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Interventions for treating fractures of the distal femur in adults (Review)

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[Intervention Review]

Interventions for treating fractures of the distal femur in adults

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ABSTRACT

Background

Fractures of the distal femur (the far end of the thigh bone just above the knee) are a considerable cause of morbidity. Various different surgical and non-surgical treatments have been used in the management of these injuries but the best treatment remains unknown.

Objectives

To evaluate the benefits and harms of interventions for treating fractures of the distal femur in adults.

Search methods

We used standard, extensive Cochrane search methods. The latest search date was October 2021.

Selection criteria

We included randomised and quasi-randomised controlled trials in adults comparing interventions for treating fractures of the distal femur. Interventions included surgical implants (retrograde intramedullary nail (RIMN), fixed-angle devices, non-locking plate fixation, locking plate, internal fixation, distal femoral replacement, mono-axial plates, poly-axial plates and condylar buttress plates) and non-surgical management.

Data collection and analysis

We used standard Cochrane methods. Our critical outcomes were validated patient-reported outcome measures (PROMs), direct adverse events, participant-reported quality of life (QoL) and pain scores. Our other important outcomes were adverse events indirectly related to intervention, symptomatic non-union, malunion and resource use. We used GRADE to assess certainty of evidence for each outcome.

Main results

We included 14 studies with 753 participants: 13 studies compared different surgical interventions, and one study compared surgical with non-surgical management. Here, we report the effects for RIMN compared with locking plates. Three studies (221 participants) reported this comparison; it included the largest study population and these are the two most commonly used devices in contemporary orthopaedic trauma practice.

Studies used three different tools to assess PROMs. We found very-low certainty evidence for lower Disability Rating Index scores after RIMN at short-term follow-up favouring RIMN (mean difference (MD) −21.90, 95% confidence interval (CI) −38.16 to −5.64; 1 study, 12 participants) and low-certainty evidence of little or no difference at long-term follow-up (standardised mean difference (SMD) −0.22, 95% CI −0.50 to

0.06; 2 studies, 198 participants). Re-expressing the SMD of the long-term follow-up data to Knee Society Score (KSS) used by one study found no clinical benefit of RIMN, based on a minimal clinically important difference of 9 points (MD 2.47, 95% CI −6.18 to 0.74). The effect on QoL was very uncertain at four months (MD 0.01, 95% CI −0.42 to 0.44; 1 study, 14 participants) and one year (MD 0.10, 95% CI −0.01 to 0.21; 1 study, 156 participants); this evidence was very low certainty.

For direct adverse events, studies reported reoperation, loss of fixation, superficial and deep infection, haematoma formation and implant loosening. Effects for all events were imprecise with the possibility of benefit or harm for both treatments. We considered reoperation the most clinically relevant. There was very low-certainty evidence of little or no difference in reoperation between the two implants (risk ratio (RR) 1.48, 95% CI 0.55 to 4.00; 1 study, 104 participants).

No studies reported pain.

For other important outcomes, we noted that people treated with RIMN may be more likely to have varus/valgus deformity (RR 2.18, 95% CI 1.09 to 4.37; 1 study, 33 participants; low-certainty evidence). However, we found no evidence of any important differences between treatments in terms of bony union, indirect adverse events, or resource use.

Other comparisons of surgical interventions included in the review were: RIMN versus single fixed-angle device (3 studies, 175 participants); RIMN versus non-locking plate fixation (1 study, 18 participants); locking plate versus single fixed-angle device (2 studies, 130 participants); internal fixation versus distal femoral replacement (1 study, 23 participants); mono-axial plates versus poly-axial plates (2 studies, 67 participants); mono-axial plate versus condylar buttress plate (1 study, 78 participants). The certainty of the evidence for outcomes in these comparisons was low to very low, and most effect estimates were imprecise.

Authors' conclusions

This review highlights the major limitations of the available evidence concerning current treatment interventions for fractures of the distal femur. The currently available evidence is incomplete and insufficient to inform clinical practice. Priority should be given to randomised controlled trials comparing contemporary treatments for people with fractures of the distal femur. At a minimum, these should report validated patient-reported functional and quality-of-life outcomes at one and two years, with an agreed core outcome set. All trials should be reported in full using the CONSORT guidelines.

PLAIN LANGUAGE SUMMARY

Treatments for breaks in the lower part of the thigh bone in adults

Key messages

For treating people with broken lower thigh bones (distal femur), we think the best comparison is a metal rod placed within the thigh bone versus a metal plate placed on the outside of the bone and fixed with screws, but other methods are used. We are uncertain which treatment is superior, but there is some evidence to suggest the rod decreases disability.

Uncertainty remains around which metal implant is best for broken bones at the lower end of the thigh bone.

Further studies are required to compare commonly used operations.

Why is treating a broken distal femur important?

Breaks (fractures) of the lower part of the thigh bone (distal femur) are debilitating and painful injuries. The reduced mobility after these injuries is also an important cause of ill-health. Sometimes these fractures happen in people who have previously had a knee replacement; this can make treatment of the fracture more complicated.

What are the options to treat a broken distal femur?

Many treatments have been used in the management of these injuries. Historically, people were treated in bed with weights holding the leg straight. More recently, surgery has been used to fix the broken femur using metal implants (surgical fixation). Methods of surgical fixation include using plates and screws on the outside the femur or rods inside the femur to hold the fracture in place while it heals. The technology of these implants has become increasingly advanced with components that 'lock' together, forming a 'locked' device. Despite these advances, the best management of these injuries remains controversial.

What did we want to find out?

We want to find out the effects of different methods for treating fractures of the lower femur in adults. Effects included: function scores, pain, quality of life (QoL) and any complications that arose as a result of the management method.

What did we do?

We searched the scientific literature for randomised controlled trials (RCTs) (studies where patients are randomly assigned a treatment group) and quasi-RCTs (where patients are assigned a treatment group with no randomisation), published up to October 2021.

We summarised each study's results, assessing our confidence in the evidence based upon the study's methods and size.

What did we find?

We found 14 relevant studies with 753 participants with these fractures. Thirteen studies compared different surgical implants and one study compared surgery with non-surgical treatment.

