated using the SD imputed for [Forster 2003](#) (two studies; 152 participants; MD at 12 months = 1.07 higher (95%CI 0.82 lower to 2.96 higher); 11% absolute change (95% CI 8% less to 30% more); 14% relative change (95% CI 11% less to 39% more); low-quality evidence). There was marked heterogeneity between these two trials ( $I^2 = 81\%$ ).

**Figure 7. Forest plot of comparison: Early pain outcomes (6-12 months).**



### Function

[Forster 2003](#) used the Lequesne index (LI) to report functional outcomes. The SD was not reported and could not be provided by the authors. An SD could not be imputed from another study included in this review. As such, an SD was imputed using a peer-reviewed article that included patients with symptomatic knee osteoarthritis ([Faucher 2002](#)). Both groups reported improved function at 12 months but there was no between-group difference observed at 12 months (one study; 32 participants; MD at 12 months = 2.50 higher (95%CI 0.53 lower to 5.53 higher); 10% absolute change (95% CI 2% less to 23% more); 25% relative change (95% CI 5% less to 53% more); low-quality evidence; [Analysis 3.2](#)).

### Radiographic structural progression

This outcome was not reported by the included studies.

### Quality of life

This outcome was not reported by the included studies.

### Serious adverse events

[Saeed 2015](#) reported no serious adverse event or withdrawals from the study for either group (one study; 120 participants; very low-quality evidence; [Analysis 3.3](#)).

[Forster 2003](#) did not comment on serious adverse events or withdrawals from the study due to adverse events.

### Re-operation rate or conversion to total knee replacement

[Forster 2003](#) reported no significant difference in conversion to TKR at 12 months between the two groups (one study; 32 participants; Peto OR at 12 months = 0.56 (95% CI 0.05 to 5.83); 5% absolute change (95% CI 25% less to 15% more); 44% relative change (95% CI 95% less to 483% more); low-quality evidence; [Analysis 3.4](#)).

[Saeed 2015](#) did not comment on re-operation rate or conversion to total knee replacement.

### Withdrawals due to adverse events

[Saeed 2015](#) reported no serious adverse events or withdrawals from

the study for either group (one study; 120 participants; very low-quality evidence; [Analysis 3.5](#)). [Forster 2003](#) did not comment on serious adverse events or withdrawals from the study due to adverse events.

### Any type of surgical intervention versus any other surgical intervention

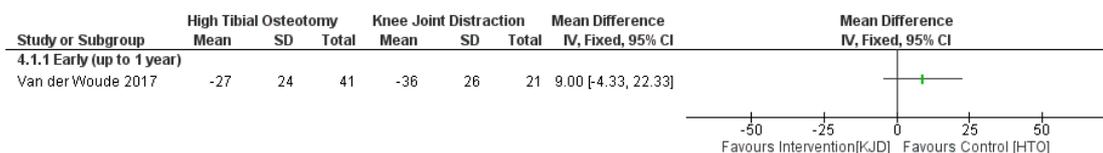
One study by [Van der Woude 2017](#) compared two types of surgical intervention; high tibial osteotomy (HTO) versus knee joint distraction (KJD). The quality of evidence for this study was considered to be low for outcomes related to pain, function, and quality of life; with one downgrade due to risk of bias issues and one downgrade for imprecision. Outcomes related to structural progression were considered moderate quality; with one downgrade for imprecision. Outcomes related to short-term serious adverse

events, re-operation rates, and withdrawals due to serious adverse events were graded very low-quality; with one downgrade due to risk of bias issues and two downgrades for serious imprecision (see [Summary of findings 3](#)).

### Pain

[Van der Woude 2017](#) used VAS to assess pain outcomes. Both groups had less pain at 12 months. There was no between-group difference in the pain score at 12 months (one study, 62 participants; MD at 12 months = 9 points worse (95% CI 4.3 better to 22.3 worse); 9% absolute decrease (95% CI 4% better to 22% worse); 14% relative decrease (95% CI 6% better to 33% worse); low-quality evidence; [Analysis 4.1](#); [Figure 8](#); [Summary of findings 3](#)).

**Figure 8. Forest plot of comparison: 3 Surgical intervention vs ANY other surgical intervention, outcome: 3.1 Pain.**



### Function

[Van der Woude 2017](#) measured function using the WOMAC function score. Both interventions led to an improvement in these scores at 12 months compared to baseline. No between-group differences were observed in function at 12 months (one study, 62 participants; MD at 12 months = 4 points worse (95% CI 13.49 worse to 5.49 better); 4% absolute improvement (95% CI 13% worse to 5% better); 8% relative improvement (95% CI 26% better to 33% worse); low-quality evidence; [Analysis 4.2](#); [Figure 8](#); [Summary of findings 3](#)).

### Radiographic structural progression

[Van der Woude 2017](#) assessed structural progression using minimum medial joint space width (minJSW). No between-group differences were observed for structural progression (MD = 0.37 greater (95% CI 0.94 greater to 0.20 smaller); 0% absolute improvement (95% CI 1% greater to 0% smaller); 56% relative im-

provement (95% CI 142% greater to 30% smaller); moderate-quality evidence; [Analysis 4.3](#); [Summary of findings 3](#)).

### Quality of life

[Van der Woude 2017](#) measured quality of life using the EQ5D index. No between-group differences were observed at 12 months (MD = 0 (95% CI 0.10 worse to 0.10 better); 0% absolute improvement (95% CI 0% worse to 0% better); 0% relative improvement (95% CI 16% worse to 16% better); low-quality evidence; [Analysis 4.4](#); [Summary of findings 3](#)).

### Serious adverse events

No participants in either group experienced a serious adverse event. Non-serious adverse events were also reported. HTO group had a total of 3 non-serious adverse events: wound infection requiring oral antibiotics (n = 2), IV antibiotics (n = 1). The KJD group had a total of 12 non-serious adverse events: pin tract infection

requiring oral antibiotics (n = 8), IV antibiotics (n = 3); broken bone pin during fixation (n = 1).

***Re-operation rate or conversion to total knee replacement***

No re-operations or conversions to total knee replacement were reported in either group.

***Withdrawals due to adverse events***

No withdrawals due to an adverse event were reported in either group.

## ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Surgical intervention compared to injectable therapy for symptomatic mild to moderate knee osteoarthritis						
<b>Patient or population:</b> Adults with symptomatic mild to moderate knee osteoarthritis defined as knee pain and radiographic evidence of non-end stage osteoarthritis (Kellgren-Lawrence grade 1, 2, 3 or equivalent on MRI/arthroscopy) <b>Setting:</b> Rheumatology clinic <b>Intervention:</b> Arthroscopic surgery (debridement ± synovectomy ± chondroplasty) <b>Comparison:</b> Closed-needle joint lavage with normal saline						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with Injectable therapy	Risk with Surgical intervention				
<b>Pain</b> Follow-up: 12 months assessed with: AIMS scale (0-10; 10 worst)	Mean pain score in control groups was 5	MD <sup>1</sup> 0.3 higher (95% CI 1.1 better to 1.7 worse)	-	32 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	0% absolute change (95% CI 10% less to 17% more) <sup>4</sup> 5% relative change (95% CI 18% less to 28% more) <sup>5</sup>
<b>Physical function</b> Follow-up: 12 months assessed with: AIMS (0-10; 10 worst)	Mean function score in control groups was 2	MD 0.30 lower (95% CI 1.10 better to 0.50 worse)	-	32 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	0% absolute change (95% CI 11% less to 5% more) 18% relative change (95% CI 65% less to 29% more) NNTB/NNTB <sup>6</sup>
<b>Radiographic structural progression</b>	-	-	-	-	-	Not reported in included studies

<b>Quality of life</b> Follow-up: 12 months assessed with: well-being Scale from: 0 to 10 (10 worst) follow-up: 12 months	The mean quality of life in control group was <b>3.3</b>	MD 0.80 (95% CI 5.30 - better to 6.90 worse)	-	32 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	8% absolute change (95% CI 53% less to 69% more) 17% relative change (95% CI 115% less to 150% more) NNTH/NTTB <sup>6</sup>
Short-term serious adverse effects from trials	-	-	-	-	-	Not reported in included studies
Re-operation rate or conversion to total knee replacement, or both	-	-	-	-	-	Not reported in included studies
Withdrawals due to adverse events	-	-	-	-	-	Not reported

\***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; OR: Odds ratio;

#### GRADE Working Group grades of evidence

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

<sup>1</sup>Mean difference

<sup>2</sup>Downgraded due to risk of bias issues

<sup>3</sup>Downgraded for imprecision with only one small study providing data

<sup>4</sup>For continuous outcomes, the absolute benefit was calculated as the improvement in the intervention group minus the improvement in the control group.

<sup>5</sup>For continuous outcomes, the relative difference in the change from baseline was calculated as the absolute benefit divided by the baseline mean of the control group, expressed as a percentage.

<sup>6</sup>Number needed to treat for an additional beneficial outcome (NNTB) or for an additional harmful outcome (NNTH) not applicable when result is not statistically significant.

**Surgical intervention compared to other surgical intervention for symptomatic mild to moderate knee osteoarthritis**

**Patient or population:** Adults with symptomatic mild to moderate knee osteoarthritis defined as knee pain and radiographic evidence of non-end stage osteoarthritis (Kellgren-Lawrence grade 1, 2, 3 or equivalent on MRI/arthroscopy)

**Setting:** Department of Orthopedics

**Intervention:** Knee joint distraction

**Comparison:** High tibial osteotomy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with High tibial osteotomy	Risk with Knee joint distraction				
Pain (Pain) assessed with: VAS Scale from: 0 to 100 (100 = worst) follow-up: mean 12 months	The mean pain score was <b>27</b>	<b>MD<sup>1</sup> 9 points worse</b> (95% CI 4.3 better to 22.3 worse)	-	62 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	No between- group difference observed 9% absolute decrease (95% CI 4% better to 22% worse) <sup>4</sup> 14% relative decrease (95% CI 6% better to 33% worse) <sup>5</sup> NNTH/NNTB <sup>6</sup>
Physical function (Function) assessed with: WOMAC- function Scale from: 0 to 100 (100 = best) follow-up: mean 12 months	The mean physical function score was <b>82</b>	<b>MD 4 points worse</b> (95% CI 13.49 worse to 5.49 better)	-	62 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	No between- group difference observed 4% absolute improvement (95% CI 13% worse to 5% better) 8% relative improvement (95% CI 26% better to 33% worse) NNTH/NNTB <sup>6</sup>

Radiographic joint structure changes (Structural progression) assessed with: Minimum Joint Space Width follow-up: mean 12 months	The mean minimum joint space width was <b>1.02</b>	<b>MD 0.37 greater</b> (0.94 greater to 0.20 smaller)	-	59 (1 RCT)	⊕⊕⊕○ MODERATE <sup>3</sup>	No between- group difference observed 0% absolute improvement (95% CI 1% greater to 0% smaller) 56% relative improvement (95% CI 142% greater to 30% smaller) NNT/NTB <sup>6</sup>
Quality of life (QoL) assessed with: EQ5D Scale from: 0 to 1 (1 = best) follow-up: mean 12 months	The mean EQ5D index was <b>0.78</b>	<b>MD 0</b> (0.10 worse to 0.10 better)	-	62 (1 RCT)	⊕⊕○○ LOW <sup>2,3</sup>	No between- group difference observed 0% absolute improvement (95% CI 0% worse to 0% better) 0% relative improvement (95% CI 16% worse to 16% better) NNT/NTB = N/A
Short-term serious adverse effects from trials (Serious adverse event) follow-up: mean 12 months	<b>0 per 1,000</b>	<b>0 per 1,000</b>	not estimable	59 (1 RCT)	⊕○○○ VERY LOW <sup>2,3</sup>	No adverse events reported in either group
Re-operation rate or conversion to total knee replacement, or both follow-up: median 12 months	<b>0 per 1,000</b>	<b>0 per 1,000</b>	not estimable	59 (1 RCT)	⊕○○○ VERY LOW <sup>2,3</sup>	No re-operations or conversions to TKR reported in either group

Withdrawals due to adverse events (Withdrawal) follow-up: mean 12 months	<b>0 per 1,000</b>	<b>0 per 1,000</b>	not estimable	59 (1 RCT)	⊕○○○ VERY LOW <sup>2,3</sup>	No withdrawals due to adverse events reported in either group
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\* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

**GRADE Working Group grades of evidence**

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

<sup>1</sup> Mean difference

<sup>2</sup> Downgraded due to risk of bias issues

<sup>3</sup>Downgraded due to imprecision (a single study providing data for the outcomes of interest). A further downgrade for dichotomous outcomes where the event rates were small

<sup>4</sup> For dichotomous outcomes, the absolute risk difference was calculated using the risk difference statistic in Review Manager and the result expressed as a percentage. For continuous outcomes, the absolute benefit was calculated as the improvement in the intervention group minus the improvement in the control group.

<sup>5</sup>The relative percent change for dichotomous data was calculated as the risk ratio - 1 and expressed as a percentage. For continuous outcomes, the relative difference in the change from baseline was calculated as the absolute benefit divided by the baseline mean of the control group, expressed as a percentage.

<sup>6</sup>Number needed to treat for an additional beneficial outcome (NNTB) or additional harmful outcome (NNTH) not applicable when result is not statistically significant

## DISCUSSION

### Summary of main results

The objective of this review was to assess the benefits and harms of surgical intervention for the management of mild to moderate knee osteoarthritis. Our definition of mild to moderate knee osteoarthritis was deliberately kept broad and included symptomatic patients in whom osteoarthritis had been confirmed but excluded people with diffuse full-thickness disease who would be considered suitable for arthroplasty surgery. Despite this broad inclusion criteria, our search yielded only five trials involving 568 participants. All the trials compared a surgical intervention with either a non-surgical intervention (Katz 2013), an injectable therapy (Chang 1993; Forster 2003; Saeed 2015), or another surgical intervention (Van der Woude 2017). No trial included a sham control group. No trial reported results beyond one year.

Summary of findings for the main comparison, Summary of findings 2, and Summary of findings 3 summarise the current evidence from randomised controlled trials for the surgical management of mild to moderate osteoarthritis of the knee. Within-group comparisons showed short-term improvements in knee pain and function could be achieved regardless of intervention (Chang 1993; Forster 2003; Katz 2013; Saeed 2015; Van der Woude 2017). The patient-reported pain and functional profiles, however, were not significantly different when between-group comparisons were made. Improvements in pain may reflect a regression to the mean for the study population as time elapses (Altman 1994).

When comparing arthroscopic partial meniscectomy and physical therapy, there may be no difference in outcomes, but we are uncertain as evidence was low-quality and only available from a single study.

When comparing surgical interventions and injectable therapies, there was low- to very low-quality evidence, from three trials, indicating we are uncertain if there are any between-group differences in patient-reported pain at six to 12 months.

When comparing high tibial osteotomy to knee joint distraction there was low-quality evidence from one trial, indicating there may be no difference between the two groups in patient-reported pain and function at one year.

Serious adverse events were reported in three of the included studies (Katz 2013; Saeed 2015; Van der Woude 2017). Adverse events following surgery are infrequent but potentially serious. There was insufficient evidence provided in this systematic review to define the risk of a serious adverse event occurring. Adequate reporting of adverse events related to surgery in future studies is strongly recommended.

Despite an extensive search, this systematic review has not been able to find any robust evidence to support surgical intervention in the management of mild to moderate symptomatic osteoarthritis of the knee. The included studies, were generally small, heterogeneous, and suffered significant biases. As such, there is also insuffi-

cient evidence to firmly oppose the use of surgery in this patient group.

### Overall completeness and applicability of evidence

As previously discussed, the available evidence in the included studies was small, heterogeneous, and insufficient to draw any firm conclusion to support or oppose the use of surgical intervention in the management of mild to moderate knee osteoarthritis.

A broadly-accepted description of mild to moderate structural knee osteoarthritis does not exist. Definitions of early osteoarthritis include those without radiographic changes (Luyten 2012). Some may consider the presence of radiographic changes in itself as being diagnostic of late or severe osteoarthritis.

Furthermore, it is possible to argue that a degenerate meniscal injury in the absence of trauma marks the onset of knee osteoarthritis regardless of whether or not the cartilage surface remains intact. Trials reporting on treatment of degenerate meniscal injuries that actively excluded subjects with osteoarthritis were not included in this review. Furthermore, only very small full-thickness cartilage lesions were considered in this review in an attempt to exclude patients with diffuse full-thickness disease who would be eligible for arthroplasty surgery. Trials investigating cartilage regeneration procedures involving larger full-thickness defects either in the presence or absence of osteoarthritis were excluded.

The definition of mild to moderate knee osteoarthritis used in this review (see Types of participants) included both clinical (symptoms) and imaging (structural) criteria. The participants in the included trials all had symptoms related to knee osteoarthritis. Chang 1993, Forster 2003, Katz 2013, and Saeed 2015 excluded subjects with Kellgren-Lawrence (KL) grade 4 knee OA. Van der Woude 2017 had a study population that included participants with severe osteoarthritis (KL grade 4). In order to meet the inclusion criteria for this review, a refined dataset was procured from the corresponding author. The remaining participants had KL grade 1, 2, or 3.

As such, the included studies had participants with symptomatic knee osteoarthritis and structural changes related to osteoarthritis that are not generally considered suitable for knee replacement surgery. The role of surgery in such individuals was the central focus of this review.

It is important to note, however, that caution should be taken when generalising the results of this review to the wider population. In the study by Katz 2013, only 26% of eligible participants were enrolled. This may have been due to either patient preference and or selective enrolment by the surgeon. Such low enrolment rates undermine the external validity of the study.

Of the five included studies, four investigated an arthroscopic procedure (Chang 1993; Forster 2003; Katz 2013; Saeed 2015). All of these arthroscopic procedures are widely available and are relevant to clinical practice. Chang 1993 investigated arthroscopic de-

bridement including meniscal resection, where necessary. Forster 2003 primarily performed an arthroscopic washout, however, debridement was performed, where necessary. Katz 2013 investigated arthroscopic partial meniscectomy using a standardised approach which allowed for the excision of loose fragments of cartilage and bone, where necessary. Saeed 2015 did not describe the extent or nature of the arthroscopic debridement undertaken in their study. Clearly, within the studies involving arthroscopic surgery, there is marked heterogeneity in the type of procedure performed both within the same study and between different studies.

Van der Woude 2017 compared two surgical procedures: knee joint distraction and high tibial osteotomy. High tibial osteotomy is a well-established surgical technique for treating knee osteoarthritis, however, Knee joint distraction is not widely practiced outside of a few specialist centres. As such, the results of this study may not be applicable to the current surgical practices of most orthopaedic knee surgeons. There were no trials found comparing either of these interventions to a sham or non-surgical control group.