Key results

Rods down the thigh versus a plate that locks (three studies, 221 participants): we are uncertain of any differences in function or QoL. There is no evidence to suggest any differences in complications.

Rods within thigh bone versus a plate that is fixed (three studies, 175 participants): we are uncertain of any differences in QoL between these two methods. We are uncertain of any differences in complications.

Rods within thigh bone versus a plate that does not lock (one study, 18 participants): we found no evidence of any differences in complications between these two methods. We did not have any data for QoL or pain.

A plate that locks versus a plate that is fixed (two studies, 130 participants): we found no evidence of fewer complications in plates that are fixed compared with a plate that locks. We did not have any data for QoL or pain.

Any surgical fixation versus a rod within thigh bone (one study, 23 participants): there were limited data available for our analysis, but there is no evidence to suggest any differences in complications between these two methods.

Comparing two different types of metal plate (two studies, 67 participants): at six months there is evidence to suggest improved patient outcome scores with a specific plate called a mono-axial plate, but this improvement was not shown at 12 months. When using x-rays to assess the function of the plates, there was evidence to suggest better x-rays with a plate called a poly-axial plate. There was no evidence to suggest differences in adverse events.

Comparing two different types of metal plates (one study, 78 participants): we are uncertain of an improved patient-reported score in a mono-axial plate compared with a condylar buttress plate.

Surgical versus non-surgical management (one study, 42 participants): there are few data reported for this comparison. However, there were more complications such as pressures sores due to the long duration of not moving associated with the non-surgical group, who stayed on average one month longer in hospital.

Main limitations of the study

Each of the studies was small and designed in a way that may affect the reliability of their findings. Most studies did not report the function scores and so it was difficult to compare. We are uncertain if these results are a true reflection of what is best for patients.

How up to date is this review?

We searched for studies published up to 26 October 2021.

Summary of findings 1. Retrograde intramedullary nail (RIMN) compared to locking plate for treating fractures of the distal femur in adults

Retrograde intramedullary nail (RIMN) compared with locking plate for treating fractures of the distal femur in adults

Patient or population: adults with fractures of the distal femur
Setting: hospitals in India, the UK and the USA
Intervention: RIMN
Comparison: locking plate

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with locking plate[a]	Risk with RIMN				
PROMs (short term) Measurements: • DRI (range 0–100, where lower values indicate less disability) Follow-up at 4 months	The mean DRI in locking plate group was **82.8** (SD 2.9)	**MD −21.90** (−38.16 to −5.64)	—	12 (1 RCT)	⊕⊖⊖⊖ **Very low[b]**	—
PROMs (long term) Measurements: • SMFA (range 0–100, higher values indicate worse function) • KSS (range 0–100, where higher values indicate better function) Follow-up at 12 and 18 months	The mean SMFA score in locking plate group was **27.4** (SD 29.4) The mean KSS in locking plate group was **74.4** (SD 10.9)	**SMD −0.22** (−0.50 to 0.06)	—	198 (2 RCTs)	⊕⊕⊖⊖ **Low[c]**	SMD re-expressed in KSS: −2.47 (95% CI −6.18 to 0.74, favours RIMN). MCID for KSS reported to be ≥ 9 points; therefore, unlikely to be a clinical important difference.
Direct adverse events (reoperation): we report reoperation for removal of implant as this is the most clinically relevant. Other adverse events with data included: loss of fixation, superficial infection, deep infection, haematoma formation, implant loosening) Follow-up: time points included 4, 12 and 18 months	**Study population** 100 per 1000	148 per 1000 (55 to 400)	**RR 1.48** (0.55 to 4.00)	114 (1 RCT)	⊕⊖⊖⊖ **Very low[d]**	There were no differences in reoperation for removal of implants, nor any of the other direct adverse events reported.

QoL (short term): using EQ-5D (range 0–1, where higher values indicate higher QoL) Follow-up at 4 months	The mean EQ-5D in locking plate group was 0.37 (SD 0.41)	**MD 0.01** (−0.42 to 0.44)	—	14 (1 RCT)	⊕⊖⊖⊖ **Very low**[d]	—
QoL (long term): using EQ-5D (range 0–1, where higher values indicate higher QoL) Follow-up at 12 months	The mean EQ-5D in locking plate group was 0.68 (SD 0.36)	**MD 0.10** (−0.01 to 0.21)	—	156 (1 RCT)	⊕⊖⊖⊖ **Very low**[d]	—
Pain	—		—	—	—	No studies reported pain.

*__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; **DRI:** Disability Rating Index; **EQ-5D:** EuroQol 5 Dimensions; **KSS:** Knee Society Score; **MCID:** minimal clinically important difference; **MD:** mean difference; **PROM:** patient-reported outcome measure; **QoL:** quality of life; **RCT:** randomised controlled trial; **RIMN:** retrograde intramedullary nail; **RR:** risk ratio; **SD:** standard deviation; **SMD:** standardised mean difference; **SMFA:** Short Musculoskeletal Function Assessment.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]The data reported here are those reported in the included studies.
[b]Downgraded three levels: twice due to imprecision because of wide CIs and a very small number of participants, and once for to study limitations due to high risk of performance bias.
[c]Downgraded two levels: once due to imprecision as the evidence was from two studies and once for study limitations due to high risk of performance bias and because of some unknown risks of bias.
[d]Downgraded three levels: once for study limitations due to high risk of performance bias and significant amounts of unknown bias in the studies, and twice levels for imprecision because there were small numbers of participants for each adverse event and wide CIs.

BACKGROUND

Description of the condition

Fractures of the distal femur (the part of the thigh bone nearest the knee) account for 4% to 6% of all femoral fractures (Kolmert 1982), and about 0.4% of all adult fractures (Court-Brown 2006). Annual incidences of between 4.5 and 11.7 per 100,000 people have been reported (Arneson 1988; Court-Brown 2006). Fractures of the distal femur typically occur in two groups of individuals: younger people sustaining high-energy trauma, such as motor vehicle accidents; and after a fall in older adults, typically women, with osteoporosis. Eighty-five per cent of distal femoral fractures occur in older adults (Martinet 2000), and this is set to increase (Hemmann 2021). Indeed, distal femur fractures in elderly people have a higher length of hospital stay and mortality rate than hip fractures (Tsai 2021). However, over recent decades, a third group has emerged – people with periprosthetic fractures occurring around previous total knee replacements. Periprosthetic fractures have a reported incidence of 0.3% to 3.5% (Meek 2011; Pitta 2018; Yoo 2015).

There are various classification systems for distal femoral fractures but fractures can broadly be classified as those that occur with or without extension into the knee joint (intra- and extra-articular). Extra-articular fractures are the most common (Martinet 2000), and these are often comminuted (Zlowodzki 2006). Fractures around the undulating growth plate of the distal femur in skeletally immature people predispose them to a high incidence of growth arrest. Children require very different surgical treatment and follow-up compared with adults with these fractures and are not included in this review (Wall 2012). For periprosthetic fractures, an additional consideration is whether the knee replacement is still functional (i.e. not loose following the injury) and the compatibility of the surgical approach and implants with the knee arthroplasty components that are in situ.

Description of the intervention

Distal femoral fractures can be treated either surgically or conservatively (non-surgically). Non-surgical treatment, which is usually reserved for less-severe injuries such as undisplaced fractures, generally involves some type of immobilisation such as hinged knee braces for more stable fractures to immobilisation in a long-leg cast for six to 12 weeks followed by bracing. Stabilisation is the initial step in the treatment of distal femoral fractures. A variety of options are available including a long-leg splint, cast, skin or skeletal traction. In people with polytrauma, an external fixator may be used until definitive treatment is possible. These interventions act to reduce discomfort and prevent any further soft tissue injury.

Definitive surgical interventions include:

- intramedullary nailing with either antegrade or retrograde approaches, usually fixed with interlocking screws;
- open reduction and plating with single fixed-angle device such as an angled blade plate (ABP) or dynamic condylar screw (DCS); indirect reduction using a mono-axial locking plate systems, for example, Less Invasive Stabilization System (LISS);
- indirect reduction using a poly-axial locking plate, for example, non-locking buttress plate;
- indirect reduction using a condylar buttress plate;
- internal fixation using plate or screws;
- external fixation with ring or axial frames;
- total knee replacement (replacement of both the distal femur and the proximal tibia). This usually requires the use of a hinged prosthesis, or a revision femoral replacement component. The use of standard femoral components is rarely possible.

Periprosthetic fractures around a total knee replacement can often be treated using the same techniques as are available when no prosthesis is in situ if the knee replacement is not loose. Certain factors need to be taken into consideration in periprosthetic fractures such as the width of the intercondylar box (to allow retrograde nail passage), the amount of bone remaining on the distal fragment and the space available for fixation devices; the lattermost may be compromised by the intercondylar box in posterior stabilised or constrained implants or stems. These factors may make certain treatments less desirable or impossible. Fractures around a loose total knee replacement mandate revision of the prosthesis rather than fixation alone. Coincident proximal prostheses such as hip replacements or metalwork from previous proximal femoral fracture fixation may make certain treatments less feasible; surgeons may favour retrograde nailing when a proximal sliding hip screw is in situ and plating where a hip arthroplasty is present in order to reduce the risk of future fracture between the implants.

How the intervention might work

Treatment of these fractures, whether surgical or non-surgical, seeks to stabilise the fracture to allow the natural healing process to occur. Bone healing requires adequate 'biology' in the form of blood supply to the fracture site – this may be made worse by surgery if soft tissues are stripped from the bone or potentially improved by surgery with bone grafting, bringing osteoprogenitor cells to the fracture site. Bone healing also requires an appropriate mechanical environment; fracture ends must be reduced and opposed enough to allow new bone to bridge the gap and the fracture must be held rigidly enough for healing to occur. How rigidly these fractures should be held depends on the fracture pattern and is still an area of debate. If fracture healing does not occur, people may experience pain and metalwork may fatigue and break.

Non-surgical interventions aim to hold the fracture in an acceptable position until it is healed enough to allow knee movement and weight-bearing. This can take a long time and prolonged immobilisation may lead to knee stiffness and pain (Crist 2008), as well as other complications such as pressure sores, chest infections and venous thromboembolic phenomena. It may be difficult to achieve adequate reduction of the fracture and holding it sufficiently still for the fracture to unite may also not be possible especially in obese people. Compared with surgery, non-surgical treatment may have a higher complication risk in terms of non-union and malunion, with serious functional consequences (Butt 1996a).

The aim of surgical treatment is to reposition the fractured bone, including reducing the articular surfaces within the knee joint if disrupted, restore limb alignment and hold it in this position until bony union. Although fractures of the distal femur may be comminuted (multifragmentary) making anatomical reduction of all fracture fragments impossible or impractical, restoration of sagittal, coronal and rotational alignment of the bone should be achievable in all cases regardless of the complexity of the fractures.

Surgical fixation should allow a mechanical environment suitable for bone healing. It should also allow earlier range of movement of the knee and potentially earlier weight-bearing. Older people with osteoporosis who are at high risk of fracture fixation failure, such as in very distal fractures or intra-articular fractures, may benefit from total knee arthroplasty (Rosen 2004), as may people with pre-existing symptomatic arthritis of the affected joint. The main disadvantage of surgical intervention is the potential for surgical complications including implant failure and additional damage to local blood supply resulting in non-union and infection (Foster 2006).

The underlying mechanisms and aims of management of periprosthetic fractures are similar to the above but consideration is required in terms of whether the knee replacement is still functional (i.e. not loose following the injury) and the potential interaction of new implants with those already in situ.

Why it is important to do this review

Fractures of the distal femur are challenging to treat. Surgical interventions include extramedullary fixation with a locking plate or intramedullary fixation with a retrograde nail or distal femur replacement (Hake 2019; Hoskins 2016; Zlowodzki 2006). Modern implants have been developed based on the three intervention principles, but there remains, however, no consensus on the most appropriate treatment, with some implants having high complication rates (Hake 2019). We reviewed the current evidence and compared the outcomes of different treatment modalities to guide best practice. This is an update of a 2015 Cochrane Review (Griffin 2015), and will help to identify where knowledge has grown and identify key areas requiring further research.