There are several surgical procedures for which we found no reported randomised trials:

1. Cartilage regeneration procedures;
2. Interpositional arthroplasty;
3. Meniscal repair or transplant;
4. Extracapsular load-modifying devices (e.g. KineSpring® (Moximed Inc, Hayward, CA, USA));
5. Knee replacement surgery (e.g. total knee replacement, partial knee replacement).

The included studies had a diverse range of comparison interventions. No studies compared a surgical intervention to a sham or placebo-intervention. As such, all participants were aware of the treatment they had received leading to the potential for performance bias.

All of the seven major outcomes (see [Types of outcome measures](#)) were included in at least one study. However, due to the very low event rates, it has not been possible to establish if surgery is associated with an increased risk of serious adverse events, incidence of total knee replacement, or withdrawals due to adverse events. Finally, osteoarthritis is a chronic condition and the follow-up period for studies included in this review was too short (six to 12 months) to be able to make any conclusions regarding the long-term outcomes for a chronic disease such as knee osteoarthritis. It is not possible to draw any conclusions from this review on the long-term efficacy of surgery in mild to moderate knee osteoarthritis in terms of progression of symptoms or pathology.

As discussed in [Excluded studies](#), several study groups were contacted to see if they could provide amended data that included only those participants relevant to our trial. The inclusion of these data may well have led to the opportunity of pooling more data and drawing more robust conclusions. We identified one ongoing study that appears to fit the inclusion criteria for our review, however, this study is still recruiting and will not be completed until

July 2019.

## Quality of the evidence

The quality of this review is limited by the small number of studies and potential for bias in the included studies. Data were available from single studies only each outcome in each of the three comparisons presented in the summary of findings tables: surgery versus exercise and physical therapy (Katz 2013; [Summary of findings for the main comparison](#)); surgery versus closed-needle joint lavage with normal saline (Chang 1993; [Summary of findings 2](#)); and one type of surgery versus another (Van der Woude 2017; [Summary of findings 3](#)). Two studies compared surgery to hyaluronic acid injection (Forster 2003; Saeed 2015) but this comparison was not presented in a summary of findings table. The quality of evidence low to very low for all outcomes, except one.

### Pain

Single studies contributed to the evidence for pain each of the three comparisons in the summary of findings tables and provided only low-quality evidence, due to imprecision and risk of bias, in particular detection bias. Two studies that compared surgery to hyaluronic acid injection (Forster 2003; Saeed 2015) provided very low-quality evidence for pain; with two downgrades for risk of bias issues and one downgrade for inconsistency between the two studies.

### Function

Low-quality evidence was available from single studies only for function each comparison (Chang 1993; Forster 2003; Katz 2013; Van der Woude 2017). Evidence was downgraded once due to risk of bias issues and once due to imprecision.

### Radiographic structural progression

A single study, Van der Woude 2017, compared two surgical interventions and provided moderate-quality evidence for radiographic structural progression (one downgrade for imprecision). The assessment of structural progression used an assessor “blinded to the order of acquisition” and, as such, the risk of detection bias for this outcome was considered to be low. In addition, the presence of selection and other biases may have less influence on the results for this outcome, compared to self-reported outcomes for example.

### Quality of life

Low-quality evidence was available for quality of life from single studies for two comparisons (Chang 1993; Van der Woude 2017) Evidence was downgraded once due to risk of bias issues and once more for imprecision.

### Serious adverse events

Single studies for three comparisons provided very low quality evidence for serious adverse events (Katz 2013; Saeed 2015; Van der Woude 2017). The evidence was downgraded once due to risk of bias issues and twice more for imprecision - due to very low event rates from single studies.

### Re-operation rate or conversion to total knee replacement

Evidence from single studies for three comparisons contributed to the assessment of serious adverse events (Forster 2003; Katz 2013; Van der Woude 2017). The quality of evidence was very low; with one downgrade due to risk of bias issues and two downgrades for imprecision: a single study contributed data for the outcome in each comparison and event rates were small.

### Withdrawals due to adverse events

Single studies for three comparisons reported serious adverse events (Katz 2013; Saeed 2015; Van der Woude 2017). The quality of evidence was very low; with one downgrade due to risk of bias issues and two downgrades for imprecision: a single study contributed data for outcome in each comparison and event rates were small. Given the low-quality of evidence presented in this review, future studies, if well-designed, may have a significant impact on our confidence in the observed treatment effects.

### Potential biases in the review process

This review was performed in accordance with the published protocol. The search strategy was broad and comprehensive with no language barrier. As such, the risk of missed trials is likely to be small but cannot be completely eliminated.

The corresponding authors for trials were contacted if some but not all their participants appeared to fit our inclusion criteria (Bisson 2017; Brouwer 2006; Duivenvoorden 2014a; Gauffin 2014; Gauffin 2017; Herrlin 2007; Herrlin 2013; Kirkley 2008; Marsh 2016; Roos 2018; Stukenborg Colsman 2001). Unfortunately, none of these studies were able to provide us with an amended dataset. The inclusion of data from these trials would have provided more data which may have allowed for more robust meta-analysis and or led to more solid conclusions being drawn.

### Agreements and disagreements with other studies or reviews

To our knowledge, this is the first systematic review to take a disease-based approach to the role of surgery in symptomatic mild to moderate knee osteoarthritis. Systematic reviews in this area typically take a procedure-based approach and have inclusion criteria that focus on subjects with either no osteoarthritis or end-stage

disease. Alternatively, some reviews allow all grades of osteoarthritis to be considered.

Brignardello-Petersen 2017 compared arthroscopic surgery to any conservative management strategy in patients with symptomatic degenerative knee disease (osteoarthritis with or without degenerative meniscal tears). Three of the 16 RCTs included in their review overlap with this review (Chang 1993; Katz 2013; Saeed 2015). The review focused on arthroscopy and provides high-quality evidence that such a procedure does not provide clinically important benefits in terms of pain and function when compared with a placebo procedure that are limited to the short term (three months).

Reichenbach 2010 performed a systematic review to assess the efficacy of joint lavage compared to a sham intervention, placebo injections, or a non-intervention control. None of their seven included studies overlapped with our review. Again, this review took a procedure-based approach including subjects with all grades of osteoarthritis. We did not consider tidal irrigation to be a surgical intervention.

Brouwer 2014 is a Cochrane review assessing the safety and efficacy of osteotomy surgery. None of the 21 included studies overlapped with our review. All indications for osteotomy were considered including end-stage osteoarthritis. No study compared osteotomy to conservative treatment.

In our opinion, subjects with symptomatic mild to moderate knee osteoarthritis represent a hard-to-treat patient group who warrant investigation in their own right. Subjects with symptomatic mild to moderate knee osteoarthritis should be handled in isolation from those with end-stage osteoarthritis who are more reliably treated with arthroplasty surgery. They should also be distinguished from those individuals who have a specific structural defect (e.g. osteochondral defect) within the knee and no demonstrable osteoarthritis. This review is the first to take a disease-based approach to identify the benefits and harms of surgical intervention for the management of symptomatic mild to moderate knee osteoarthritis.

## AUTHORS' CONCLUSIONS

### Implications for practice

We found very low-quality evidence from five trials involving 568 participants. There was low-quality evidence that surgery offers no benefits over physical therapy or injectable therapy in terms of pain (Chang 1993, Forster 2003; Katz 2013; Saeed 2015; Van der Woude 2017) and function (Forster 2003; Katz 2013; Van der Woude 2017) in the short term (six to 12 months).

Knee joint distraction and high tibial osteotomy led to short-term improvements (12 months) in pain and function but neither intervention was superior to the other (Van der Woude 2017).

Due to the very low quality of evidence provided in this systematic review, the risks associated with surgery are uncertain. This review has not been able to comment on the effects of surgical intervention in this patient group beyond 12 months.

### Implications for research

This systematic review has highlighted key deficiencies in the literature regarding the surgical management of symptomatic mild to moderate knee osteoarthritis. An awareness of this patient group as being distinct from those patients with end-stage or no osteoarthritis is necessary if these deficiencies are to be rectified. Subjects with end-stage osteoarthritis should not be grouped with subjects with relatively minor degenerative changes unless there is a clear and justifiable reason for doing so. In such instances, post hoc analysis of the effect of grade of osteoarthritis on outcome frequently leads to a loss of statistical power and failure to make firm conclusions.

The biases seen in our included studies can be mitigated by clearly stating both the method of randomisation and concealment. Blinding participants is generally not possible unless a sham type procedure is being proposed. However, assessor-reported outcomes including structural progression lend themselves to blinding. The challenges associated with patient preference and cross-over will need to be anticipated when designing trials and interpreting their results. Adverse events need to be clearly reported so that potential harms of surgical intervention can be easily identified.

For the surgical interventions included in this review, the low quality evidence failed to find any benefit of surgery over non-surgical

intervention. Surgical interventions are not without risk and at present the evidence to support their use is of low quality. There have been no sham trials for this condition and only one trial that compared surgical intervention with physical therapy (Katz 2013). There have been no trials reporting outcomes beyond 12 months. Despite an awareness of a treatment gap (London 2011) in the wider orthopaedic community, this group of patients have not been well-studied. If further research is undertaken in this population, sham-controlled trials should be prioritised over non-blinded studies in order to improve the quality of evidence available. However, it could also be argued that the value of performing future higher quality trials using the same comparators is debatable. It is possible further well-designed placebo controlled trials would result in effect estimates similar to those seen in this review or trending more toward no effect, similar to the pattern seen in shoulder surgery (Karjalainen 2019).

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### REFERENCES

#### References to studies included in this review

##### Chang 1993 {published data only}

Chang RW, Falconer J, Dyer AR, Arnold WJ, Stulberg SD. Prerandomization: an alternative to classic randomization: the effects on recruitment in a controlled trial of arthroscopy for osteoarthritis of the knee. *Journal of Bone and Joint Surgery - American Volume* 1990;**72**:1451–5.

\* Chang RW, Falconer J, Stulberg SD, Arnold WJ, Manheim LM, Dyer AR. A randomized, controlled trial of arthroscopic surgery versus closed-needle joint lavage for patients with osteoarthritis of the knee. *Arthritis and Rheumatism* 1993;**36**(3):289–96.

##### Forster 2003 {published data only}

Forster MC, Straw R. A prospective randomised trial comparing intra-articular Hyalgan injection and arthroscopic washout for knee osteoarthritis. *Knee* 2003;**10**(3):291–3.

##### Katz 2013 {published data only}

Englund M, Zhang F, Guermazi A, Roemer FW, Losina E, Katz JN. The effect of arthroscopic partial meniscectomy

in patients with osteoarthritis on meniscal body extrusion. *Arthritis Rheumatol* 2015; Vol. 67 (suppl 10).

\* Katz JN, Brophy RH, Chaisson CE, De Chaves L, Cole BJ, Dahm DL, et al. Surgery versus physical therapy for a meniscal tear and osteoarthritis. *New England Journal of Medicine* 2013;**368**(18):1675–84.

Katz JN, Chaisson CE, Cole B, Guermazi A, Hunter DJ, Jones M, et al. The MeTeOR Trial (Meniscal Tear in Osteoarthritis Research): rationale and design features. *Contemporary Clinical Trials* 2012;**33**(6):1189–96.

Katz JN, Chaisson CE, Cole B, Laurel DF, Jones M, Levy B, et al. The meteor trial: preliminary results of an RCT of arthroscopic partial meniscectomy vs physical therapy in patients greater than 45. *Arthritis and Rheumatism* 2012; **64**:s1123.

NCT00597012. Comparing knee cartilage surgery versus standard physical therapy in treating people with a meniscal tear and osteoarthritis. [clinicaltrials.gov/ct2/show/record/NCT00597012?term=00597012&rank=1](http://clinicaltrials.gov/ct2/show/record/NCT00597012?term=00597012&rank=1) (first received 17 January 2008).

**Saeed 2015** {published data only}

Saeed K, Khan SA, Ahmed I. Efficacy of intra articular hyaluronic acid versus arthroscopic debridement in terms of improvement in pain score in Kellgran-Lawrence grading II & III osteoarthritis of knee joint. *Pakistan Journal of Medical and Health Sciences* 2015;**9**(3):1011–5.

**Van der Woude 2017** {published and unpublished data}

NTR2761. Knee joint distraction in comparison with high tibial osteotomy in treatment of knee osteoarthritis. <https://www.trialregister.nl/trial/2761>. Netherlands Trial Register, (first received 16 May 2011).

Van Der Woude JT, Van Heerwaarden RJ, Spruijt S, Wiegant K, Van Roermund PM, Saris DB, et al. Knee joint distraction compared with high tibial osteotomy: a randomized controlled trial. *Annals of the Rheumatic Diseases* 2015;**74**:108.

\* Van der Woude J, Wiegant K, Van Heerwaarden RJ, Spruijt S, Van Roermund PM, Custers R, et al. Knee joint distraction compared with high tibial osteotomy: a randomized controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017;**25**(3):876–86.

## References to studies excluded from this review

**Aae 2017** {published data only}

Aae TF, Randsborg PH, Breen AB, Visnes H, Vindfeld S, Sivertsen EA, et al. Norwegian Cartilage Project - a study protocol for a double-blinded randomized controlled trial comparing arthroscopic microfracture with arthroscopic debridement in focal cartilage defects in the knee. *BMC Musculoskeletal Disorders* 2016;**17**:292.

**Adeyemi 2017** {published data only}

Adeyemi A, Nherera L, Trueman P, Cano J. Cost-effectiveness analysis of coblation technology vs mechanical debridement with a shaver in the treatment of knee cartilage lesions - a Spanish payer perspective. *Value in Health* 2017;**20**(7):A584.

**Adler 1970** {published data only}

Adler E, Wolf E, Taustein I. A double blind trial with cartilage and bone marrow extract in degenerative gonarthrosis. *Acta Rheumatologica Scandinavica* 1970;**16**(1):6–11.

**Akizuki 1997** {published data only}

Akizuki S, Yasukawa Y, Takizawa T. Does arthroscopic abrasion arthroplasty promote cartilage regeneration in osteoarthritic knees with eburnation? A prospective study of high tibial osteotomy with abrasion arthroplasty versus high tibial osteotomy alone. *Arthroscopy* 1997;**13**(1):9–17.

**Alpayci 2011** {published data only}

Alpayci M, Hiz O, Ediz L, Ozkan Y. The effect of traction in the treatment of knee osteoarthritis: a prospective randomized controlled trial [Diz osteoartritinde traksiyon tedavisinin etkisi: prospektif randomize kontrollu califma]. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi* 2011;**57**:259.

**Alpayci 2013** {published data only}

Alpayci M, Ozkan Y, Yazmalar L, Hiz O, Ediz L. A randomized controlled trial on the efficacy of intermittent

and continuous traction for patients with knee osteoarthritis. *Clinical Rehabilitation* 2013;**27**(4):347–54.

**Arden 2008** {published data only}

Arden NK, Reading IC, Jordan KM, Thomas L, Platten H, Hassan A, et al. A randomised controlled trial of tidal irrigation vs corticosteroid injection in knee osteoarthritis: the KIVIS Study. *Osteoarthritis and Cartilage* 2008;**16**(6):733–9.

**Aslan 2012** {published data only}

Aslan A, Kirdemir V, Atay T, Baykal YB, Aytekin O, Aydogan FC. The efficacy of intra-articular injection of hyaluronic acid with supplemental peroral vitamin E following arthroscopic debridement in the treatment of knee osteoarthritis: a prospective, randomized, controlled study [Diz osteoartritli hastalarda artroskopik debridman sonrası eklemici hyaluronik asitle birlikte peroral E vitamini tedavisinin etkinligi: prospektif, randomize, kontrollu calisma]. *Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi* 2012;**58**(3):199–203. DOI: 10.4274/tftr.36693

**Atay 2008** {published data only}

Atay T, Aslan A, Baydar ML, Ceylan B, Baykal B, Kirdemir V. The efficacy of low- and high-molecular-weight hyaluronic acid applications after arthroscopic debridement in patients with osteoarthritis of the knee

[Gonartrozlu hastalarda artroskopik debridman sonrası dü ük ve yüksek molekül ağı rlı klı hiyalüronik asit uygulamaları nı n etkinliđ i]. *Acta Orthopaedica et Traumatologica Turcica* 2008;**42**(4):228–33.

**Benedetto 1993** {published data only}

Benedetto KP, Rangger C. Arthroscopic partial meniscectomy: 5-year follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy* 1993;**1**(3–4):235–8.

**Besselink 2017** {published data only}

Besselink, N, Van Heerwaarden R, Van Der Woude J, Wiegant K, Spruijt S, Lafeber F, et al. Axial alignment of the knee - importance in cartilage repair? High tibial osteotomy vs. distraction. *Annals of the Rheumatic Diseases* 2017;**76**:978–9.

**Bisson 2017** {published data only}

Bisson LJ, Kluczynski MA, Wind WM, Fineberg MS, Bernas GA, Rauh MA, et al. Design of a randomized controlled trial to compare debridement to observation of chondral lesions encountered during partial meniscectomy: the ChAMP (Chondral Lesions And Meniscus Procedures) trial. *Contemporary Clinical Trials* 2015;**45**:281–6.  
\* Bisson LJ, Kluczynski MA, Wind WM, Fineberg MS, Bernas GA, Rauh MA, et al. Patient outcomes after observation versus debridement of unstable chondral lesions during partial meniscectomy: the CHondral lesions And Meniscus Procedures (ChAMP) randomized controlled trial. *Journal of Bone and Joint Surgery: American Volume* 99;**13**:1078–85.

**Bloembergen 2017** {published data only}

\* Bloembergen CH, Graaf VA. Preliminary results of the escape trial: early surgery versus conservative treatment with optional delayed meniscectomy for patients over 45 years with non-obstructive meniscal tears. *Osteoporosis International* 2017;**28**:s635–6.  
Van De Graaf VA, Scholtes VAB, Wolterbeek N, Noorduyt JCA, Neeter C, Van Tulder MW, et al. Cost-effectiveness of early surgery versus conservative treatment with optional delayed meniscectomy for patients over 45 years with non-obstructive meniscal tears (ESCAPE study): protocol of a randomised controlled trial. *BMJ Open* 2016;**6**(6):no pagination.

**Börjesson 2005** {published data only}

Börjesson M, Weidenhielm L, Mattsson E, Olsson E. Gait and clinical measurements in patients with knee osteoarthritis after surgery: a prospective 5-year follow-up study. *Knee* 2005;**12**(2):121–7. DOI: 10.1016/j.knee.2004.04.002

**Bradley 2002** {published data only}

Bradley JD, Heilman DK, Katz BP, Gsell P, Wallick JE, Brandt KD. Tidal irrigation as treatment for knee osteoarthritis: a sham-controlled, randomized, double-blinded evaluation. *Arthritis and Rheumatism* 2002;**46**(1):100–8.