OBJECTIVES

To assess the effects (benefits and harms) of interventions for treating fractures of the distal femur in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and quasi-RCTs (method of allocating participants to a treatment that is not strictly random, e.g. by hospital number) evaluating one or more interventions for treating fractures of the distal femur (including periprosthetic). Studies published as conference abstracts were included if data presented were sufficient.

Types of participants

We included adults with an acute fracture of the distal femur. We anticipated that the distal femur would be defined variably perhaps using a classification system such as AO (distal femur = category 33) (Marsh 2007; Müller 1990), or perhaps more simply as principally beyond the isthmus or involving the distal metaphysis. We excluded trials exclusively reporting on children (skeletally immature participants) but we would have included those containing adults with a subgroup of children where the proportion of children was small and similar in the intervention groups, or there were separate data for the adult subpopulation. Iatrogenic fractures typically sustained during arthroplasty surgery were not eligible. However, acute periprosthetic fractures around established arthroplasties were included.

We also planned to include, but present separately, trials including adults with periprosthetic fractures. As treatment options for participants with an intact knee replacement are distinct from those for a loose knee replacement, our initial intention was to consider these separately.

Types of interventions

Any and all comparisons between those interventions described in the Description of the intervention were eligible for this review. Interventions were grouped as:

- retrograde intramedullary implants (RIMN);
- single fixed-angle device (e.g. dynamic condylar screw (DCS) or blade plate);
- non-locking (buttress) plates;
- locking plates;
- internal fixation (using either a plate or screws);
- distal femoral replacement (DFR);
- mono-axial plates;
- poly-axial plates;
- condylar buttress plate;
- non-surgical treatment.

Comparisons

The interventions were then grouped to allow for comparisons between studies. The following were the separate comparison groups:

- RIMN versus locking plate;
- RIMN versus single fixed-angle device;
- RIMN versus non-locking (buttress) plate;
- locking plate versus single fixed-angle device;
- internal fixation versus DFR;
- mono-axial plate versus poly-axial plate;
- mono-axial plate versus condylar buttress plate;
- surgical versus non-surgical management.

Types of outcome measures

The primary focus was on long-term functional outcome, preferably measured at one year or more.

Critical outcomes

We extracted information on the following four 'critical' outcomes.

- Validated patient-reported functional outcomes of the knee (e.g. Western Ontario and McMaster Universities Arthritis Index (WOMAC), Oxford Knee Score (OKS))
- Adverse events directly related to intervention (e.g. reoperations, wound infection, implant failure, damage to neurovascular structures, peri-implant fractures)
- Participant-reported quality of life (e.g. EuroQol 5 Dimensions (EQ-5D))
- Pain, using validated scores (e.g. Visual Analogue Scale (VAS))

Other important outcomes

We extracted information on the following 'important' outcomes.

- Adverse events indirectly related to interventions (e.g. pneumonia, urinary tract infections, acute kidney injury)
- Symptomatic non-union
- Malunion
- Resource use

For adverse events, we did not report composite measures because of potential unit of analysis errors. Therefore, we chose to report the effect estimate of those deemed as most clinically relevant.

Timing of outcome assessment

We expected most studies to report outcomes at several follow-up times. We considered less than six months as short-term, between six and 12 months as intermediate, and 12 months or greater as long-term follow-up.

Search methods for identification of studies

Electronic searches

We identified studies through systematic search strategies, as outlined in Chapter 4 of the *Cochrane Handbook of Systematic Reviews of Interventions* (Lefebvre 2021). We searched the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; CRS Web; 2021, Issue 10);
- MEDLINE (Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to 25 October 2021);
- Embase (Ovid; 1980 to 26 October 2021 week 42).

At the time of the search, CENTRAL was fully up-to-date with all records from the Bone, Joint and Muscle Trauma Group's Specialised Register and so it was not necessary to search this separately.

For this update, we limited the searches to 2014 onwards. Details of the search strategies used for previous versions of the review are given in Griffin 2015. We placed no restrictions on language or publication status.

The MEDLINE strategy followed guidelines outlined within the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2021). The subject-specific strategy was combined with the sensitivity-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE (Lefebvre 2021). Appendix 1 shows the search strategies for CENTRAL, MEDLINE and Embase.

We also searched the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch/Default.aspx) and ClinicalTrials.gov (clinicaltrials.gov/) for ongoing and recently completed trials (26 October 2021) (see Appendix 1), and identified conference abstracts by searching the *Bone & Joint Journal* Orthopaedic Proceedings (online.boneandjoint.org.uk/search/advanced; 2014 to 26 October 2021) (see Appendix 1).

Searching other resources

We checked the reference lists from identified trials for any additional relevant trials.

Data collection and analysis

Any review author who was or is a co-applicant, study author, or holds or held an advisory role on any studies was excluded from screening and selection decisions, data extraction and study quality assessment.

Selection of studies

Two review authors (HC and HS) independently identified potentially eligible trials from the electronic search results. We obtained full texts of all potentially eligible studies and two review authors independently reviewed them. We discussed any disagreements with a third review author. We contacted trial authors by email to request further information on study methods. Where there were disagreements concerning eligibility, we reached consensus through discussion amongst all review authors.

Data extraction and management

Two review authors (HC and HS) independently extracted data from each included trial report using a prepiloted data collection form. We recorded details of study methods, participants, interventions and outcomes. We resolved any disagreements through discussion. One review author (HC) entered data into Review Manager 5, and a second review author (HS) checked entries (Review Manager 2014). There were no attempts to mask the trial reports.

Assessment of risk of bias in included studies

Two review authors (HC and HS) independently assessed risk of bias in included studies using Cochrane's RoB 1 tool (Higgins 2011). This tool assesses the following domains.

- Sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of participants and personnel (performance bias)
- Blinding of outcome assessors (detection bias)
- Incomplete outcome data (attrition bias)
- Selective reporting (reporting bias)
- Other risks of bias

Each domain was ranked as: high, low or unclear risk of bias. Where disagreement existed concerning the assessment, we reached consensus through discussion amongst all review authors.

Measures of treatment effect

For dichotomous outcomes, we used risk ratios (RR) with 95% confidence intervals (CI). For continuous data we calculated mean differences (MD) with 95% CI. Where outcomes were measured using different scales, we calculated standardised mean differences (SMD) with 95% CI.

Unit of analysis issues

We were aware of potential unit of analyses issues arising from inclusion of participants with bilateral fractures. Hartin 2006 and Patterson 2020 reported one person each with bilateral fractures, though this was clear in the reports.

We expected that most studies would report outcomes at several follow-up times. We had planned to present these within the short-, intermediate- and long-term follow-up categories stipulated in Types of outcome measures; however, there were inadequate data available to perform separate analyses at each time point.

As expected, studies reported simple parallel-group designs. If other designs had been reported (e.g. cluster-randomised designs), we would have used generic inverse variance methods to combine data where appropriate.

Dealing with missing data

We contacted study authors where data were unclear or missing in manuscripts.

Where data continued to be missing for binary outcomes, we planned to class these outcomes as treatment failures (worst-case analysis). Similarly, where there were missing data for continuous outcomes, we planned to make a conservative estimate of the treatment effect by attributing outcomes in the treatment group values two standard deviations (SD) from the mean of the distribution. We aimed to present effect sizes with and without these adjustments ('as-reported' and 'worst-case analyses') in order to check the effect of these assumptions (see Sensitivity analysis). Unfortunately, there were insufficient data available in the reports of the studies to apportion data loss to one or other of the treatment groups.

Where SDs were not specifically reported, we determined these from standard errors, CIs or exact P values, if available.

Assessment of heterogeneity

We first assessed the degree of statistical heterogeneity between studies visually from inspection of the forest plot. We tested heterogeneity more formally using the Chi^2 test and I^2 statistic (Higgins 2003). We set a conservative P value for Chi^2 of less than 0.1 to indicate significant heterogeneity between studies. We interpreted values of I^2 statistic as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% indicated considerable heterogeneity (Deeks 2011).

Assessment of reporting biases

We planned to investigate the potential for publication bias and explore possible small-study biases using funnel plots. However, we had insufficient studies (fewer than 10) for most outcomes (Sterne 2017). To assess outcome reporting bias, we screened clinical trials registers for protocols and registration documents of included studies that were prospectively published, and we sourced all clinical trials register documents that were reported in the study reports of included studies. We used evidence of prospective registration to judge whether studies were at risk of selective reporting bias.

Data synthesis

There were insufficient studies to report the results for the three patient populations (normal (native) knee, intact knee replacement, loose knee replacement) described in Types of participants separately, as we had planned. Where appropriate, we pooled results of comparable groups of trials using a fixed-effect model. This model was chosen since there were few studies suitable for pooling, there was little statistical heterogeneity and little clinical diversity between studies. Where we performed a meta-analysis, we presented a summary estimate of the effect size with 95% CI.

Subgroup analysis and investigation of heterogeneity

Possible subgroup analyses that were specified a priori included:

- age:
  - over 60 years (as a surrogate for osteoporosis);
- fracture severity:
  - extra-articular versus intra-articular;
  - by fracture classification (e.g. main categories of the AO classification) if there were sufficient data;
  - open (Gustilo and Anderson Grade II or III) versus closed (closed or Gustilo and Anderson Grade I) (Gustilo 1976).

There were insufficient data to support the reporting of such analyses. We had planned to investigate whether the results of subgroups were significantly different by inspecting the overlap of CIs and performing the test for subgroup differences available in Review Manager 5 (Review Manager 2014).

We had planned that if one or more studies appeared to be a clear outlier, we would have checked the data for these studies carefully for errors or other methodological or clinical reasons why they might have differed from the other studies. If there had been good reasons why the studies differed from the majority then we would have noted this, and removed the studies from the main meta-analyses. There were insufficient data to facilitate such analyses.

Sensitivity analysis

If there had been sufficient data available, we planned to perform sensitivity analyses to examine various aspects of trial and review methodology, 'worst case' and as 'reported analyses' as described in Dealing with missing data, the selection of statistical model (fixed-effect versus random-effects) for pooling, the effects of excluding trials at high or unclear risk of bias, such as selection bias arising from the lack of allocation concealment, and exclusion of 'outlier' trials.

Summary of findings and assessment of the certainty of the evidence

Two review authors (HC and HS) used the GRADE approach to assess the certainty of the body of evidence associated with the critical outcomes (see the *Cochrane Handbook for Systematic Reviews of Interventions*; Section 12.2; Schünemann 2011). These included:

- validated patient-reported functional outcomes of the knee;
- adverse events directly related to intervention (e.g. reoperations, wound infection, implant failure, damage to neurovascular structures, peri-implant fracture);
- participant-reported quality of life (e.g. EQ-5D);
- pain, using validated scores (e.g. VAS).

The GRADE approach assesses the certainty of evidence based upon the quality of the supporting evidence as based on five domains.

- Study limitations (risk of bias)

- Indirectness (directness of the evidence)
- Inconsistency (heterogeneity of the data)
- Imprecision (precision of the effect estimates)
- Risk of publication bias

The certainty is rated as high, moderate, low or very low, being downgraded by one or two levels depending on presence and extent of concerns in the five GRADE domains. We prepared a summary of findings table for the comparison of RIMN versus locking plate using GRADE profiler software (GRADEpro GDT). We used footnotes to describe reasons for downgrading the certainty of the evidence for each outcome.