**Brittberg 2013** {published data only}

Brittberg M, Saris D, Caron J, Emans P, Kili S, Bezuidenhoudt M, et al. Matrix-induced autologous chondrocyte implant vs. microfracture: prospective, randomized trial in European patients, 2-year follow up. *Arthroscopy* 2013;**1**:e179–80.

**Brouwer 2005a** {published data only}

Brouwer RW, Bierma-Zeinstra SMA, Van Koeveeringe AJ, Verhaar JAN. Patellar height and the inclination of the tibial plateau after high tibial osteotomy. The open versus the closed-wedge technique. *Journal of Bone and Joint Surgery - Series B* 2005;**87**(9):1227–32.

**Brouwer 2006** {published data only}

Brouwer RW, Bierma-Zeinstra SMA, Van Raaij TM, Verhaar JAN. Osteotomy for medial compartment arthritis of the knee using a closing wedge or an opening wedge controlled by a Puddu plate. A one-year randomised, controlled study. *Journal of Bone and Joint Surgery - Series B* 2006;**88**(11):1454–9.

**Campbell 2010** {published data only}

Campbell MK, Skea ZC, Sutherland AG, Cuthbertson BH, Entwistle VA, McDonald AM, et al. Effectiveness and cost-effectiveness of arthroscopic lavage in the treatment of osteoarthritis of the knee: a mixed methods study of the feasibility of conducting a surgical placebo-controlled trial (the KORAL study). *Health Technology Assessment* 2010;**14**(5):1–115.

**Cho 2013** {published data only}

Cho SW, Kim DH, Lee GC, Lee SH, Park SH. Comparison between autogenous bone graft and allogeneous cancellous bone graft in medial open wedge high tibial osteotomy with

2-year follow-up. *Knee Surgery & Related Research* 2013;**25**(3):117–25.

**Collins 2017** {published data only}

Collins JE, Losina E, Guermazi A, Katz JN. The risk of osteoarthritis progression after arthroscopic partial meniscectomy (APM); data from an RCT of APM vs. physical therapy. *Osteoarthritis and Cartilage* 2017;**25**:no pagination.

**Dallari 2007** {published data only}

Dallari D, Savarino L, Stagni C, Cenni E, Cenacchi A, Fornasari PM, et al. Enhanced tibial osteotomy healing with use of bone grafts supplemented with platelet gel or platelet gel and bone marrow stromal cells. *Journal of Bone and Joint Surgery, American Volume* 2007;**89**(11):2413–20. DOI: 10.2106/JBJS.F.01026

**Dawes 1987** {published data only}

Dawes PT, Kirlow C, Haslock I. Saline washout for knee osteoarthritis: results of a controlled study. *Clinical Rheumatology* 1987;**6**(1):61–3.

**Duif 2015** {published data only}

Duif C, Vogel T, Topcuoglu F, Spyrou G, Von Schulze Pellengahr C, Lahner M. Does intraoperative application of leukocyte-poor platelet-rich plasma during arthroscopy for knee degeneration affect postoperative pain, function and quality of life? A 12-month randomized controlled double-blind trial. *Archives of Orthopaedic and Trauma Surgery* 2015;**135**(7):971–7.

**Duivenvoorden 2014** {published data only}

Duivenvoorden T, Brouwer R, Bos K, Reijman M, Bierma-Zeinstra S, Verhaar J. Better survival of valgus opening-wedge high tibial osteotomy: 10-year results of a RCT comparing closing wedge and opening wedge technique. *Osteoarthritis and Cartilage* 2014;**22**:S468.

**Duivenvoorden 2014a** {published data only}

Duivenvoorden T, Brouwer RW, Baan A, Bos PK, Reijman M, Bierma-Zeinstra SM, et al. Comparison of closing-wedge and opening-wedge high tibial osteotomy for medial compartment osteoarthritis of the knee: a randomized controlled trial with a six-year follow-up. *Journal of Bone and Joint Surgery, American Volume* 2014;**96**(17):1425–32.

**Ferruzzi 2012** {published data only}

Ferruzzi A, Buda R, Timoncini A, Giannini S. Autologous chondrocyte implantation and microfractures associated to high tibial osteotomy in the treatment of varus knee with severe osteoarthritis: a clinical study at 10-year follow-up. *Journal of Orthopaedics and Traumatology* 2012;**13**:S63–4.

**Ferruzzi 2014** {published data only}

Ferruzzi A, Buda R, Cavallo M, Timoncini A, Natali S, Giannini S. Cartilage repair procedures associated with high tibial osteotomy in varus knees: clinical results at 11 years' follow-up. *Knee* 2014;**21**(2):445–50.

**Freitag 2015** {published data only}

Freitag J, Ford J, Bates D, Boyd R, Hahne A, Wang Y, et al. Adipose derived mesenchymal stem cell therapy in the treatment of isolated knee chondral lesions: design of a

randomised controlled pilot study comparing arthroscopic microfracture versus arthroscopic microfracture combined with postoperative mesenchymal stem cell injections. *BMJ Open* 2015;**5**(12):e009332.

**Frias 2004** {published data only}

Frias G, Caracuel MA, Escudero A, Rumbao J, Perez-Gujo V, Castro MDC, et al. Assessment of the efficacy of joint lavage versus joint lavage plus corticoids in patients with osteoarthritis of the knee. *Current Medical Research and Opinion* 2004;**20**(6):861–7.

**Frias 2009** {published data only}

Frias G, Font P, Munoz-Gomariz E, Caracuel MA, Escudero A, Castro MC, et al. Assessing the efficacy of non-arthroscopic joint lavage in patients with osteoarthritis of the knee [Valoracion de la eficacia del lavado articular no artroscopico en pacientes con artrosis de rodilla]. *Reumatologia Clinica* 2009;**5**(5):189–93.

**Fu 2015** {published data only}

Fu B. Clinical observation on the curative effect of knee osteoarthritis with minimally invasive arthroscopic operation and local injection. *Journal of Dalian Medical University* 2015;**37**(3):286–8.

**Gaasbeek 2010** {published data only}

Gaasbeek RDA, Nicolaas L, Rijnberg WJ, Van Loon CJM, Van Kampen A. Correction accuracy and collateral laxity in open versus closed wedge high tibial osteotomy. A one-year randomised controlled study. *International Orthopaedics* 2010;**34**(2 SPECIAL ISSUE):201–7.

**Gauffin 2014** {published data only}

Gauffin H, Tagesson S, Meunier A, Magnusson H, Kvist J. Knee arthroscopic surgery is beneficial to middle-aged patients with meniscal symptoms: a prospective, randomised, single-blinded study. *Osteoarthritis and Cartilage* 2014;**22**(11):1808–16.

**Gauffin 2017** {published data only}

Gauffin H, Sonesson S, Meunier A, Magnusson H, Kvist J. Knee arthroscopic surgery in middle-aged patients with meniscal symptoms: a 3-year follow-up of a prospective, randomized study. *American Journal of Sports Medicine* 2017;**45**(9):2077–84.

**Gouin 2010** {published data only}

Gouin F, Yaouanc F, Waast D, Melchior B, Delecrcin J, Passuti N. Open wedge high tibial osteotomies: Calcium-phosphate ceramic spacer versus autologous bonegraft. *Orthopaedics and Traumatology: Surgery and Research* 2010;**96**(6):637–45.

**Gudas 2002** {published data only}

Gudas R, Simonaityte R, Riauba L, Pocius G, Kalesinskas R. Treatment of joint surface pathology by Pridie drilling

[Są narinių paviršių patologijos chirurginio gydymo efektyvumas naudojant Pridie tunelizaciją]. *Medicina (Kaunas)* 2002;**38**(7):720–9.

**Gudas 2012** {published data only}

Gudas R, Gudaite A, Pocius A, Gudiene A, Cekanauskas E, Monastyreckiene E, et al. Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. *American Journal of Sports Medicine* 2012;**40**(11):2499–508.

**Han 2010** {published data only}

Han MT, Wang F, Sun JK, Tang ZH. Comparative study on impacted high tibial osteotomy and conventional high tibial osteotomy for the treatment of flexional medial knee osteoarthritis in aged patients. *Zhongguo Gu Shang [China Journal of Orthopaedics and Traumatology]* 2010;**23**(2):107–10.

**Hede 1992** {published data only}

Hede A, Larsen E, Sandberg H. Partial versus total meniscectomy: a prospective, randomised study with long-term follow-up. *Journal of Bone and Joint Surgery - Series B* 1992;**74**(1):118–21.

**Heir 2013** {published data only}

Heir S, Ulstein S, Aroen A, Harald Rotterud J, Loken S, Engebretsen L. Microfracture technique vs mosaic plasty: no difference in knee scores at 5-11 years follow-up in a prospective randomized clinical trial. *Arthroscopy* 2013;**1**:e136.

**Hempfling 2007** {published data only}

Hempfling H. Intra-articular hyaluronic acid after knee arthroscopy: a two-year study. *Knee Surgery, Sports Traumatology, Arthroscopy* 2007;**15**(5):537–46.

**Herrlin 2007** {published data only}

Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surgery, Sports Traumatology, Arthroscopy* 2007;**15**(4):393–401.

**Herrlin 2013** {published data only}

Herrlin SV, Wange PO, Lapidus G, Hallander M, Werner S, Weidenhielm L. Is arthroscopic surgery beneficial in treating non-traumatic, degenerative medial meniscal tears? A five year follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy* 2013;**21**(2):358–64.

**Hiemstra 2012** {published data only}

Hiemstra LA, Kerslake S, Heard SM, Buchko GL. Postoperative pain and function in patients having a knee arthroscopy with viscosupplementation or placebo injection at the time of surgery: a pilot study. *Clinical Journal of Sport Medicine* 2012;**22**(3):300.

**Hubbard 1996** {published data only}

Hubbard MJ. Articular debridement versus washout for degeneration of the medial femoral condyle. A five-year study. *Journal of Bone and Joint Surgery, British Volume* 1996;**78**(2):217–9.

**Huizinga 2014** {published data only}

Huizinga MR, Brouwer RW, Van Raaij TM. High tibial osteotomy: closed wedge versus combined wedge

- osteotomy. *BMC Musculoskeletal Disorders* 2014;**15**(124): no pagination.
- Jarvinen 2014** *{published data only}*  
Jarvinen T, Sihvonen R, Paavola M, Malmivaara A, Itala A, Joukainen A, et al. Arthroscopic partial meniscectomy vs sham surgery for degenerative meniscus tear. *Arthroscopy* 2014;**1**:e38.
- Jung 2014** *{published data only}*  
Jung WH, Takeuchi R, Chun CW, Lee JS, Ha JH, Kim JH, et al. Efficacy of periarticular multimodal drug injection after medial opening-wedge high tibial osteotomy: a randomized, controlled study. *Arthroscopy* 2014;**30**(10): 1261–8.
- Kalunian 2000** *{published data only}*  
Kalunian KC, Moreland LW, Klashman DJ, Brion PH, Concoff AL, Myers S, et al. Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial. *Osteoarthritis and Cartilage* 2000;**8**(6):412–8.
- Kang 2005** *{published data only}*  
Kang JG, Wang ML, Zhang XN. Treatment of knee osteoarthritis with arthroscopic debridement and intra-articular sodium hyaluronate injection. *Journal of Jilin University Medicine Edition* 2005;**31**(5):802–5.
- Kim 2017** *{published data only}*  
Kim MS, Koh IJ, Choi YJ, Pak KH, In Y. Collagen augmentation improves the quality of cartilage repair after microfracture in patients undergoing high tibial osteotomy: a randomized controlled trial. *American Journal of Sports Medicine* 2017;**45**(8):1845–55.
- Kirkley 2008** *{published data only}*  
Anonymous. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *New England Journal of Medicine*; 20:361 2009.  
\* Kirkley A, Birmingham TB, Litchfield RB, Giffin JR, Willits K, Wong CJ, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *New England Journal of Medicine* 2008;**359**(11):1097–1107.
- Knutsen 2004** *{published data only}*  
Knutsen G, Isaksen V, Johansen O, Engebretsen L, Ludvigsen TC, Drogset JO, et al. Autologous chondrocyte implantation compared with microfracture in the knee: a randomized trial. *Journal of Bone and Joint Surgery - Series A* 2004;**86**(3):455–64.
- Knutsen 2007** *{published data only}*  
Knutsen G, Drogset JO, Engebretsen L, Grontvedt T, Isaksen V, Ludvigsen TC, et al. A randomized trial comparing autologous chondrocyte implantation with microfracture: findings at five years. *Journal of Bone and Joint Surgery - Series A* 2007;**89**(10):2105–12.
- Kulshrestha 2016** *{published data only}*  
Kulshrestha V, Datta B, Kumar S, Mittal G. Outcome of unicompartmental knee arthroplasty vs total knee arthroplasty for early medial compartment arthritis: a randomized study. *Journal of Arthroplasty* 2016;**17**:no pagination.
- Lee 2013** *{published data only}*  
Lee GW, Son JH, Kim JD, Jung GH. Is platelet-rich plasma able to enhance the results of arthroscopic microfracture in early osteoarthritis and cartilage lesion over 40 years of age?. *European Journal of Orthopaedic Surgery and Traumatology* 2013;**23**(5):581–7.
- Linke 2007** *{published data only}*  
Linke RD, Ulmer M, Imhoff AB. Replacement of the meniscus with a collagen implant (CMI). *European Journal of Trauma & Emergency Surgery* 2007;**33**(4):435–40.
- Liu 2004** *{published data only}*  
Liu YJ, Dong Y, Liu LF. Staging treatment of osteoarthritis: a three-year follow-up of randomized control. *Chinese Journal of Clinical Rehabilitation* 2004;**8**(8):1426–7.
- Luchikhina 2014** *{published data only}*  
Luchikhina LV, Mendel OI, Antonov DA. Knee osteoarthritis combination therapy with hyaluronic acid, chondroitine sulfate and glucosamine after arthroscopic lavage: long-term results. *Osteoarthritis and Cartilage* 2014;**22**:S480.
- Luites 2009** *{published data only}*  
Luites JWH, Brinkman JM, Wymenga AB, Van Heerwaarden RJ. Fixation stability of opening- versus closing-wedge high tibial osteotomy: a randomised clinical trial using radiostereometry. *Journal of Bone and Joint Surgery - Series B* 2009;**91**(11):1459–65.
- Magyar 1999** *{published data only}*  
Magyar G, Ahl TL, Vibe P, Toksvig-Larsen S, Lindstrand A. Open-wedge osteotomy by hemicallotaxis or the closed-wedge technique for osteoarthritis of the knee. *Journal of Bone and Joint Surgery - Series B* 1999;**81**(3):444–8.
- Marmotti 2013** *{published data only}*  
Marmotti A, Castoldi F, Rossi R, Marengo S, Risso A, Ruella M, et al. Bone marrow-derived cell mobilization by G-CSF to enhance osseointegration of bone substitute in high tibial osteotomy. *Knee Surgery, Sports Traumatology, Arthroscopy* 2013;**21**(1):237–48. DOI: 10.1007/s00167-012-2150-z
- Marsh 2016** *{published data only}*  
\* Marsh J, Birmingham TB, Giffin JR, Isaranuwachai W, Hoch JS, Litchfield R, et al. Cost-effectiveness analysis of arthroscopic surgery compared to non-operative management for osteoarthritis of the knee. *Osteoarthritis and Cartilage* 2015;**23**(A31):no pagination.  
Marsh JD, Birmingham TB, Giffin JR, Isaranuwachai W, Hoch J, Feagan BG, et al. Cost-effectiveness analysis of arthroscopic surgery compared with non-operative management for osteoarthritis of the knee. *BMJ Open* 2016;**6** (1)(e009949):no pagination.
- Merchan 1993** *{published data only}*  
Merchan EC, Galindo E. Arthroscope-guided surgery versus nonoperative treatment for limited degenerative osteoarthritis of the femorotibial joint in patients over 50 years of age: a prospective comparative study. *Arthroscopy* 1993;**9**(6):663–7.