RESULTS

Description of studies

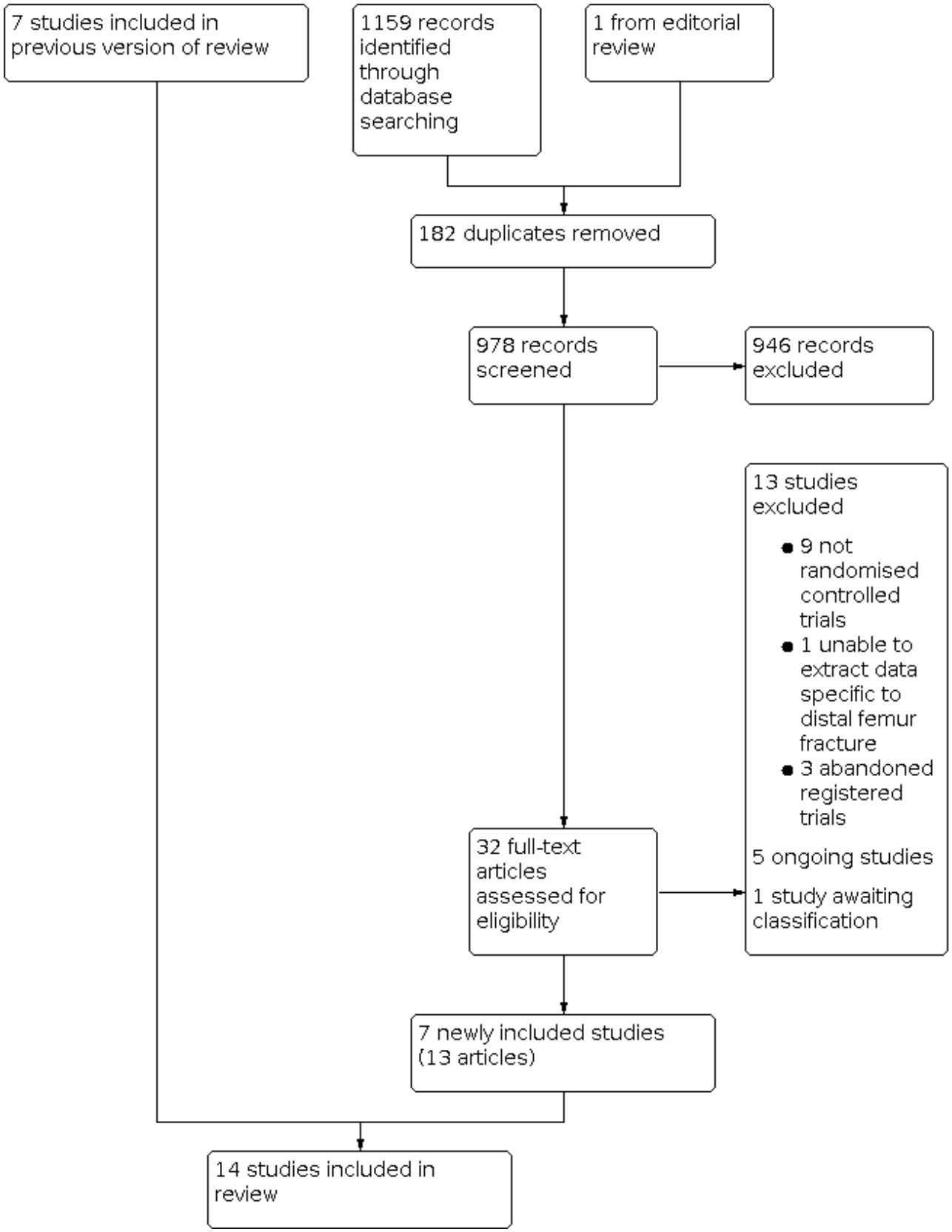
See Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; and Characteristics of ongoing studies table.

Results of the search

For this update (to 26 October 2021), we screened 1159 records from CENTRAL (265), MEDLINE (534), Embase (216), WHO ICTRP (54) ClinicalTrials.gov (76) and *Bone & Joint Journal* Orthopaedic Proceedings (14), and one from editorial review.

We removed 182 duplicates and screened the titles and abstracts of 978 records. Of these, we excluded 946 records and assessed 32 full-text articles for eligibility. A summary of the study selection process is shown in Figure 1.

Figure 1. Study flow diagram.



The 2015 Cochrane Review identified seven trials (Butt 1996b; Canadian Orthopaedic Trauma Society 2016; Christodoulou 2005; Dar 2009; DeCoster 1995; Hartin 2006; Tornetta 2013), which we also included in this review update. In 2015, there were five ongoing trials. One is now completed and included in the current review (Patterson 2020), two are now excluded due to the studies being terminated (NCT01553630; NCT01693367), and two are still ongoing (NCT01766648; NCT01973712).

In addition to Patterson 2020, the new search highlighted six further new studies (Gill 2017; Griffin 2019; Hanschen 2014; Hull 2019; Kanakaris 2019; Xu 2015), resulting in seven new studies for this update and 14 included studies overall. There are three new ongoing trials (ACTRN12617000493347; ACTRN12619001023145; NCT04076735), bringing the total of ongoing trials to five.

We excluded 13 studies overall (Firoozabadi 2012; Gao 2013; NCT01693367; Han 2011; Horneff 2013; Liu 2014; Markmiller 2004; Petsatodis 2010; NCT00578019; Thomas 1981; Tornetta 2000; Vallier 2012; NCT01553630).

Included studies

The 14 included studies involved 753 adults (755 fractures) and no children (Butt 1996b; Canadian Orthopaedic Trauma Society 2016; Christodoulou 2005; Dar 2009; DeCoster 1995; Gill 2017; Griffin 2019; Hanschen 2014; Hartin 2006; Hull 2019; Kanakaris 2019; Patterson 2020; Tornetta 2013; Xu 2015). These are summarised below, with a full summary for each study detailed in the Characteristics of included studies table.

Design

There were seven RCTs (Canadian Orthopaedic Trauma Society 2016; Gill 2017; Hanschen 2014; Hartin 2006; Patterson 2020; Tornetta 2013; Xu 2015), two randomised feasibility trials (Griffin 2019; Hull 2019), and one pilot RCT (Kanakaris 2019). Four studies were quasi-RCTs (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995).

Study size

The study population sizes at allocation varied but were generally small: 18 participants (DeCoster 1995), 22 participants (Hull 2019), 22 participants with 23 fractures (Hartin 2006), 23 participants (Griffin 2019), 27 participants (Hanschen 2014), 40 participants (Kanakaris 2019), 42 participants (Butt 1996b; Gill 2017), 52 participants (Canadian Orthopaedic Trauma Society 2016), 73 participants (Dar 2009), 78 participants with 79 fractures (Patterson 2020), 78 participants (Xu 2015), 80 participants (Christodoulou 2005), 156 participants (Tornetta 2013).

Setting

All studies were conducted in a hospital setting. Seven were single-centre studies: Butt 1996b in the UK, Christodoulou 2005 in Greece, Dar 2009 and Gill 2017 in India, Xu 2015 in China, and DeCoster 1995 and Patterson 2020 in the USA. Five were multicentre trials: Hartin 2006 conducted a two-centre trial in Australia, Kanakaris 2019 conducted a four-centre trial in the UK, Hanschen 2014 conducted a four-centre trial in Germany, Canadian Orthopaedic Trauma Society 2016 conducted a seven-centre trial in Canada, and Tornetta 2013 conducted a 22-centre trial in the USA. The randomised feasibility studies were both multicentre, conducted in seven-centres in the UK (Griffin 2019; Hull 2019).

The opening year of participant recruitment ranged from 1988 in Butt 1996b to August 2017 in Griffin 2019. DeCoster 1995 and Tornetta 2013 did not report the period of recruitment.

Participants

Twelve studies reported information on gender: Christodoulou 2005 (25 men, 47 women), Dar 2009 (41 men, 27 women), Gill 2017 (29 men, 13 women), Griffin 2019 (7 men, 16 women), Hanschen 2014 (8 men, 19 women), Hartin 2006 (7 men, 16 women), Hull 2019 (0 men, 23 women), Kanakaris 2019 (6 men, 34 women), Canadian Orthopaedic Trauma Society 2016 (18 men, 34 women), Patterson 2020 (31 men, 47 women), Tornetta 2013 (71 men, 55 women), Xu 2015 (54 men, 24 women).

The participants' ages varied between 16 and 98.8 years. Kanakaris 2019 restricted their participants to greater than 60 years, while Butt 1996b and Hull 2019 restricted participants to greater than 65 years. Hull 2019 had the highest mean age of 90 years, reporting mostly injuries occurring due to low-energy falls in people who were mostly in nursing homes requiring walking aids. Griffin 2019 initially included people aged greater than 50 years with an isolated, acute fracture of the distal femur. However, the minimum age for inclusion was lowered to greater than 18 years following review of the screening data and input from the Trial Steering Committee. The mean age of participants was 35 years in DeCoster 1995, all of whom had open fractures resulting from high-energy trauma. Gill 2017 reported mean ages of 39 and 36 years for the two treatment arms, and most participants in this trial experienced high-energy trauma. Hartin 2006 excluded people who were skeletally immature but reported no maximum age limit.

Studies recruited participants with different types of fractures. Butt 1996b included participants with displaced fractures of the distal femur. Xu 2015 included participants with type C fractures of distal femurs. Christodoulou 2005, Gill 2017, and Hartin 2006, included participants with supracondylar distal femur fractures. Tornetta 2013 and Dar 2009 recruited only participants with AO/ASIF 33A1–3 (extra-articular) or C1 (simple complete articular) fractures of the distal femur. DeCoster 1995 included AO/ASIF type A3, C1–C3 fractures. Kanakaris 2019 included AO/OTA 33–A1 to C3 fractures. Griffin 2019 included AO/OTA A1–3, B1 and C2–3 fractures. Hanschen 2014 recruited participants with AO/OTA type A–C fractures. Canadian Orthopaedic Trauma Society 2016 recruited only participants with fractures classified as AO/OTA 33A1–33C2, excluding 33C3 fractures in the RCT due to no consensus on appropriate management. Patterson 2020 excluded 33C3.3 cases with coronal plane fractures to the medial or lateral (or both) condyle, people with insufficient lateral cortex remaining for blade insertion, periprosthetic fractures, and Gustilo and Anderson IIIC open fractures. Hull 2019 provided no breakdown in fracture classifications.

There was variability between studies involving participants with open versus closed fractures. Dar 2009 and Hull 2019 included participants with only closed distal femur fractures, whereas DeCoster 1995 included only participants with open distal femur fractures. Gill 2017, Hanschen 2014, and Patterson 2020 included open and closed fractures, but Gill 2017 excluded closed fractures with Gustilo-Anderson fractures grade 3B and 3C,

whereas Patterson 2020 only excluded grade 3C. All other studies only included closed fractures.

Three studies specifically included fragility fractures. Kanakaris 2019 included displaced distal femoral fractures in people with osteoporosis, or above or below a total knee or hip arthroplasty. Two studies used age as a surrogate for fragility fractures: Hull 2019 included people with fractures aged 65 years or above and Griffin 2019 initially included only people aged 50 years or greater, but this had to be changed to 18 years or greater by the trial steering committee.

Three studies reported at least one periprosthetic fracture in each treatment arm, but these could not be separated for analysis (Griffin 2019; Hanschen 2014; Hartin 2006). All other studies did not include periprosthetic or fragility fractures.

Interventions

Surgical management

Thirteen studies compared different methods of surgical treatment (Canadian Orthopaedic Trauma Society 2016; Christodoulou 2005; Dar 2009; DeCoster 1995; Gill 2017; Griffin 2019; Hanschen 2014; Hartin 2006; Hull 2019; Kanakaris 2019; Patterson 2020; Tornetta 2013; Xu 2015).

Retrograde intramedullary nail versus locking plate

Three studies (210 participants) compared RIMN with a locking plate (Gill 2017; Griffin 2019; Tornetta 2013). Gill 2017 compared a locked compressive plate to a RIMN. Griffin 2019 locked the RIMN proximally and distally, and used at least one locking screw distal to the fracture for the locking plate. Tornetta 2013 reported a comparison between two commonly used contemporary implants – a reamed, locked RIMN and a locking plate.

Retrograde intramedullary nail versus single fixed-angle device

Three studies (159 participants) compared RIMN with fixation using a single fixed-angle device (Christodoulou 2005; Dar 2009; Hartin 2006). Christodoulou 2005 used the intercondylar notch approach with the RIMN, locking the nail with two proximal and two or three distal screws. The plate group received a 95° ABP with or without primary autologous bone grafting. Dar 2009 and Hartin 2006 reported similar comparisons between RIMN and DCS; fractures were reduced closed and the DCS inserted percutaneously in Dar 2009 and an open approach in Hartin 2006.