- Moseley 1996** *{published data only}*  
Moseley JB, Wray NP, Kuykendall D, Willis K, Landon G. Arthroscopic treatment of osteoarthritis of the knee: a prospective, randomized, placebo-controlled trial: results of a pilot study. *American Journal of Sports Medicine* 1996;**24**(1):28–34.
- Moseley 2002** *{published data only}*  
Chambers K, Schulzer M, Sobolev B. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *Arthroscopy* 2002;**18**(7):683–7.  
\* Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *New England Journal of Medicine* 2002;**347**(2):81–8.
- Myrnerets 1980** *{published data only}*  
Myrnerets R. High tibial osteotomy with overcorrection of varus malalignment in medial gonarthrosis. *Acta Orthopaedica Scandinavica* 1980;**51**(3):557–60.
- Nakamura 2001** *{published data only}*  
Nakamura E, Mizuta H, Kudo S, Takagi K, Sakamoto K. Open-wedge osteotomy of the proximal tibia with hemicallotasis. *Journal of Bone and Joint Surgery - Series B* 2001;**83**(8):1111–5.
- Narkbunnam 2012** *{published data only}*  
Narkbunnam R, Chareancholvanich K, Pornrattanamaneewong C. Efficacy and safety of continuous intra-articular hyaluronic acid injection (Hyalgan) in treatment of knee osteoarthritis patients who underwent high tibial osteotomy, clinical and MRI evaluation. *Osteoarthritis and Cartilage* 2012;**20**:S292–3.
- Nerhus 2017a** *{published data only}*  
Nerhus TK, Ekeland A, Solberg G, Sivertsen EA, Madsen JE, Heir S. Radiological outcomes in a randomized trial comparing opening wedge and closing wedge techniques of high tibial osteotomy. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017;**25**(3):910–7.
- Nerhus 2017b** *{published data only}*  
Nerhus TK, Ekeland A, Solberg G, Olsen BH, Madsen JE, Heir S. No difference in time-dependent improvement in functional outcome following closing wedge versus opening wedge high tibial osteotomy: a randomised controlled trial with two-year follow-up. *Bone & Joint Journal* 2017;**99-B**(9):1157–66.
- Osman 2014** *{published data only}*  
Osman WS, Yousef MG, El Gebeily MA, Metwaly RG. Tibial slope and patellar height changes following high tibial osteotomy. *Osteoarthritis and Cartilage* 2014;**22**:S194–5.
- Osteras 2011** *{published data only}*  
Osteras H, Torstensen TA, Selven E, Haugerud L. High dosage medical exercise therapy or arthroscopic treatment for patients with degenerative meniscus injury: a pilot study. *Physiotherapy* 2011;**97**:eS946–7.
- Ou 2008** *{published data only}*  
Ou ZX, Jin JC, Huang D. Comparative study on effects of combined massage-smouldering-washing therapy and mini-invasive surgery in treating knee osteoarthritis. *Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi [Chinese Journal of Integrated Traditional and Western Medicine]* 2008;**28**(10):925–8.
- Parmigiani 2010** *{published data only}*  
Parmigiani L, Furtado RNV, Lopes RV, Ribeiro LHC, Natour J. Joint lavage associated with triamcinolone hexacetonide injection in knee osteoarthritis: a randomized double-blind controlled study. *Clinical Rheumatology* 2010;**29**(11):1311–5.
- Pascale 2011** *{published data only}*  
Pascale W, Luraghi S, Perico L, Pascale V. Do microfractures improve high tibial osteotomy outcome?. *Orthopedics* 2011;**34**(7):e251–5.
- Ravaud 1999** *{published data only}*  
Ravaud P, Moulinier L, Giraudeau B, Ayrat X, Guerin C, Noel E, et al. Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial. *Arthritis and Rheumatism* 1999;**42**(3):475–82.
- Raynauld 2002** *{published data only}*  
Raynauld JP, Torrance GW, Band PA, Goldsmith CH, Tugwell P, Walker V, et al. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (part 1 of 2): clinical results. *Osteoarthritis and Cartilage* 2002;**10**(7):506–17.
- Rodkey 2009** *{published data only}*  
Rodkey WG, Briggs KK, Steadman JR. Anatomic location of partial medial meniscectomy correlates with two-year function and activity levels. *Osteoarthritis and Cartilage* 2009;**17**:S251.
- Rodkey 2009a** *{published data only}*  
Rodkey WG, Briggs KK, Steadman JR. Six-year results of collagen meniscus implants emphasizing location and meniscus remaining. *Osteoarthritis and Cartilage* 2009;**17**:S251.
- Roos 2018** *{published data only}*  
Hare KB, Lohmander LS, Christensen R, Roos EM. Arthroscopic partial meniscectomy in middle-aged patients with mild or no knee osteoarthritis: a protocol for a double-blind, randomized sham-controlled multi-centre trial. *BMC Musculoskeletal Disorders* 2013;**14**(71):no pagination.  
\* Roos EM, Hare KB, Nielsen SM, Christensen R, Lohmander LS. Better outcome from arthroscopic partial meniscectomy than skin incisions only? A sham-controlled randomised trial in patients aged 35-55 years with knee pain and an MRI-verified meniscal tear. *BMJ Open* 2018;**8**(2):no pagination.
- Russell 2003** *{published data only}*  
Russell ID, Baker D, Johnson SR. A comparison of Synvisc and arthroscopic lavage in the management of osteoarthritis of the knee [abstract]. *Journal of Bone and Joint Surgery - British Volume* 2003;**85** Suppl 2:106.

- Saris 2008** *{published data only}*  
Saris DB, Vanlauwe J, Victor J, Almqvist KF, Verdonk R, Bellemans J, et al. Treatment of symptomatic cartilage defects of the knee: characterized chondrocyte implantation results in better clinical outcome at 36 months in a randomized trial compared to microfracture. *American Journal of Sports Medicine* 2009;**37**:10S–19S.  
\* Saris DBF, Vanlauwe J, Victor J, Haspl M, Bohnsack M, Fortems Y, et al. Characterized chondrocyte implantation results in better structural repair when treating symptomatic cartilage defects of the knee in a randomized controlled trial versus microfracture. *American Journal of Sports Medicine* 2008;**36**(2):235–46.
- Schultz 1999** *{published data only}*  
Schultz W, Gobel D. Articular cartilage regeneration of the knee joint after proximal tibial valgus osteotomy: a prospective study of different intra- and extra-articular operative techniques. *Knee Surgery, Sports Traumatology, Arthroscopy* 1999;**7**(1):29–36.
- Shaofei 2017** *{published data only}*  
Shaofei Z, Junliang Z, Zhongxin X, Peng H, Xing Z. Comparative analysis of the medium-term effect of the medial unicompartmental arthroplasty through medial approach next to patellar and high tibial osteotomy on medial compartment osteoarthritis of the knee. *Biomedical Research* 2017;**28**(7):3276–80.
- Shive 2015** *{published data only}*  
Shive MS, Stanish WD, McCormack R, Forriol F, Mohtadi N, Pelet S, et al. BST-CarGel treatment maintains cartilage repair superiority over microfracture at 5 years in a multicenter randomized controlled trial. *Cartilage* 2015;**6**(2):62–72.
- Sihvonen 2013** *{published data only}*  
Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Nurmi H, et al. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. *New England Journal of Medicine* 2013;**369**:2515–24.
- Smith 2003** *{published data only}*  
Smith M, Wetherall M, Darby T, Esterman A, Roberts-Thomson P, Coleman M, et al. Erratum: a randomized placebo-controlled trial of arthroscopic lavage versus lavage plus intra-articular corticosteroids in the management of symptomatic osteoarthritis of the knee. *Rheumatology* 2003;**42**(6):814.
- Smith 2018** *{published data only}*  
Smith NA, Achten J, Parsons N, Wright D, Parkinson B, Thompson P, et al. Meniscal transplantation and its effect on osteoarthritis risk: an abridged protocol for the MeTEOR study: a comprehensive cohort study incorporating a pilot randomised controlled trial. *Bone & Joint Research* 2015;**4**(6):93–8.  
\* Smith NA, Parsons N, Wright D, Hutchinson C, Metcalfe A, Thompson P, et al. A pilot randomized trial of meniscal allograft transplantation versus personalized physiotherapy for patients with a symptomatic meniscal deficient knee compartment. *Bone & Joint Journal* 2018;**100-B**(1):56–63.
- Spahn 2010** *{published data only}*  
Spahn G, Klinger HM, McKley T, Hofmann GO. Four-year results from a randomized controlled study of knee chondroplasty with concomitant medial meniscectomy: mechanical debridement versus radiofrequency chondroplasty. *Arthroscopy* 2010;**26**(9 Suppl 1):S73–S80+e164.
- Spahn 2016** *{published data only}*  
Spahn G, Hofmann GO, Von Engelhardt LV. Mechanical debridement versus radiofrequency in knee chondroplasty with concomitant medial meniscectomy: 10-year results from a randomized controlled study. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016;**24**(5):1560–8.
- Stensrud 2015** *{published data only}*  
Stensrud S, Risberg MA, Roos EM. Effect of exercise therapy compared with arthroscopic surgery on knee muscle strength and functional performance in middle-aged patients with degenerative meniscus tears: a 3-mo follow-up of a randomized controlled trial. *American Journal of Physical Medicine & Rehabilitation* 2015;**94**(6):460–73.
- Stukenborg Colsman 2001** *{published data only}*  
Stukenborg-Colsman C, Wirth CJ, Lazovic D, Wefer A. High tibial osteotomy versus unicompartmental joint replacement in unicompartmental knee joint osteoarthritis: 7-10-year follow-up prospective randomised study. *Knee* 2001;**8**(3):187–94.
- Van Egmond 2016** *{published data only}*  
Van Egmond N, Van Grinsven S, Van Loon CJ, Gaasbeek RD, Van Kampen A. Better clinical results after closed-compared to open-wedge high tibial osteotomy in patients with medial knee osteoarthritis and varus leg alignment. *Knee Surgery, Sports Traumatology, Arthroscopy* 2016;**24**(1):34–41.
- Van Oosterhout 2006** *{published data only}*  
Van Oosterhout M, Sont JK, Bajema IM, Breedveld FC, Van Laar JM. Arthroscopic lavage plus corticosteroids is more effective than joint aspiration plus corticosteroids in patients with arthritis of the knee. *Nederlands Tijdschrift Voor Geneeskunde* 2008;**152**(36):1973–1980.  
\* Van Oosterhout M, Sont JK, Bajema IM, Breedveld FC, Van Laar JM. Comparison of efficacy of arthroscopic lavage plus administration of corticosteroids, arthroscopic lavage plus administration of placebo, and joint aspiration plus administration of corticosteroids in arthritis of the knee: a randomized controlled trial. *Arthritis Care and Research* 2006;**55**(6):964–70.
- Vermesan 2013** *{published data only}*  
Vermesan D, Prejbeanu R, Laitin S, Damian G, Deleanu B, Abbinante A, et al. Arthroscopic debridement compared to intra-articular steroids in treating degenerative medial meniscal tears. *European Review for Medical and Pharmacological Sciences* 2013;**17**(23):3192–6.
- Volz 2017** *{published data only}*  
Volz M, Schaumburger J, Frick H, Grifka J, Anders S. A randomized controlled trial demonstrating sustained benefit of autologous matrix-induced chondrogenesis over

microfracture at five years. *International Orthopaedics* 2017; **41**(4):797–804.

**Ward 1998** {published data only}

Ward PJ, Ramos JL, Fernandez GN, Palazon J. A prospective randomised controlled trial of cannula versus arthroscopic lavage in patients with osteoarthritis of the knee [Abstract]. *Journal of Bone and Joint Surgery - British Volume* 1998;**80** Suppl 1:46.

**Yim 2013** {published data only}

Yim JH, Seon JK, Song EK, Choi JI, Kim MC, Lee KB, et al. A comparative study of meniscectomy and nonoperative treatment for degenerative horizontal tears of the medial meniscus. *American Journal of Sports Medicine* 2013;**41**(7): 1565–70.

**Zhang 2018** {published data only}

Zhang YF, Liu H. Clinical efficacy of knee arthroscopy in the treatment of degenerative knee osteoarthritis. *Biomedical Research* 2018;**29**(5):958–61.

**Zhao 2018** {published data only}

Zhao B, Yu Y, Liu W, Du J. Efficacy of arthroscopic loose body removal for knee osteoarthritis. *Experimental and Therapeutic Medicine* 2018;**15**(2):1666–71.

**Zorzi 2011** {published data only}

Zorzi AR, Da Silva HG, Muszkat C, Marques LC, Cliquet Jr A, De Miranda JB. Opening-wedge high tibial osteotomy with and without bone graft. *Artificial Organs* 2011;**35**(3): 301–7.

## References to ongoing studies

**NCT02003976** {published data only}

NCT02003976. A Randomized Trial Comparing High Tibial Osteotomy Plus Non-Surgical Treatment and Non-Surgical Treatment Alone. [clinicaltrials.gov/show/NCT02003976](http://clinicaltrials.gov/show/NCT02003976) First received 6th December 2013.

## Additional references

**Altman 1991**

Altman R. Classification of disease: osteoarthritis. *Seminars in Arthritis and Rheumatism* 1991;**20**(6):40–7.

**Altman 1994**

Bland JM, Altman DG. Statistics Notes: Some examples of regression towards the mean. *BMJ* 1994;**309**:780.

**Amin 2005**

Amin S, LaValley M, Guermazi A, Grigoryan M, Hunter D, Clancy M, et al. The relationship between cartilage loss on magnetic resonance imaging and radiographic progression in men and women with knee osteoarthritis. *Arthritis & Rheumatology* 2005;**52**(10):3152–9.

**Bailie 2008**

Bailie A, Lewis P, Brumby S, Roy S, Paterson R, Campbell D. The Unispacer knee implant: early clinical results. *Journal of Bone and Joint Surgery, British Volume* 2008;**90** (4):446–50.

**Brahmachari 2009**

Brahmachari B, Chatterjee S, Ghosh A. Efficacy and safety of diacerein in early knee osteoarthritis: a randomized placebo-controlled trial. *Clinical Rheumatology* 2009;**28** (10):1193–8.

**Briem 2007**

Briem K, Ramsey D, Newcomb W, Rudolph K, Snyder L. Effects of the amount of valgus correction for medial compartment knee osteoarthritis on clinical outcome, knee kinetics and muscle co-contraction after opening wedge high tibial osteotomy. *Journal of Orthopaedic Research* 2007; **25**(3):311–8.

**Brignardello-Petersen 2017**

Brignardello-Petersen R, Guyatt GH, Buchbinder R, Poolman RW, Schandelmaier S, Chang Y, et al. Knee arthroscopy versus conservative management in patients with degenerative knee disease: a systematic review. *BMJ Open* 2017;**7**(5):no pagination.

**Brouwer 2014**

Brouwer RW, Huizinga MR, Duivenvoorden T, Van Raaij TM, Verhagen AP, Bierma-Zeinstra SMA, et al. Osteotomy for treating knee osteoarthritis. *Cochrane Database of Systematic Reviews* 2014, Issue 12. DOI: 10.1002/14651858.CD004019.pub4

**Buckwalter 1998**

Buckwalter J, Mankin H. Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. Part II. *Journal of the American Academy of Orthopaedic Surgeons. Global Research and Reviews* 1998;**47**:487–504.

**Cates 2008** [Computer program]

Dr Christopher Cates. Visual Rx. Version 3. Dr Christopher Cates, 2008.

**Clarius 2010**

Clarius M, Becker J, Schmitt H, Seeger J. The UniSpacer <sup>TM</sup>: correcting varus malalignment in medial gonarthrosis. *International Orthopaedics* 2010;**34**(8):1175–9.

**Clifford 2011**

Clifford A, O'Connell M, Gabriel S, Miller L, Block J. The KineSpring load absorber implant: rationale, design and biomechanical characterization. *Journal of Medical Engineering & Technology* 2011;**35**(1):65–71.

**Coventry 1993**

Coventry M, Ilstrup D, Wallrichs S. Proximal tibial osteotomy. *Journal of Bone and Joint Surgery, American Volume* 1993;**75-A**(2):196–201.

**Cross 2014**

Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Annals of the Rheumatic Diseases* 2014;**73**(7):1323–1330.

**Deeks 2011**

Deeks J, Higgins J, Altman D (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March

- 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).
- Department for Work and Pensions 2007**  
Department for Work and Pensions, UK. Disability living allowance - cases in payment caseload (thousands): main disabling condition by gender of claimant. 83.244.183.180/100pc/dla/disabled/ccsex/a\_carate\_r\_disabled\_c\_ccsex\_nov07.html (accessed 16 June 2015).
- Dowsey 2012**  
Dowsey M, Nikpour M, Dieppe P, Choong P. Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. *Osteoarthritis and Cartilage* 2012;**20**(10):1095–102.
- Faucher 2002**  
Faucher M, Poiraudou S, Lefevre-Colau MM, Rannou F, Fermanian J, Revel M. Algo-functional assessment of knee osteoarthritis: comparison of the test-retest reliability and construct validity of the Womac and Lequesne indexes. *Osteoarthritis & Cartilage* 2002;**10**:602–10.
- Ghogomu 2014**  
Ghogomu E, Maxwell L, Buchbinder R, Rader T, Pardo Pardo J, Johnston R, et al. Updated method guidelines for Cochrane musculoskeletal group systematic reviews and metaanalyses. *Journal of Rheumatology* 2014;**41**(2):194–205.
- GRADEpro 2015 [Computer program]**  
GRADE Working Group, McMaster University (developed by Evidence Prime, Inc.). GRADEpro GDT. Version accessed prior to 26 June 2019. GRADE Working Group, McMaster University (developed by Evidence Prime, Inc.), 2015.
- Hayashi 2012**  
Hayashi D, Englund M, Roemer F, Niu J, Sharma L, Felson D, et al. Knee malalignment is associated with an increased risk for incident and enlarging bone marrow lesions in the more loaded compartments: the MOST study. *Osteoarthritis and Cartilage* 2012;**20**(11):1227–33.
- Higgins 2011**  
Higgins J, Altman D, Sterne J (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors), *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).
- Higgins 2011a**  
Higgins J, Deeks J (editors). Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).
- Hunter 2008**  
Hunter D, Lo G, Gale D, Grainger A, Guermazi A, Conaghan P. The reliability of a new scoring system for knee osteoarthritis MRI and the validity of bone marrow lesion assessment: BLOKS (Boston Leeds Osteoarthritis Knee Score). *Annals of the Rheumatic Diseases* 2008;**67**(2):206–11.
- Hunter 2011**  
Hunter D, Guermazi A, Lo G, Grainger A, Conaghan P, Boudreau R, et al. Evolution of semiquantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis and Cartilage* 2011;**19**(8):990–1002.
- ICRS 2000**  
International Cartilage Repair Society. ICRS cartilage Injury evaluation package. [www.cartilage.org/\\_files/contentmanagement/ICRS\\_evaluation.pdf](http://www.cartilage.org/_files/contentmanagement/ICRS_evaluation.pdf) (accessed 20 July 2015).
- Jang 2013**  
Jang S, Kim J, Cha S. Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. *European Journal of Orthopaedic Surgery and Traumatology* 2013;**23**(5):573–80.
- Javaid 2009**  
Javaid M, Lynch J, Tolstykh I, Guermazi A, Roemer F, Aliabadi P, et al. Pre-radiographic MRI findings are associated with onset of knee symptoms: the Most study. *Osteoarthritis and Cartilage* 2010;**18**:323–8.
- JLA 2015**  
The James Lind Alliance. Tackling treatment uncertainties together. [www.jla.nihr.ac.uk/top-10-priorities/](http://www.jla.nihr.ac.uk/top-10-priorities/) (accessed 28 November 2018).
- Jones 2014**  
Jones L, Bottomley N, Harris K, Jackson W, Price A, Beard D. The clinical symptom profile of early radiographic knee arthritis: a pain and function comparison with advanced disease. *Knee Surgery, Sports Traumatology, Arthroscopy* 2014 Oct 2 [Epub ahead of print].
- Karjalainen 2019**  
Karjalainen TV, Jain NB, Page CM, Lähdeoja TA, Johnston RV, Salamh P, Kavaja L, Ardern CL, Agarwal A, Vandvik PO, Buchbinder R. Subacromial decompression surgery for rotator cuff disease. *Cochrane Database of Systematic Reviews* 2019, Issue 1. DOI: 10.1002/14651858.CD005619.pub3
- Kellgren 1957**  
Kellgren J, Lawrence J. Radiological assessment of osteoarthritis. *Annals of the Rheumatic Diseases* 1957;**16**:494–502.
- Koeck 2009**  
Koeck F, Perlick L, Luring C, Beckmann J, Linhardt O, Grifka J. Leg axis correction with ConforMIS iForma™ (interpositional device) in unicompartmental arthritis of the knee. *International Orthopaedics* 2009;**33**(4):955–60.
- Lafeber 2006**  
Lafeber F, Intema F, Van Roermund P, Marijnissen A. Unloading joints to treat osteoarthritis, including joint distraction. *Current Opinions Rheumatology* 2006;**18**:519–25.

**Laupattarakasem 2008**

Laupattarakasem W, Laopaiboon M, Laupattarakasem P, Sumananont C. Arthroscopic debridement for knee osteoarthritis. *Cochrane Database of Systematic Reviews* 2008, Issue 1. DOI: 10.1002/14651858.CD005118.pub2

**London 2011**

London N, Miller L, Block J. Clinical and economic consequences of the treatment gap in knee osteoarthritis management. *Medical Hypotheses* 2011;**76**(6):887–92.

**London 2013**

London N, Smith J, Miller L, Block J. Midterm outcomes and predictors of clinical success with the KineSpring knee implant system. *Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders* 2013;**6**:19–28.

**Luyten 2012**

Luyten F, Denti M, Filardo G, Kon E, Engebretsen L. Definition and classification of early osteoarthritis of the knee. *Knee Surgery, Sports Traumatology, Arthroscopy* 2012;**20**(L):401–6.

**Marijnissen 2008**

Marijnissen ACA, Vincken KL, Vos PAJM, Saris DBF, Viergever MA, Bijlsma JWJ, et al. Knee Images Digital Analysis (KIDA): a novel method to quantify individual radiographic features of knee osteoarthritis in detail. *Osteoarthritis & Cartilage* 2008;**16**:234–43.

**Murphy 2008**

Murphy L, Schwartz T, Helmick C, Renner J, Tudor G, Koch G, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis and Rheumatism* 2008;**59**(9):1207–13.

**Murray 2012**

Murray C, Vos T, Lozano R, Naghavi M, Flaxman A, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; Vol. 380, issue 9859:2197–223.

**Nelson 2013**

Nelson F, Zvirbulis R, Pilla A. Non-invasive electromagnetic field therapy produces rapid and substantial pain reduction in early knee osteoarthritis: a randomized double-blind pilot study. *Rheumatology International* 2013;**33**(8):2169–73.

**Niinimäki 2011**

Niinimäki T, Murray D, Partanen J, Pajala A, Leppilähti J. Unicompartmental knee arthroplasties implanted for osteoarthritis with partial loss of joint space have high reoperation rates. *Knee* 2011;**18**(6):432–5.

**Peterfy 2004**

Peterfy C, Guermazi A, Zaim S, Tirman P, Miaux Y, White D, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis. *Osteoarthritis and Cartilage* 2004;**12**(3):177–90.

**Reichenbach 2010**

Reichenbach S, Rutjes A, Nuesch E, Trelle S, Juni P. Joint lavage for osteoarthritis of the knee. *Cochrane Database*

*of Systematic Reviews* 2010, Issue 5. DOI: 10.1002/14651858.CD007320.pub2

**RevMan 2012 [Computer program]**

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.2. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

**Roos 2001**

Roos E, Ostenberg A, Roos H, Ekdahl C, Lohmander S. Long-term outcome of meniscectomy: symptoms, function, and performance tests in patients with or without radiographic osteoarthritis compared to matched controls. *Osteoarthritis and Cartilage* 2001;**9**(4):316–24.

**Schünemann 2011a**

Schünemann H, Oxman A, Higgins J, Vist G, Glasziou P, Guyatt G. Chapter 11: Presenting results and ‘Summary of findings’ tables. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).

**Schünemann 2011b**

Schünemann H, Oxman A, Vist G, Higgins J, Deeks J, Glasziou P, et al. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).

**Sharma 2001**

Sharma L, Song J, Felson D, Cahue S, Shamiyeh E, Dunlop D. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA* 2001;**286**:188–95.

**Sharma 2013**

Sharma L, Chmiel J, Almagor O, Felson D, Guermazi A, Roemer F, et al. The role of varus and valgus alignment in the initial development of knee cartilage damage by MRI: the MOST study. *Annals of the Rheumatic Diseases* 2013;**72**(2):235–40.

**Sterne 2011**

Sterne J, Egger M, Moher D (editors). Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from [handbook.cochrane.org](http://handbook.cochrane.org).

**Tanamas 2009**

Tanamas S, Hanna F, Cicuttini F, Wluka A, Berry P, Urquhart D. Does knee malalignment increase the risk of development and progression of knee osteoarthritis? A systematic review. *Arthritis and Rheumatism* 2009;**61**(4):459–67.

**Wiegant 2013**

Wiegant K, Van Roermund P, Intema F, Eckstein F, Mastbergen S, Lafeber F. Sustained clinical and structural

benefit after joint distraction in the treatment of severe knee osteoarthritis. *Osteoarthritis and Cartilage* 2013;**21**(11): 1660–7.

\* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

#### Chang 1993

Methods	<p><b>Study design:</b> Randomised controlled two-armed trial</p> <p><b>Study grouping:</b> Parallel group trial</p> <p><b>Interventions:</b> Arthroscopic surgery versus closed-needle joint lavage</p>
Participants	<p>Overall:</p> <ul style="list-style-type: none"> <li>• Mean Age (yrs): 63 (<math>\pm</math>12)</li> <li>• % Female: 72</li> <li>• KL grade 1: 19%</li> <li>• KL grade 2: 31%</li> <li>• KL grade 3: 50%</li> </ul> <p><b>Number of participants:</b> Number screened = "more than 200"; number randomised = 34; number included in analysis = 32</p> <p><b>Included criteria:</b></p> <ol style="list-style-type: none"> <li>1. Persistent knee pain for longer than 3 months, despite conservative medical and rehabilitation management, which restricted work, athletic, or self-care activities to an extent unacceptable to the patient</li> <li>2. Weight-bearing knee radiographs showing grade 1, 2, or 3 changes as described by Kellgren and Lawrence</li> <li>3. Age &gt; 20 years</li> <li>4. Willingness to attend follow-up visits at 3 and 12 months</li> <li>5. Willingness to give written informed consent</li> </ol> <p>Note: In patients with bilateral disease, the more symptomatic knee was designated the study knee</p> <p><b>Excluded criteria:</b></p> <ol style="list-style-type: none"> <li>1. Knee surgery within 6 months of study entry</li> <li>2. Total knee replacement</li> <li>3. Any concurrent illness which would influence functional assessment of the knee or preclude arthroscopic surgery, e.g. severe intermittent claudication or cardiac disease</li> <li>4. Kellgren class 4 changes or radiographs</li> </ol> <p><b>Pretreatment:</b> The only statistically significant difference between groups (<math>P &lt; 0.05</math>) was the initial mean AIMS Physical Activity score. A higher AIMS Physical Activity score (lower physical activity level) was seen in the arthroscopy group (6.9, SD 2.0) compared to the control group (5.3, SD 2.1)</p>
Interventions	<p><b>Intervention Characteristics</b></p> <p>Arthroscopic surgery: Arthroscopy was done under general anaesthesia. A diagnostic evaluation was performed and then any of the following interventions were performed arthroscopically:</p> <ol style="list-style-type: none"> <li>1. Debridement of torn meniscus and removal of meniscal and cruciate fragments;</li> <li>2. Removal of proliferative synovium;</li> <li>3. Excision of loose articular fragment.</li> </ol> <p>Patients were instructed on partial weight-bearing for 10 days (3 weeks if osteochondral defect noted)</p>

	<p>Closed-needle joint lavage: Tidal knee lavage was performed under local anaesthesia. 1 litre of saline was injected into and aspirated from the knee in aliquots of 40-120 cc depending on the size of the knee capsule</p> <p>Both groups received identical non-narcotic analgesia and physical therapy</p>
<p>Outcomes</p>	<p><b>Outcomes included in this review:</b></p> <p><i>Arthritis Impact Measurement Scales (AIMS) scales: Pain</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-10</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Change from baseline</li> </ul> <p><i>Arthritis Impact Measurement Scales (AIMS) scales: Function</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-10</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Change from baseline</li> </ul> <p><i>Visual Analogue Scale (VAS): well-being</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-10</li> <li>● <b>Unit of measure:</b> cm</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Change from baseline</li> </ul> <p><b>Other outcomes reported in the trial:</b></p> <ul style="list-style-type: none"> <li>● Active and passive range of knee motion</li> <li>● Knee joint swelling</li> <li>● Knee joint tenderness</li> <li>● Physician's global assessment of disease activity</li> <li>● Economic measures</li> </ul>
<p>Identification</p>	<p><b>Sponsorship source:</b> Supported by grant 9040 from the Robert Wood Johnson Foundation, by MAC grant AR-30692 from the NIH (NIAMS), and by the Percy Surgical Research Trust of Lutheran General Hospital</p> <p><b>Country:</b> USA</p> <p><b>Setting:</b> The Rheumatology-Orthopedic Knee Clinic of the Northwestern Medical Faculty Foundation (Northwestern University Medical School) and the Division of Rheumatology of the Lutheran General Medical Group (Lutheran General Hospital)</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> Rowland W. Chang, MD</p> <p><b>Institution:</b> Multipurpose Arthritis Center, Northwestern University</p> <p><b>Email:</b> N/A</p> <p><b>Address:</b> Multipurpose Arthritis Center, Northwestern University, 303 East Chicago Avenue, #3-315, Chicago, IL 6061 1</p> <p><b>Trial registration:</b> not reported</p>
<p>Notes</p>	<ul style="list-style-type: none"> <li>● Adverse events not reported in this study</li> </ul>

**Chang 1993** (Continued)

<i>Risk of bias</i>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Method for random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Sealed envelope mentioned in another study referenced in their methodology - but did not report if the envelopes were opaque, sequentially numbered, or kept from investigators
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants or personnel
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Judgement Comment: Patient-reported outcomes were at high risk of bias as subjects were aware of the treatment they received
Blinding of outcome assessment (detection bias) Assessor-reported outcomes	Low risk	Quote: "a single assessor not associated with the procedures and blinded to the patient's treatment regimen" . Outcomes included range of motion, knee swelling, knee tenderness, which were not included in the review
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small number of participants lost to follow-up
Selective reporting (reporting bias)	Low risk	No study protocol available. Had acceptable outcomes including pain and functional assessment, global assessment
Other bias	Low risk	No other source of bias identified

**Forster 2003**

Methods	<p><b>Study design:</b> Randomised controlled two-armed trial</p> <p><b>Study grouping:</b> Parallel group</p> <p><b>Interventions:</b> Arthroscopic surgery versus hyaluronic acid injections</p>
Participants	<p><b>Baseline Characteristics</b></p> <p>Arthroscopic washout</p> <ul style="list-style-type: none"> <li>• <i>Mean Age (yrs):</i> 63</li> </ul> <p>Hyalgan Injection</p>

	<ul style="list-style-type: none"> <li>• <i>Mean Age (yrs):</i> 60</li> </ul> <p><b>Number of participants:</b> Number screened = not reported; number randomised = 38; number included in analysis = 32</p> <p><b>Included criteria:</b></p> <ol style="list-style-type: none"> <li>1. Symptomatic knee osteoarthritis</li> <li>2. Radiographic evidence of some remaining joint space on weight-bearing films</li> <li>3. Fit for regional or general anaesthesia</li> </ol> <p><b>Excluded criteria:</b></p> <ol style="list-style-type: none"> <li>1. Patients with mechanical symptoms</li> <li>2. Intra-articular injection within the last 6 months</li> <li>3. Previous arthroscopic surgery</li> <li>4. Hypersensitivity to avian proteins</li> </ol> <p><b>Pretreatment:</b> The pre-intervention Knee Society Function Score was significantly worse in the arthroscopy group (Mann-Whitney test; <math>P = 0.05</math>). There was no significant difference between the groups in terms of age, amount of analgesic or nonsteroidal anti-inflammatory tablets used, pre-intervention Visual Analogue Scale, or pre-intervention Lequesne Index</p>
Interventions	<p><b>Intervention Characteristics</b></p> <p>Arthroscopic washout: Arthroscopic washout under general or spinal anaesthesia. Knee joints were washed out with at least 2 L 0.9% saline. Debridement of the articular surface or menisci was undertaken if clinically necessary. Large chondral flaps or meniscal fragments were excised but stable, degenerate menisci were left intact</p> <p>Hyalgan Injection: Five intra-articular injections of 20 mg Hyalgan at 1-week intervals. Any joint effusion was aspirated prior to injection under aseptic conditions</p>
Outcomes	<p><b>Outcomes included in this review:</b></p> <p><i>Visual Analogue Scale (VAS)</i></p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Continuous outcome</li> <li>• <b>Reporting:</b> Fully reported</li> <li>• <b>Scale:</b> 0-10</li> <li>• <b>Direction:</b> Lower is better</li> <li>• <b>Data value:</b> End point</li> </ul> <p><i>Lequesne Index</i></p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Continuous outcome</li> <li>• <b>Reporting:</b> Fully reported</li> <li>• <b>Scale:</b> 0-24</li> <li>• <b>Direction:</b> Lower is better</li> <li>• <b>Data value:</b> End point</li> </ul> <p>Re-operation or conversion to TKR</p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Adverse event</li> <li>• <b>Reporting:</b> Fully reported</li> <li>• <b>Direction:</b> Lower is better</li> <li>• <b>Data value:</b> End point</li> </ul> <p><b>Other outcomes reported in the trial:</b></p> <ul style="list-style-type: none"> <li>• Knee Society function score</li> </ul>

Identification	<p><b>Sponsorship source:</b> No funding reported</p> <p><b>Country:</b> UK</p> <p><b>Setting:</b> Derbyshire Royal Infirmary, London Road, Derby, UK. Boston Pilgrim Hospital, Sibsey Road, Boston, Lincolnshire, UK</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> M. C. Forster</p> <p><b>Institution:</b> Glenfield Hospital, Leicester, UK</p> <p><b>Email:</b> mcfoster@doctors.org.uk</p> <p><b>Address:</b> 9 Lambourne Avenue, Ashbourne, Derbyshire DE6 1BP, UK</p> <p><b>Trial registration:</b> not reported</p>	
Notes	<ul style="list-style-type: none"> <li>• Serious adverse events and withdrawals from the study due to adverse events were not reported.</li> <li>• The Standard Deviation (SD) was not reported and could not be provided by the authors. As such, the SD was imputed from another study included in this review (<a href="#">Van der Woude 2017</a>).</li> <li>• Lequesne index (LI) was used to report functional outcomes. The SD was not reported and could not be provided by the authors. An SD could not be imputed from another study included in this review. As such, an SD was imputed using a peer-reviewed article that included patients with symptomatic knee osteoarthritis <a href="#">Faucher 2002</a>.</li> </ul>	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No comment regarding sequence generation
Allocation concealment (selection bias)	Unclear risk	Quote: "each patient was randomised by sealed envelope to receive either a course of Hyalgan injections or an arthroscopic washout." The study did not report if the envelopes were opaque, sequentially numbered, or kept from investigators
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement Comment: No blinding of participants or personnel to the intervention received
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Judgement Comment: Patient-reported outcomes were at high risk of bias as subjects were aware of the treatment they received
Blinding of outcome assessment (detection bias) Assessor-reported outcomes	Low risk	Knowledge of treatment allocation should not have influenced the interpretation of outcomes related to re-operation or conver-

**Forster 2003** (Continued)

		sion to TKR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Four patients moved during the study and were lost to follow-up (2 from the arthroscopy group and 2 from the Hyalgan group). Two patients randomised to the arthroscopy group declined surgery.”
Selective reporting (reporting bias)	Low risk	Judgement Comment: No trial protocol available. Acceptable outcomes including patient-reported pain and function
Other bias	High risk	Quote: “The pre-intervention function score was significantly worse in the arthroscopy group (Mann-Whitney test; P = 0.05).”

**Katz 2013**

Methods	<p><b>Study design:</b> Randomised controlled two-armed trial</p> <p><b>Study grouping:</b> Parallel group</p> <p><b>Interventions:</b> Arthroscopic partial meniscectomy versus physical therapy</p>
Participants	<p><b>Baseline Characteristics</b></p> <p>Arthroscopic partial meniscectomy</p> <ul style="list-style-type: none"> <li>● Mean Age (yrs): 59 (SD 7.9)</li> <li>● % Female: 55.9</li> <li>● KL grade 0: 21.1%</li> <li>● KL grade 1: 16.1%</li> <li>● KL grade 2: 23%</li> <li>● KL grade 3: 28%</li> <li>● BMI: 30 (SD 6.1)</li> <li>● Mental Health Index 5 Score: 74.8 (SD 12.9)</li> <li>● Race or ethnic group- White: 85.7%</li> <li>● Race or ethnic group- Black: 9.3%</li> <li>● Race or ethnic group- Hispanic: 1.2%</li> <li>● Race or ethnic group- Other: 3.7%</li> </ul> <p>Physical Therapy</p> <ul style="list-style-type: none"> <li>● Mean Age (yrs): 57.8 (SD 6.8)</li> <li>● % Female: 57.4</li> <li>● KL grade 0: 21.3</li> <li>● KL grade 1: 20.7</li> <li>● KL grade 2: 23.1</li> <li>● KL grade 3: 23.1</li> <li>● BMI: 30 (SD 6.1)</li> <li>● Mental Health Index 5 Score: 74.0 (SD 13.9)</li> <li>● Race or ethnic group- White: 84%</li> <li>● Race or ethnic group- Black: 10.1%</li> </ul>

	<ul style="list-style-type: none"> <li>● Race or ethnic group- Hispanic: 3%</li> <li>● Race or ethnic group- Other: 3%</li> </ul> <p><b>Number of participants:</b> Number screened = 14,430; number randomised = 351; number included in analysis = 320</p> <p><b>Inclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. Age 45 years or greater</li> <li>2. Symptoms for at least four weeks, managed with one or more of: medications, activity limitations or PT</li> <li>3. Symptoms consistent with torn meniscus (at least one of the following: clicking, catching, popping, giving way, pain with pivot or torque, pain that is episodic, pain that is acute and localised to one joint line)</li> <li>4. Availability of knee radiograph and MRI</li> <li>5. Evidence on knee MRI of osteophytes or full-thickness cartilage defect; or plain radiographic evidence of osteophytes or joint space narrowing</li> <li>6. Evidence on knee MRI of a meniscal tear that extends to the surface of the meniscus</li> <li>7. Willingness to undergo randomisation and ability to understand and sign an informed consent document</li> </ol> <p><b>Exclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. Chronically locked knee (e.g. patient cannot flex or extend the knee; a clear indication for APM)</li> <li>2. Kellgren-Lawrence grade 4</li> <li>3. Inflammatory arthritis or clinically symptomatic chondrocalcinosis</li> <li>4. Injection with visco supplementation in past four weeks in index knee</li> <li>5. Contraindication to surgery or physical therapy</li> <li>6. Bilateral symptomatic meniscal tear</li> <li>7. Prior surgery on index knee</li> </ol> <p><b>Pretreatment:</b> The two groups were similar with respect to age, sex, race or ethnic group, baseline Kellgren-Lawrence grade of radiographic severity, and baseline WOMAC physical-function score</p>
Interventions	<p><b>Intervention Characteristics</b></p> <p>Arthroscopic partial meniscectomy: Arthroscopic partial meniscectomy was performed by trimming the damaged meniscus back to a stable rim. Surgeons removed loose fragments of cartilage and bone, but did not penetrate the subchondral bone Postoperatively, participants were allowed to weight-bear, as able. Physical therapy was initiated using the same protocol as the control group</p> <p>Physical Therapy: Land-based, individualised physical therapy with progressive home exercise for patients with knee OA. Three-stage program was designed to address inflammation, range of motion, concentric and eccentric muscle strength, muscle-length restrictions, aerobic conditioning, functional mobility, proprioception, and balance. Generally, the program lasted 6 weeks</p> <p>The use of nonsteroidal anti-inflammatories, paracetamol, and intra-articular glucocorticoid injections was permitted in both groups over the course of the trial</p>
Outcomes	<p><b>Outcomes included in this review:</b></p> <p>WOMAC- Function</p> <ul style="list-style-type: none"> <li>● Outcome type: Continuous outcome</li> </ul>

	<ul style="list-style-type: none"> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-100</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p><i>KOOS - Pain</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-100</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p><i>Serious adverse events</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p>Re-operation or conversion to TKR</p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p>Withdrawals due to adverse events</p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p><b>Other outcomes reported in the trial:</b></p> <ul style="list-style-type: none"> <li>● Short Form Health Survey (SF-36): physical activity score</li> </ul>
<p>Identification</p>	<p><b>Sponsorship source:</b> Supported by grants (R01AR055557, K24AR057827, and P60AR047782) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health</p> <p><b>Country:</b> USA</p> <p><b>Setting:</b> Seven US tertiary referral centres.</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> J. N. Katz</p> <p><b>Institution:</b> Brigham and Women's Hospital</p> <p><b>Email:</b> jnkatz@partners.org</p> <p><b>Address:</b> Orthopedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham and Women's Hospital, 75 Francis St., BC-4016, Boston, MA 02115</p> <p><b>Trial registration:</b> ClinicalTrials.gov Identifier: NCT00597012</p>
<p>Notes</p>	<ul style="list-style-type: none"> <li>● Over the 12-month period of follow-up, serious adverse events occurred in 3 participants assigned to arthroscopic partial meniscectomy (fatal pulmonary embolism n = 1, myocardial infarction n = 1, hypoxaemia n = 1) and 2 participants assigned to physical therapy alone (sudden death n = 1, stroke n = 1)</li> </ul>
<p><i>Risk of bias</i></p>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were then randomly assigned in a 1:1 ratio to a treatment group with the use of a secure program on the trial website." Quote: "Randomization was conducted in blocks of varying size within each site, stratified according to sex and the extent of osteoarthritis on baseline radiography"
Allocation concealment (selection bias)	Low risk	Judgement Comment: Randomisation was performed by a research coordinator in real time using a secure website, thus ensuring concealment until the time of allocation to treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "After randomisation, the patient was informed about the treatment assignment; the surgeon was informed as part of the surgical booking process."
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Quote: "Surgeons, patients, and research staff were aware of the treatment assignments." As participants were aware of their treatment group, this may overestimate their measurement of self-reported outcomes
Blinding of outcome assessment (detection bias) Assessor-reported outcomes	Low risk	Knowledge of treatment allocation should not have influenced the interpretation of outcomes related to serious adverse events, re-operation, or conversion to TKR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small number of participants lost to follow-up
Selective reporting (reporting bias)	Low risk	Judgement Comment: Outcomes described in the trial protocol were reported
Other bias	High risk	"by 6 months of follow-up, 51 patients assigned to physical therapy alone (30.2%) had undergone surgery" demonstrating a high-rate of cross-over

Methods	<p><b>Study design:</b> Randomised controlled two-armed trial</p> <p><b>Study grouping:</b> Parallel group</p> <p><b>Interventions:</b> Arthroscopic surgery versus hyaluronic injections</p>
Participants	<p><b>Baseline Characteristics</b></p> <p>Overall</p> <ul style="list-style-type: none"> <li>• % Female: 81.7%</li> <li>• KL grade 2: 61.7%</li> <li>• KL grade 3: 38.3%</li> <li>• Age (40-45yrs): 18.33%</li> <li>• Age (45-50yrs): 20.83%</li> <li>• Age (56-60yrs): 26.66%</li> <li>• Age &gt; 60yrs: 34.16%</li> </ul> <p><b>Number of participants:</b> Number screened = not reported; number randomised = 120; number included in analysis = 120</p> <p><b>Inclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. History of knee pain</li> <li>2. &lt; 40 years of age</li> <li>3. K-L grade 2 &amp; 3</li> </ol> <p><b>Exclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. History of injury or accident</li> <li>2. Prior intervention like intra-articular steroid injections within three months</li> </ol> <p><b>Pretreatment:</b> None reported</p>
Interventions	<p><b>Intervention Characteristics</b></p> <p>Arthroscopic debridement: Arthroscopic debridement was performed using two portals under spinal anaesthesia. All debridements were performed by a single surgeon</p> <p>Hyaluronic acid injection: Intra-articular injections were given weekly for 5 weeks. Dose of injection not reported</p>
Outcomes	<p><b>Outcomes included in this review:</b></p> <p><i>Knee Society pain Score</i></p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Continuous outcome</li> <li>• <b>Reporting:</b> Partially reported</li> <li>• <b>Scale:</b> 0-50</li> <li>• <b>Direction:</b> Higher is better</li> <li>• <b>Data value:</b> End point</li> <li>• <b>Notes:</b> Data were not appropriately formatted. However, the number of individuals with each score was given and could be used to obtain a mean and standard deviation.</li> </ul> <p><i>Serious adverse events</i></p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Adverse event</li> <li>• <b>Reporting:</b> Fully reported</li> <li>• <b>Direction:</b> Lower is better</li> <li>• <b>Data value:</b> End point</li> </ul> <p>Withdrawals due to adverse events</p> <ul style="list-style-type: none"> <li>• <b>Outcome type:</b> Adverse event</li> <li>• <b>Reporting:</b> Fully reported</li> </ul>

	<ul style="list-style-type: none"> <li>• <b>Direction:</b> Lower is better</li> <li>• <b>Data value:</b> End point</li> </ul> <b>Other outcomes reported in the trial:</b> <ul style="list-style-type: none"> <li>• N/A</li> </ul>	
Identification	<p><b>Sponsorship source:</b> None reported</p> <p><b>Country:</b> India</p> <p><b>Setting:</b> Department of Orthopedic Surgery, Ch. Rehmat Ali Memorial Trust Hospital</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> Dr. Kamran Saeed</p> <p><b>Institution:</b> Department of Orthopaedic, Continental Medical College, Township, Lahore</p> <p><b>Email:</b> kamranortho@yahoo.com</p> <p><b>Address:</b> Punjab Government Employee's Cooperative Housing Society, College Road, Lahore</p> <p><b>Trial registration:</b> not reported</p>	
Notes	<ul style="list-style-type: none"> <li>• Quote: "No serious complication was seen in any of the case."</li> </ul>	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement Comment: No blinding of participants or personnel
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Judgement Comment: Patient-reported outcomes were at high risk of bias as patients were aware of the treatment they received
Blinding of outcome assessment (detection bias) Assessor-reported outcomes	Low risk	Knowledge of treatment allocation should not have influenced the interpretation of outcomes related to serious adverse events
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement Comment: No loss to follow-up over 6 months. No documented cross-over of patients from one treatment to the other

Selective reporting (reporting bias)	High risk	Judgement Comment: Knee Society pain score was the single outcome assessed. However, in the methodology, the authors discussed the use of the Knee Society score to assess range of motion, function, and stability. These were not included in the analyses. The authors mentioned that there were no serious complications but did not pre-define the complications they were looking for or explain how they assessed for them
Other bias	Low risk	No other source of bias identified

## Van der Woude 2017

Methods	<p><b>Study design:</b> Randomised controlled two-armed trial</p> <p><b>Study grouping:</b> Parallel group</p> <p><b>Interventions:</b> High tibial osteotomy versus knee joint distraction</p>
Participants	<p><b>Baseline Characteristics</b></p> <p>Knee joint distraction</p> <ul style="list-style-type: none"> <li>• Mean Age (yrs): 51.2 (SD 1.1)</li> <li>• % Female: 27%</li> <li>• KL grade 1: 28.6%</li> <li>• KL grade 2: 19%</li> <li>• KL grade 3: 52.4%</li> <li>• BMI: 27.5 (SD 0.7)</li> <li>• Tibiofemoral axis (degrees): 5.8 (SD 0.6)</li> </ul> <p>High Tibial Osteotomy</p> <ul style="list-style-type: none"> <li>• Mean Age (yrs): 49.4 (SD 1.0)</li> <li>• % Female: 40%</li> <li>• KL grade 1: 12.5%</li> <li>• KL grade 2: 30%</li> <li>• KL grade 3: 57.5%</li> <li>• BMI: 27.2 (SD 0.5)</li> <li>• Tibiofemoral axis (degrees): 6.2 (SD 0.3)</li> </ul> <p><b>Number of participants:</b> Number screened = not reported; number randomised = 69; number included in analysis = 62 (only those participants with KL1-3 included in this review)</p> <p><b>Inclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. Osteoarthritis of the medial compartment of the knee</li> <li>2. A tibiofemoral angle of less than 10° of varus</li> <li>3. Age &lt; 65years</li> <li>4. Intact knee ligaments</li> <li>5. Normal range of motion (minimum of 120° flexion)</li> <li>6. A body mass index (BMI) &lt; 35</li> </ol> <p><b>Exclusion criteria:</b></p> <ol style="list-style-type: none"> <li>1. Patients with contralateral knee OA needing treatment were excluded</li> </ol>

	<ol style="list-style-type: none"> <li>2. Those with primary patellofemoral OA</li> <li>3. Bi-compartmental OA</li> <li>4. A history of inflammatory or septic arthritis</li> <li>5. A (partial) lateral meniscectomy</li> <li>6. Inability to cope with an external fixator</li> <li>7. Complete joint space absence on X-ray</li> <li>8. Post-traumatic fibrosis due to a fracture of the tibial plateau</li> <li>9. Inability to undergo MRI examination</li> <li>10. Previous surgery on the same knee within the past 6 months</li> </ol> <p><b>Pretreatment:</b> Randomisation of 2:1 for HTO versus knee joint distraction was obligated by the medical ethics committee, considering knee joint distraction as an experimental treatment. No significant difference between the groups for key variables including: age, gender, BMI, KL grade, tibiofemoral angle, or laterality</p>
Interventions	<p><b>Intervention Characteristics</b></p> <p><b>Knee joint distraction:</b> Performed using an external distraction device. Two dynamic monotubes (Triax, Stryker, 45 kg spring with 2.5 mm displacement) were fixed in a standard fashion to bone pins. Intraoperatively, the tubes were distracted 2 mm. Post-operatively, the tubes were distracted by 1 mm per day until a total distraction of 5 mm was achieved. Patients were then allowed to fully weight-bear with crutches for stability. After 6 weeks (on average), the bone pins were removed. Patients were then instructed to partially weight-bear gradually increasing their weight-bearing to full weight-bearing at 6 weeks</p> <p><b>High Tibial Osteotomy:</b> Bi-plane medial-based opening-wedge osteotomy was performed, including a distal release of the superficial fibres of the medial collateral ligament. A TomoFix (Depuy Synthes, Switzerland) or Synthes locking compression plate (Depuy Synthes, Switzerland) were used for fixation. In all cases, the target correction was a weight-bearing axis of 62%. Three cases required bone graft to fill the gap. Partial weight-bearing was allowed for 6 weeks and then weight-bearing was progressed thereafter as able</p>
Outcomes	<p><b>Outcomes included in this review:</b></p> <p><i>Visual Analogue Scale (VAS): pain</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-100</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p><i>WOMAC- Function</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-100</li> <li>● <b>Data value:</b> End point</li> </ul> <p><i>EQ-5D</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> 0-1</li> <li>● <b>Direction:</b> Higher is better</li> <li>● <b>Data value:</b> End point</li> </ul>

	<p><i>Serious adverse events</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p>Re-operation or conversion to TKR</p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p>Withdrawals due to adverse events</p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Adverse event</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> End point</li> </ul> <p><b>Other outcomes included in the trial:</b></p> <ul style="list-style-type: none"> <li>● The intermittent and constant osteoarthritis pain score (ICOAP)</li> <li>● Visual analogue scale for pain (VAS)</li> <li>● Short Form 36 (SF-36) health survey</li> <li>● Knee flexion</li> </ul>	
Identification	<p><b>Sponsorship source:</b> This study was funded by ZonMw (The Netherlands Organisation for Health Research and Development)</p> <p><b>Country:</b> The Netherlands</p> <p><b>Setting:</b> Limb and Knee Reconstruction Unit, Maartenskliniek Woerden. Department of Orthopedics, UMC Utrecht, Utrecht</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> F. P. J. G. Lafeber</p> <p><b>Institution:</b> University Medical Center Utrecht</p> <p><b>Email:</b> f.lafeber@umcutrecht.nl</p> <p><b>Address:</b> Rheumatology and Clinical Immunology, University Medical Center Utrecht, F02.217, PO Box85500, 3508 GAUtrecht, The Netherlands</p> <p><b>Trial registration:</b> <a href="https://www.trialregister.nl/trial/2761">https://www.trialregister.nl/trial/2761</a></p>	
Notes	<ul style="list-style-type: none"> <li>● KL 0-4 included and corresponding author provided data on trial with KL4 (severe OA) excluded.</li> <li>● No participants in either group experienced a serious adverse event, a withdrawal due to an adverse event, a return to theatre or conversion to TKR.</li> </ul>	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Quote: "Randomization of 2:1 for HTO versus knee joint distraction was performed in blocks of six at each of the institutes using standard randomisation software. In order to minimize the number of knee joint distraction treatments, the medical ethics

		committee, considering knee joint distraction an experimental treatment, obligated this randomizations ratio.”
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement Comment: Participants and personnel were not blinded to the treatment received
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Judgement Comment: Patient-reported outcomes were at high risk of bias as patients were aware of the treatment they received
Blinding of outcome assessment (detection bias) Assessor-reported outcomes	Low risk	Judgement Comment: Risk of detection bias was low for assessor-reported outcomes as assessors were blinded to the treatment allocation when assessing radiographic structural progression. Knowledge of treatment allocation should not have influenced the interpretation of outcomes related to re-operation, conversion to TKR, or serious adverse events
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement Comment: No loss to follow-up at 1 year
Selective reporting (reporting bias)	Low risk	Judgement Comment: Acceptable outcomes reported. Trial protocol included a primary outcome based on cartilage changes on MRI; these results were expected 2 yrs postoperatively
Other bias	High risk	Quote: “Noteworthy is the difference in female gender between the HTO group and the knee joint distraction group (40% vs 27%). One could imagine that this relative difference influenced the outcome in the HTO group.”

AIMS: Arthritis Impact Measurement Scale

APM: Arthroscopic Partial Meniscectomy

BMI: Body Mass Index

HTO: High tibial Osteotomy

ICOAP: Intermittent and Constant Osteoarthritis Pain score

KL: Kellgren Lawrence

LI: Lequesne Index  
 MRI: Magnetic Resonance Imaging  
 N/A: Not applicable  
 OA: Osteoarthritis  
 PT: Physical Therapy  
 SD: Standard Deviation  
 SF-36: Short Form-36 (health survey)  
 TKR: Total Knee Replacement  
 VAS: Visual Analogous Scale  
 WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

### Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
<a href="#">Aae 2017</a>	This study included participants with articular cartilage defects but excluded participants with knee OA
<a href="#">Adeyemi 2017</a>	Not a randomised controlled trial
<a href="#">Adler 1970</a>	Included no surgical intervention
<a href="#">Akizuki 1997</a>	Not a randomised controlled trial
<a href="#">Alpayci 2011</a>	Included no surgical intervention
<a href="#">Alpayci 2013</a>	Included no surgical intervention
<a href="#">Arden 2008</a>	Included no surgical intervention
<a href="#">Aslan 2012</a>	Included no surgical intervention
<a href="#">Atay 2008</a>	Excluded as subjects were randomised to receive or not receive a non-surgical intervention after the surgical procedure had been performed
<a href="#">Benedetto 1993</a>	Not a randomised controlled trial
<a href="#">Besselink 2017</a>	Not a randomised controlled trial
<a href="#">Bisson 2017</a>	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
<a href="#">Bloembergen 2017</a>	Included subjects with no radiographic, arthroscopic or MRI description of OA
<a href="#">Bradley 2002</a>	Included no surgical intervention
<a href="#">Brittberg 2013</a>	Included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria

(Continued)

Brouwer 2005a	Not a randomised controlled trial
Brouwer 2006	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Börjesson 2005	Not a randomised controlled trial
Campbell 2010	Not a randomised controlled trial
Cho 2013	Not a randomised controlled trial
Collins 2017	Not a randomised controlled trial
Dallari 2007	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Dawes 1987	Included no surgical intervention
Duif 2015	Included subjects with severe osteoarthritis
Duivenvoorden 2014	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Duivenvoorden 2014a	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Ferruzzi 2012	Included subjects with severe osteoarthritis
Ferruzzi 2014	Not a randomised controlled trial
Freitag 2015	The protocol for a trial which was terminated early due to recruitment difficulties
Frias 2004	Included no surgical intervention
Frias 2009	Included no surgical intervention
Fu 2015	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Gaasbeek 2010	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Gauffin 2014	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Gauffin 2017	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received

(Continued)

Gouin 2010	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Gudas 2002	Not a randomised controlled trial
Gudas 2012	This study included participants with articular cartilage defects but excluded participants with knee OA
Han 2010	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Hede 1992	Included subjects with no radiographic, arthroscopic or MRI description of OA
Heir 2013	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Hempfling 2007	Included subjects with severe osteoarthritis
Herrlin 2007	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Herrlin 2013	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Hiemstra 2012	Excluded as subjects were randomised to receive or not receive a non-surgical intervention after the surgical procedure had been performed
Hubbard 1996	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Huizinga 2014	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Jarvinen 2014	This study included participants with degenerate meniscal tears but excluded participants with knee OA
Jung 2014	Excluded as subjects were randomised to receive or not receive a non-surgical intervention after the surgical procedure had been performed
Kalunian 2000	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Kang 2005	This study did not include symptoms as part of their inclusion criteria
Kim 2017	This study did not include symptoms as part of their inclusion criteria

(Continued)

Kirkley 2008	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Knutsen 2004	This study included participants with articular cartilage defects but excluded participants with knee OA
Knutsen 2007	This study included participants with articular cartilage defects but excluded participants with knee OA
Kulshrestha 2016	Included subjects with severe osteoarthritis
Lee 2013	Included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria
Linke 2007	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Liu 2004	Included subjects with severe osteoarthritis
Luchikhina 2014	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Luites 2009	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Magyar 1999	Included subjects with severe osteoarthritis
Marmotti 2013	Not a randomised controlled trial
Marsh 2016	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Merchan 1993	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Moseley 1996	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Moseley 2002	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Myrnerets 1980	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Nakamura 2001	None of the review's outcomes were measured.
Narkbunnam 2012	This study was excluded as it did not define the severity of radiographic OA within their included subjects

(Continued)

Nerhus 2017a	None of the review's outcomes were measured.
Nerhus 2017b	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Osman 2014	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Osteras 2011	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Ou 2008	Included subjects with no radiographic evidence of knee osteoarthritis
Parmigiani 2010	Included no surgical intervention
Pascale 2011	Included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria
Ravaud 1999	Included no surgical intervention
Raynauld 2002	Included no surgical intervention
Rodkey 2009	Included subjects with no radiographic, arthroscopic or MRI description of OA
Rodkey 2009a	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Roos 2018	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
Russell 2003	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Saris 2008	Included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria
Schultz 1999	Not a randomised controlled trial
Shaofei 2017	This study did not include symptoms as part of their inclusion criteria
Shive 2015	Included subjects with full thickness cartilage defects which were too large to meet our inclusion criteria
Sihvonen 2013	Did not include participants with osteoarthritis
Smith 2003	This study was excluded as it did not define the severity of radiographic OA within their included subjects
Smith 2018	This study was excluded as it did not define the severity of radiographic OA within their included subjects

(Continued)

<a href="#">Spahn 2010</a>	This study included participants with articular cartilage defects but excluded participants with knee OA
<a href="#">Spahn 2016</a>	This study included participants with articular cartilage defects but excluded participants with knee OA
<a href="#">Stensrud 2015</a>	Included subjects with no radiographic, arthroscopic or MRI description of OA
<a href="#">Stukenborg Colsman 2001</a>	All grades of OA included. Authors were contacted to provide an amended dataset including only those participants relevant to the study. No response was received
<a href="#">Van Egmond 2016</a>	Not a randomised controlled trial
<a href="#">Van Oosterhout 2006</a>	This study included subjects with inflammatory arthropathy only
<a href="#">Vermesan 2013</a>	This study was excluded as it did not define the severity of radiographic OA within their included subjects
<a href="#">Volz 2017</a>	This study included participants with articular cartilage defects but excluded participants with knee OA
<a href="#">Ward 1998</a>	Included subjects with severe osteoarthritis
<a href="#">Yim 2013</a>	Included subjects with no radiographic evidence of knee osteoarthritis
<a href="#">Zhang 2018</a>	This study was excluded as it did not define the severity of radiographic OA within their included subjects
<a href="#">Zhao 2018</a>	Not a randomised controlled trial
<a href="#">Zorzi 2011</a>	Included subjects with severe osteoarthritis

MRI: Magnetic Resonance Imaging

OA: Osteoarthritis

### Characteristics of ongoing studies [ordered by study ID]

#### [NCT02003976](#)

Trial name or title	A Randomized Trial Comparing High Tibial Osteotomy Plus Non-Surgical Treatment and Non-Surgical Treatment Alone
Methods	<b>Study design:</b> Randomized controlled trial <b>Study grouping:</b> Parallel group

Participants	<p><b>Inclusion Criteria:</b></p> <ol style="list-style-type: none"> <li>1. Is the subject either:25-55 years old?Older than 55 but still active (ex. physical labour, regular recreational activities)?</li> <li>2. Does this subject present with varus alignment? (Based on hip to ankle x-rays).</li> <li>3. Does this subject have clinical Knee OA? (MAA &lt;-2° on full limb standing AP) according to the Altman classification primarily involving the medial compartment of the knee?</li> <li>4. Patient is a good candidate for high tibial osteotomy and will be receiving a PEEK plate, or if receiving an alternate plate, agrees to have the plate removed prior to 1 year postoperative.</li> </ol> <p><b>Exclusion Criteria:</b></p> <ol style="list-style-type: none"> <li>1. Has this subject had a previous HTO or joint replacement in either limb?</li> <li>2. Is this subject likely to undergo bilateral HTO within the 2 year follow up period?</li> <li>3. Does this subject have an unstable knee or ligament?</li> <li>4. Does this subject have inflammatory or infectious arthritis of the knee?</li> <li>5. Radiographic disease too advanced for HTO (i.e., diffuse lateral compartment, patellofemoral joint OA and/or severe enough disease to suggest that joint replacement is the better surgical option) and/or Kellgren and Lawrence grade 4.</li> <li>6. The subject's disease is not advanced enough (symptomatically or radiographically) to warrant HTO.</li> <li>7. Does this subject have a major medical illness with life expectancy &lt;2 years or with an unacceptably high operative risk?</li> <li>8. Does this subject have a major neurological deficit that would affect gait?</li> <li>9. Is this subject possibly pregnant or planning pregnancy?</li> <li>10. Is this subject unable to read English?</li> <li>11. Does this subject have a psychiatric illness that limits informed consent?</li> <li>12. Is the subject unlikely to comply with study protocol?</li> </ol>
Interventions	<p>Medial Opening Wedge High Tibial Osteotomy (HTO) Non-Surgical Treatment Program</p>
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> <li>• MRI articular cartilage morphology [ Time Frame: Change from baseline to 24 months post operative ]3 Tesla MRI measure of medial tibiofemoral articular cartilage thickness</li> </ul> <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> <li>• Knee Injury and Osteoarthritis Outcome Score (KOOS) [ Time Frame: Change from baseline to 24 months post operative ]5 subdomains: pain, symptoms, activities of daily living, sport and recreation, quality of life</li> <li>• Western Ontario Meniscal Evaluation Tool (WOMET) [ Time Frame: Change from baseline to 24 months post operative ]</li> <li>• Biological Markers of Disease Progression [ Time Frame: Baseline, 12 and 24 months post operative ]Synovial fluid, serum and urine biological markers</li> <li>• Numeric Rating Scale for Pain [ Time Frame: Baseline, 12 and 24 months post operative ]0 (no pain) - 10 (worst possible pain)</li> <li>• Gait Biomechanics [ Time Frame: Baseline, 12 and 24 months post operative ]Knee frontal, sagittal and transverse plane kinematics and kinetics tested during level walking in a motion analysis laboratory. The measure of most interest is the peak external knee adduction moment during stance phase of walking, expressed in %BW*Ht.</li> <li>• Isometric Strength Testing [ Time Frame: Baseline, 12 and 24 months post operative ]Isometric quadriceps and hamstrings strength tested using an isokinetic dynamometer.</li> <li>• Intermittent and Constant Osteoarthritis Pain Index (ICOAP) [ Time Frame: Change from baseline to</li> </ul>

**NCT02003976** (Continued)

	24 months post operative ] <ul style="list-style-type: none"><li>• Short-Form 12 (SF12) [ Time Frame: Change from baseline to 24 months post operative ]</li><li>• Western Ontario and McMaster Universities Arthritis Index (WOMAC) [ Time Frame: Change from baseline to 24 months post operative ]3 sub domains: pain, symptoms, function</li></ul>
Starting date	September 2014
Contact information	Fowler Kennedy Sport Medicine Clinic, Western University London, Ontario, Canada, N6A 3K7 <a href="mailto:alorber2@uwo.ca">alorber2@uwo.ca</a>
Notes	Estimated Study Completion Date: July 2019

*AP:Anterior Posterior*

HTO: High Tibial Osteotomy

ICOAP: Intermittent and Constant Osteoarthritis Pain score

KOOS: Knee Injury and Osteoarthritis Outcome Score

MAA: Mechanical Axis Alignment

MRI: Magnetic Resonance Imaging

OA: Osteoarthritis

PEEK: all polyetheretherketone

SF12: Short form 12 (health survey)

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

WOMET: Western Ontario Meniscal Evaluation Tool

## DATA AND ANALYSES

### Comparison 1. Surgical intervention vs non-surgical intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Early (up to 1 year)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Function	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Adverse events	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
3.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Re-operation rate or TKR (6-12 months)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
4.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Withdrawals due to adverse events (6-12 months)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
5.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

### Comparison 2. Surgical intervention vs injectable therapy (saline irrigation)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Early (up to 1 year)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Function	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Quality of life	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

### Comparison 3. Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Early (up to 1 year)	2	152	Std. Mean Difference (IV, Random, 95% CI)	0.51 [-0.39, 1.41]
2 Function	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Adverse events	1		Risk Difference (M-H, Fixed, 95% CI)	Totals not selected
3.1 Early (up to 1 year)	1		Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Re-operation rate or TKR (6-12 months)	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected

4.1 Early (up to 1 year)	1	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Withdrawals due to adverse events (6-12 months)	1	Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
5.1 Early (up to 1 year)	1	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

#### Comparison 4. Surgical intervention vs ANY other surgical intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Function	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Structural progression	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Quality of life	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Early (up to 1 year)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Adverse events	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
5.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Re-operation rate or TKR (6-12 months)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
6.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Withdrawals due to adverse events (6-12 months)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
7.1 Early (up to 1 year)	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

#### Analysis 1.1. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 1 Pain.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 1 Surgical intervention vs non-surgical intervention

Outcome: 1 Pain



### Analysis 1.2. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 2 Function.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 1 Surgical intervention vs non-surgical intervention

Outcome: 2 Function

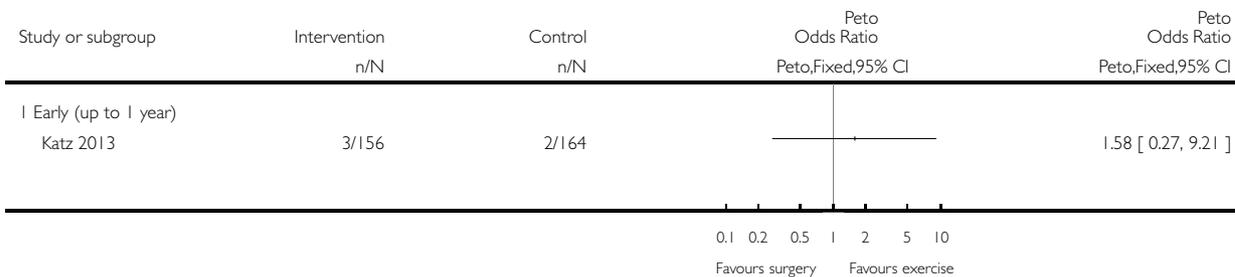


### Analysis 1.3. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 3 Adverse events.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 1 Surgical intervention vs non-surgical intervention

Outcome: 3 Adverse events

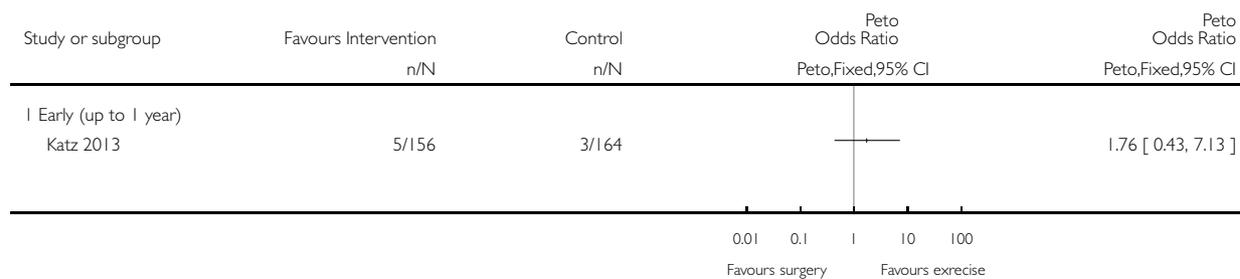


**Analysis 1.4. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 4 Re-operation rate or TKR (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 1 Surgical intervention vs non-surgical intervention

Outcome: 4 Re-operation rate or TKR (6-12 months)



**Analysis 1.5. Comparison 1 Surgical intervention vs non-surgical intervention, Outcome 5 Withdrawals due to adverse events (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 1 Surgical intervention vs non-surgical intervention

Outcome: 5 Withdrawals due to adverse events (6-12 months)

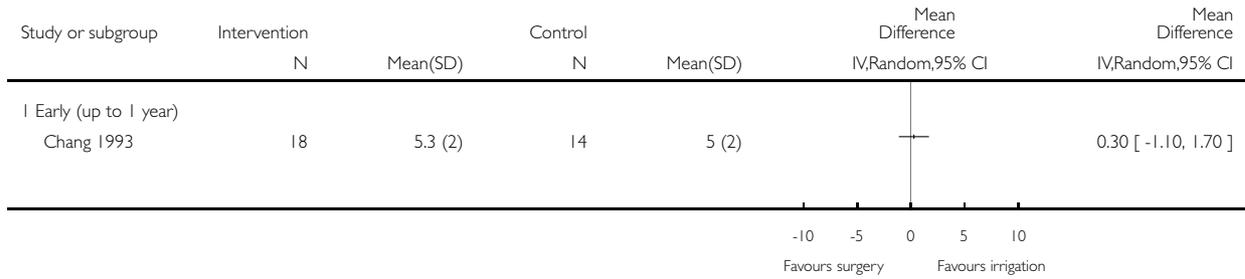


### Analysis 2.1. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 1 Pain.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 2 Surgical intervention vs injectable therapy (saline irrigation)

Outcome: 1 Pain

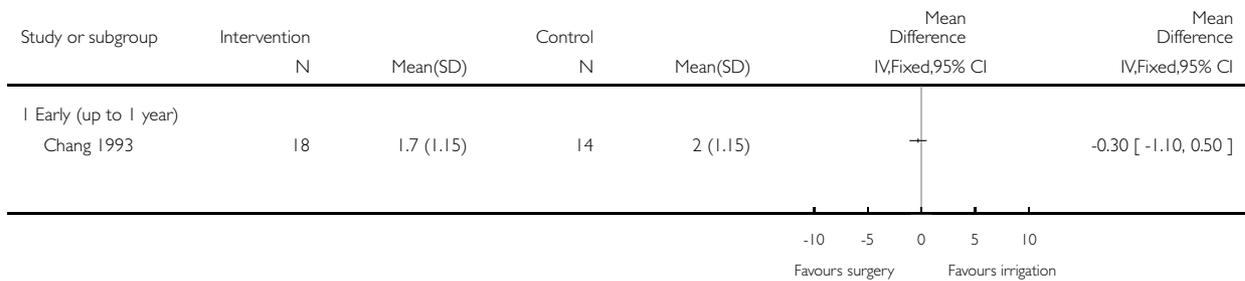


### Analysis 2.2. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 2 Function.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 2 Surgical intervention vs injectable therapy (saline irrigation)

Outcome: 2 Function

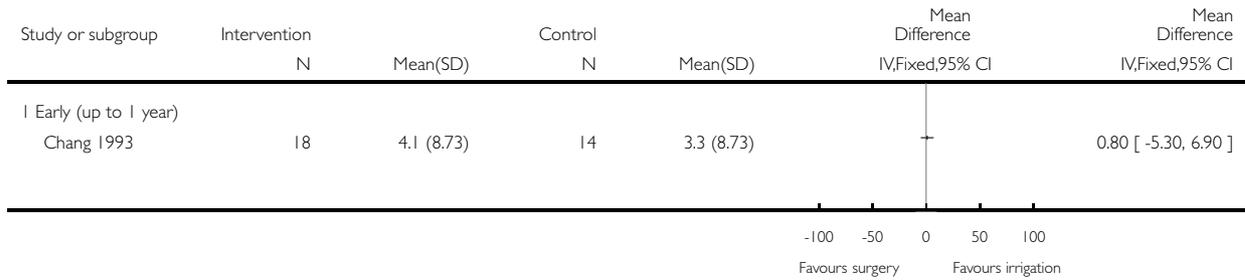


### Analysis 2.3. Comparison 2 Surgical intervention vs injectable therapy (saline irrigation), Outcome 3 Quality of life.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 2 Surgical intervention vs injectable therapy (saline irrigation)

Outcome: 3 Quality of life

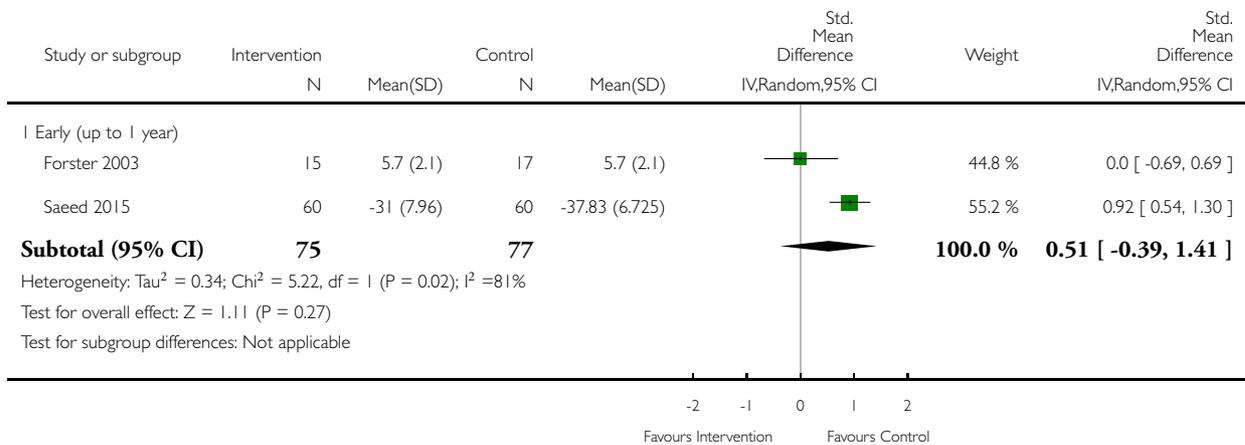


### Analysis 3.1. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 1 Pain.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 3 Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome: 1 Pain



### Analysis 3.2. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 2 Function.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 3 Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome: 2 Function

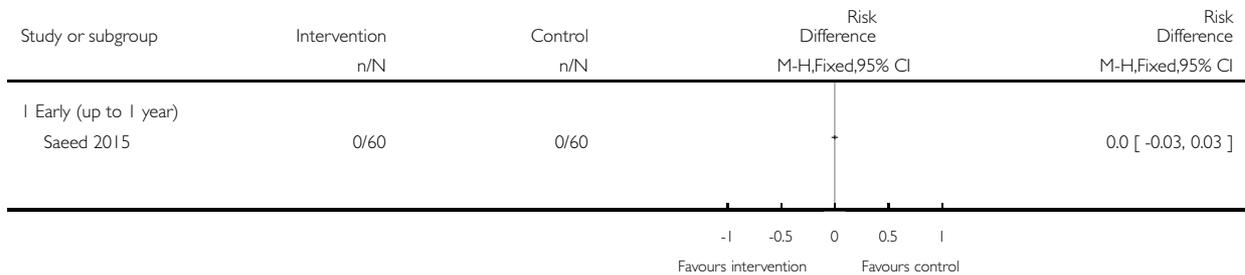


### Analysis 3.3. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 3 Adverse events.

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 3 Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome: 3 Adverse events

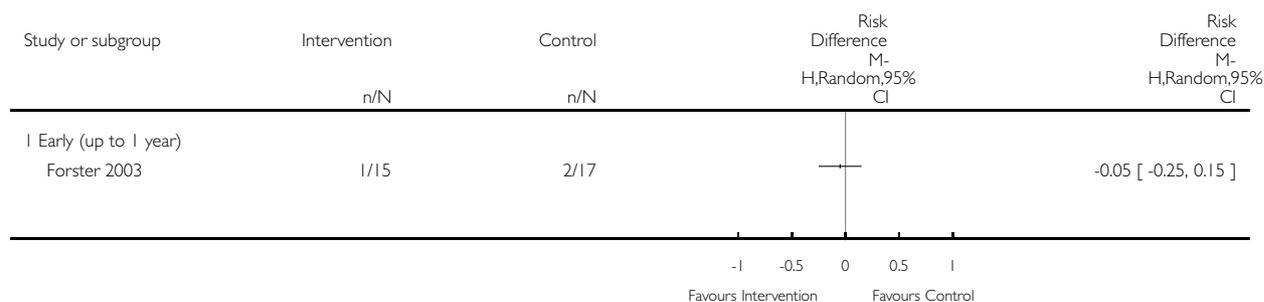


**Analysis 3.4. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 4 Re-operation rate or TKR (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 3 Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome: 4 Re-operation rate or TKR (6-12 months)

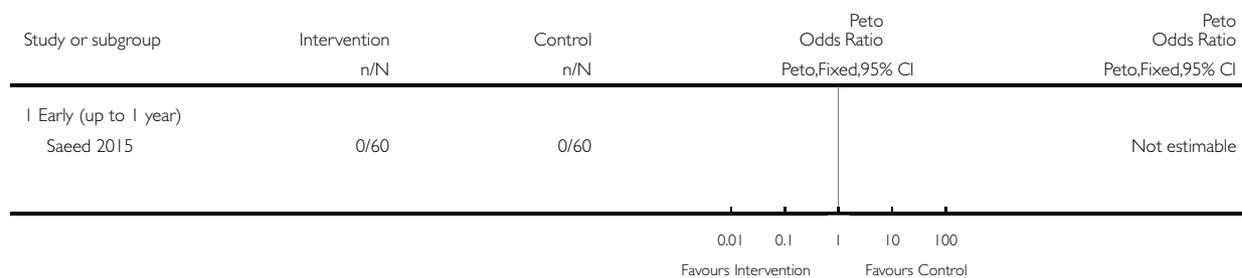


**Analysis 3.5. Comparison 3 Surgical intervention vs injectable therapy (hyaluronic acid), Outcome 5 Withdrawals due to adverse events (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 3 Surgical intervention vs injectable therapy (hyaluronic acid)

Outcome: 5 Withdrawals due to adverse events (6-12 months)

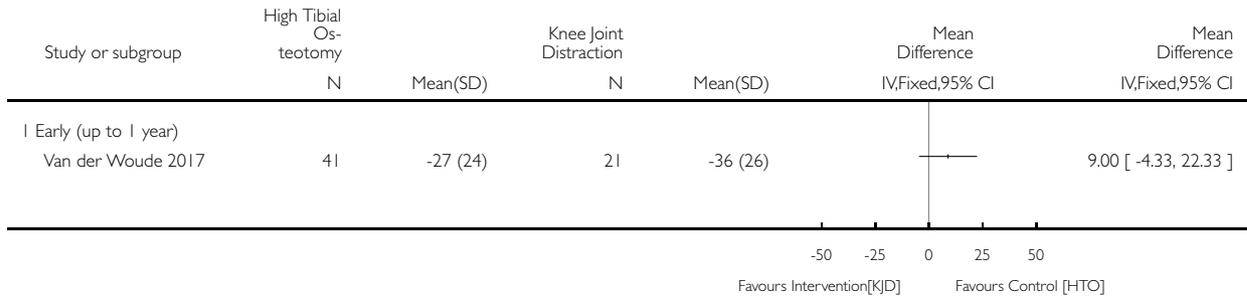


**Analysis 4.1. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 1 Pain.**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 1 Pain

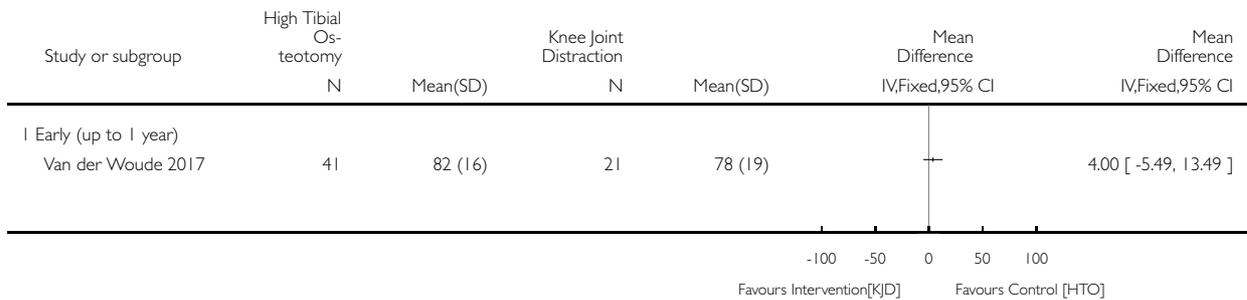


**Analysis 4.2. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 2 Function.**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 2 Function

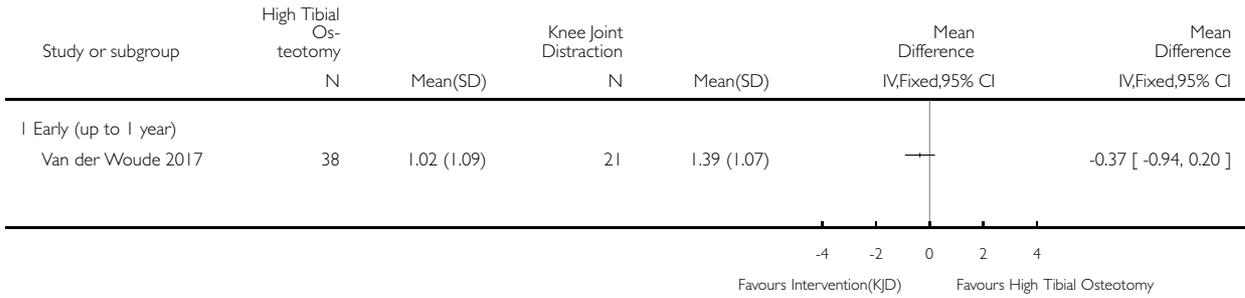


**Analysis 4.3. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 3 Structural progression.**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 3 Structural progression

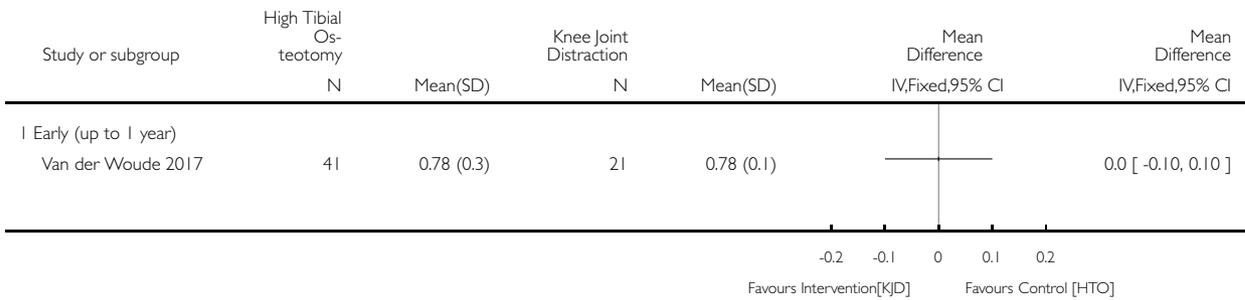


**Analysis 4.4. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 4 Quality of life.**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 4 Quality of life

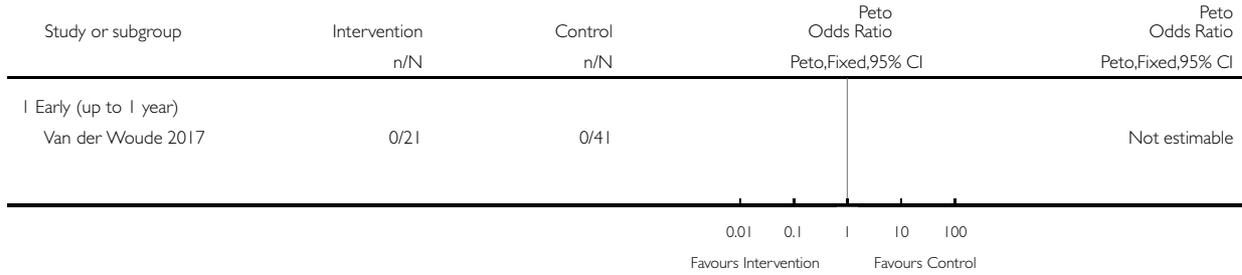


**Analysis 4.5. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 5 Adverse events.**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 5 Adverse events

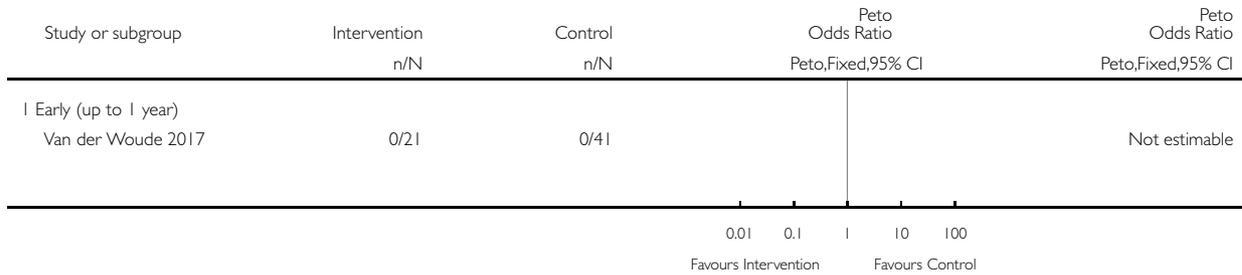


**Analysis 4.6. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 6 Re-operation rate or TKR (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 6 Re-operation rate or TKR (6-12 months)

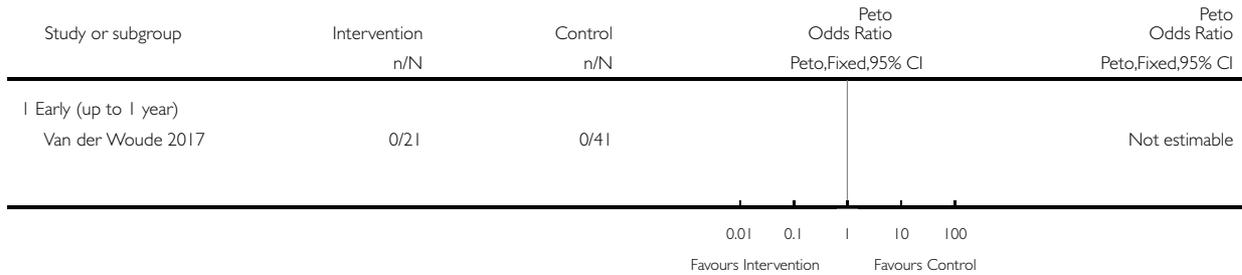


**Analysis 4.7. Comparison 4 Surgical intervention vs ANY other surgical intervention, Outcome 7 Withdrawals due to adverse events (6-12 months).**

Review: Surgical interventions for symptomatic mild to moderate knee osteoarthritis

Comparison: 4 Surgical intervention vs ANY other surgical intervention

Outcome: 7 Withdrawals due to adverse events (6-12 months)



## APPENDICES

### Appendix I. MEDLINE search strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1974 to Present> -----

- 
- 1 exp osteoarthritis/
  - 2 osteoarthr\$.tw.
  - 3 (degenerative adj2 arthritis).tw.
  - 4 arthrosis.tw.
  - 5 or/1-4
  - 6 exp Surgical Procedures, Operative/
  - 7 exp surgery/
  - 8 su.fs.
  - 9 (surgery\$ or surgeries or surgical or operat\$).tw.
  - 10 (arthroplast\$ or hemiarthroplast\$ or (joint\$ adj2 replace\$)).tw.
  - 11 Debridement/
  - 12 debride\$.tw.
  - 13 repair\$.tw.
  - 14 (surface\$ adj replace\$).tw.
  - 15 resurfac\$.tw.
  - 16 arthroscop\$.tw.
  - 17 (needle\$ adj4 debridement).tw.
  - 18 (needle\$ adj4 irrigation).tw.
  - 19 (needle\$ adj4 lavage).tw.
  - 20 (needle\$ adj4 washout).tw.

21 (Joint adj4 lavage).tw.  
 22 Meniscectomy.tw.  
 23 Chondroplast\$.tw.  
 24 gonarthrosis\$.tw.  
 25 osteotom\$.tw.  
 26 (device adj4 knee).tw.  
 27 knee prosthesis.mp. [mesh]  
 28 (knee\* and (arthroplast\* or implant\* or replace\* or prosth\* or endoprosthe\*)).tw.  
 29 or/6-28  
 30 randomized controlled trial.pt.  
 31 controlled clinical trial.pt.  
 32 randomized.ab.  
 33 placebo.ab.  
 34 drug therapy.fs.  
 35 randomly.ab.  
 36 trial.ab.  
 37 groups.ab.  
 38 or/30-37  
 39 (animals not (humans and animals)).sh.  
 40 38 not 39  
 41 5 and 29 and 40

## Appendix 2. Embase search strategy

Database: Embase <1974 to 2018 May 24>

-----  
 1 exp osteoarthritis/  
 2 osteoarthr\$.tw.  
 3 (degenerative adj2 arthritis).tw.  
 4 arthrosis.tw.  
 5 or/1-4  
 6 exp surgery/  
 7 su.fs.  
 8 (surgery\$ or surgeries or surgical or operat\$).tw.  
 9 (arthroplast\$ or hemiarthroplast\$ or (joint\$ adj2 replace\$)).tw.  
 10 Debridement/  
 11 debride\$.tw.  
 12 repair\$.tw.  
 13 (surface\$ adj replace\$).tw.  
 14 resurfac\$.tw.  
 15 arthroscop\$.tw.  
 16 (needle\$ adj4 debridement).tw.  
 17 (needle\$ adj4 irrigation).tw.  
 18 (needle\$ adj4 lavage).tw.  
 19 (needle\$ adj4 washout).tw.  
 20 (Joint adj4 lavage).tw.  
 21 Meniscectomy.tw.  
 22 Chondroplast\$.tw.  
 23 gonarthrosis\$.tw.  
 24 osteotom\$.tw.  
 25 (device adj4 knee).tw.  
 26 knee prosthesis/

27 (knee\* and (arthroplast\* or implant\* or replace\* or prosth\* or endoprosth\*)).tw.  
 28 or/6-27  
 29 random\$.tw.  
 30 factorial\$.tw.  
 31 crossover\$.tw.  
 32 cross over.tw.  
 33 cross-over.tw.  
 34 placebo\$.tw.  
 35 (doubl\$ adj blind\$).tw.  
 36 (singl\$ adj blind\$).tw.  
 37 assign\$.tw.  
 38 allocat\$.tw.  
 39 volunteer\$.tw.  
 40 crossover procedure/  
 41 double blind procedure/  
 42 randomized controlled trial/  
 43 single blind procedure/  
 44 or/29-43  
 45 5 and 28 and 44

### Appendix 3. Cochrane Library search strategy

Cochrane Library

Date Run: 24/05/18

1 MeSH descriptor: [Osteoarthritis] explode all trees  
 2 osteoarthr\*  
 3 (degenerative near/2 arthritis)  
 4 arthrosis  
 5 #1 or #2 or #3 or #4  
 6 MeSH descriptor: [Surgical Procedures, Operative] explode all trees  
 7 MeSH descriptor: [General Surgery] explode all trees  
 8 Any MeSH descriptor with qualifier(s): [Surgery - SU]  
 9 (surgery\* or surgeries or surgical or operat\*)  
 10 (arthroplast\* or hemiarthroplast\* or (joint\* and replace\*))  
 11 Debridement  
 12 debride\*  
 13 repair\*  
 14 (surface\* and replace\*)  
 15 resurfac\*  
 16 arthroscop\*  
 17 (needle\* near/4 debridement)  
 18 (needle\* near/4 irrigation)  
 19 (needle\* near/4 lavage)  
 20 (needle\* near/4 washout)  
 21 Joint near/4 lavage  
 22 Meniscectomy  
 23 Chondroplast\*  
 24 gonarthrosis\*  
 25 osteotom\*  
 26 (device near/4 knee)  
 27 MeSH descriptor: [Knee Prosthesis] explode all trees  
 28 knee\* and (arthroplast\* or implant\* or replace\* or prosth\* or endoprosth\*)

29 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28  
30 #5 and #29

## **CONTRIBUTIONS OF AUTHORS**

Jonathan S Palmer: lead author, writing of manuscript, co-ordination of team

A Paul Monk: development of review

Sally Hopewell: development of review and statistical expertise

Lee E Bayliss: statistical expertise

William Jackson: clinical expertise

David J Beard: methodological expertise

Andrew J Price: clinical expertise and protocol development

## **DECLARATIONS OF INTEREST**

Jonathan S Palmer: none known

A Paul Monk: none known

Sally Hopewell: none known

Lee E Bayliss: none known

William Jackson: He is a specialist knee surgeon working for Oxford University NHS Trust. He is involved in treating patients with early knee arthritis. He lectures to surgeons on all aspects of knee surgery and is involved in developing new procedures and techniques to improve treatments for patients with knee conditions; as part of it, his institution got a patent for instrumentation to perform knee replacements and applied for a patent for an HTO system. He got payments from Biomet and Depuy J&J (medical devices companies) for lectures and holds stocks of Smith and Nephew PLC, a medical device company.

David J Beard: none known

Andrew J Price: none known

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## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The title of the review was changed from “Surgical interventions for early structural knee osteoarthritis” to “Surgical interventions for symptomatic mild to moderate knee osteoarthritis”. This title better reflects the inclusion criteria for the review.