Retrograde intramedullary nail versus non-locking buttress plate

DeCoster 1995 (18 participants) compared RIMN versus indirect reduction and non-fixed-angle buttress plate fixation. Both groups reduced articular fragments and held them with lag screws. Participants started range of motion exercises immediately postoperatively and weight-bearing was allowed when there was radiographic evidence of callus.

Locking plate versus single fixed-angle device

Two studies (130 participants) compared a locking pate device and a single, fixed-angle device (Canadian Orthopaedic Trauma Society 2016; Patterson 2020). Canadian Orthopaedic Trauma Society 2016 used a locking plate system (LISS) with a DCS fixed-angle plate. Patterson 2020 compared two fixed-angle implants: a locking condylar plate (LCP) and a 95° ABP.

Internal fixation versus distal femoral replacement

Hull 2019 (22 participants) compared internal fixation (lateral locking plate or locked RIMN) and DFR. The treatment for those allocated to internal fixation was dependent on the usual practice of the treating surgeon.

Mono-axial plate versus poly-axial plate

Two studies (67 participants) compared a mono-axial plate (LISS) and a poly-axial plate (Hanschen 2014; Kanakaris 2019). Hanschen 2014 fixed the plate using either mono-axial or poly-axial screws. In the mono-axial system, additional lag screws were inserted.

Mono-axial plate versus condylar buttress plate

Xu 2015 (78 participants) compared a mono-axial plate (LISS) and a condylar buttress plate. The LISS used three to five screws to lock the plate at the proximal and distal ends. The condyle support plate was fitted on the lateral side of the femur, with the proximal end fixed with cortical screws and the distal end fixed with cancellous bone screws.

Surgical versus non-surgical management

One study (42 older adults) compared surgical and non-surgical interventions (Butt 1996b). Butt 1996b reported outcomes after DCS fixation, with or without medial bone grafting, compared with non-surgical treatment. The non-operative treatment consisted of skeletal traction with Denham pin and Thomas splint, followed by splint removal and Perkin's exercises at three to four weeks, followed by a functional cast brace at six to eight weeks.

Outcomes

All studies reported at least one of the critical review outcomes. Length of follow-up ranged between four months (Griffin 2019) and 30 months (Dar 2009). Butt 1996b and Canadian Orthopaedic Trauma Society 2016 did not provide follow-up schedules. Four studies did not report patient-reported outcome measures (PROMs) (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995). Of the studies that did report PROMs, there was variability in terms of outcome measures reported. Reported PROMs were: OKS (Hanschen 2014; Hull 2019; Kanakaris 2019), EQ-5D (Griffin 2019; Hull 2019; Tornetta 2013; Kanakaris 2019), Disability Rating Index (DRI) (Griffin 2019; Hull 2019), Musculoskeletal Function Assessment (MFA) (Patterson 2020), short MFA (SMFA) (Canadian Orthopaedic Trauma Society 2016; Tornetta 2013), Evanich score (Xu 2015), Tegner Score (Hanschen 2014), Lysholm (Hanschen 2014), Knee Society Score (KSS) (Gill 2017), and 36-Item Short Form (SF-36) (Hartin 2006). In the methods, one study noted using VAS at each follow-up, but this was not reported in the results (Gill 2017).

Other clinical outcome measures included categories based on Schatzker and Lambert criteria (full extension, loss of flexion, valgus/varus/rotational deformity, pain, joint congruency) (Schatzker 1979) reported in Butt 1996b and Christodoulou 2005. Hanschen 2014 also assessed the degree of knee flexion, and radiological assessment reported via the Rasmussen score (Rasmussen 1973). Five studies reported a measure of resource use (Christodoulou 2005; Gill 2017; Griffin 2019; Hull 2019; Xu 2015). Hull 2019 in the trial protocol stated that they would also report range of motion in flexion and extension using a goniometer, but this was not reported in the manuscript.

All trials reported adverse events, though there was variability in which specific events were reported and whether directly or indirectly related to the implant.

Sources of funding and declarations of interest

Nine studies declared any conflicts of interest. Of these, five reported no conflicts of interest (Butt 1996b; Gill 2017; Hull 2019; Kanakaris 2019; Patterson 2020). The remaining four studies reported a conflict of interest. Griffin 2019 reported that one study author was a member of the board that funded the study. Hanschen 2014 reported one study author was a surgical instructor for the company producing the implants. Canadian Orthopaedic Trauma Society 2016 reported some study authors being affiliated with industry companies and members of editorial boards. Tornetta 2013 reported a disclosure of being affiliated with industry.

Two studies were funded by the National Institute for Health Research (Griffin 2019; Hull 2019), while two studies received funding by industry sponsor providing implants (Canadian Orthopaedic Trauma Society 2016; Kanakaris 2019). Patterson 2020 received no funding.

For the remaining studies, there was no information from the manuscripts, trial registers or personal communication with the authors about sources of funding or conflicts of interest.

Excluded studies

We excluded 13 studies (see Characteristics of excluded studies). Nine studies were from the Griffin 2015 review (Firoozabadi 2012; Gao 2013; Han 2011; Horneff 2013; Markmiller 2004; Petsatodis 2010; Thomas 1981; Tornetta 2000; Vallier 2012). Four studies were from this review update following full-text review (NCT01693367; NCT00578019; NCT01553630; Liu 2014). NCT01693367 was abandoned due to one of the interventions (distal locking screw) being removed from the market. Liu 2014 was a letter to the editor. NCT00578019 was abandoned due to the Primary Investigator moving institutions. NCT01553630 was abandoned due to low enrolment.

Studies awaiting classification

One study (100 participants) is awaiting classification (Mahar 2021; Characteristics of studies awaiting classification table). This trial compared LISS to RIMN in a single-centre study in Pakistan in people aged 20 to 60 years with closed AO33A fractures. The primary and secondary objectives were not stated, but the manuscript presented mean time to union, Neer classification and complications (presence of shoulder pain, superficial infection, delayed union, non-union, shoulder stiffness and elbow stiffness). We were unsuccessful in receiving details of ethical approval or protocol (or both) to ascertain the randomisation process as this information has not yet been released.

Ongoing studies

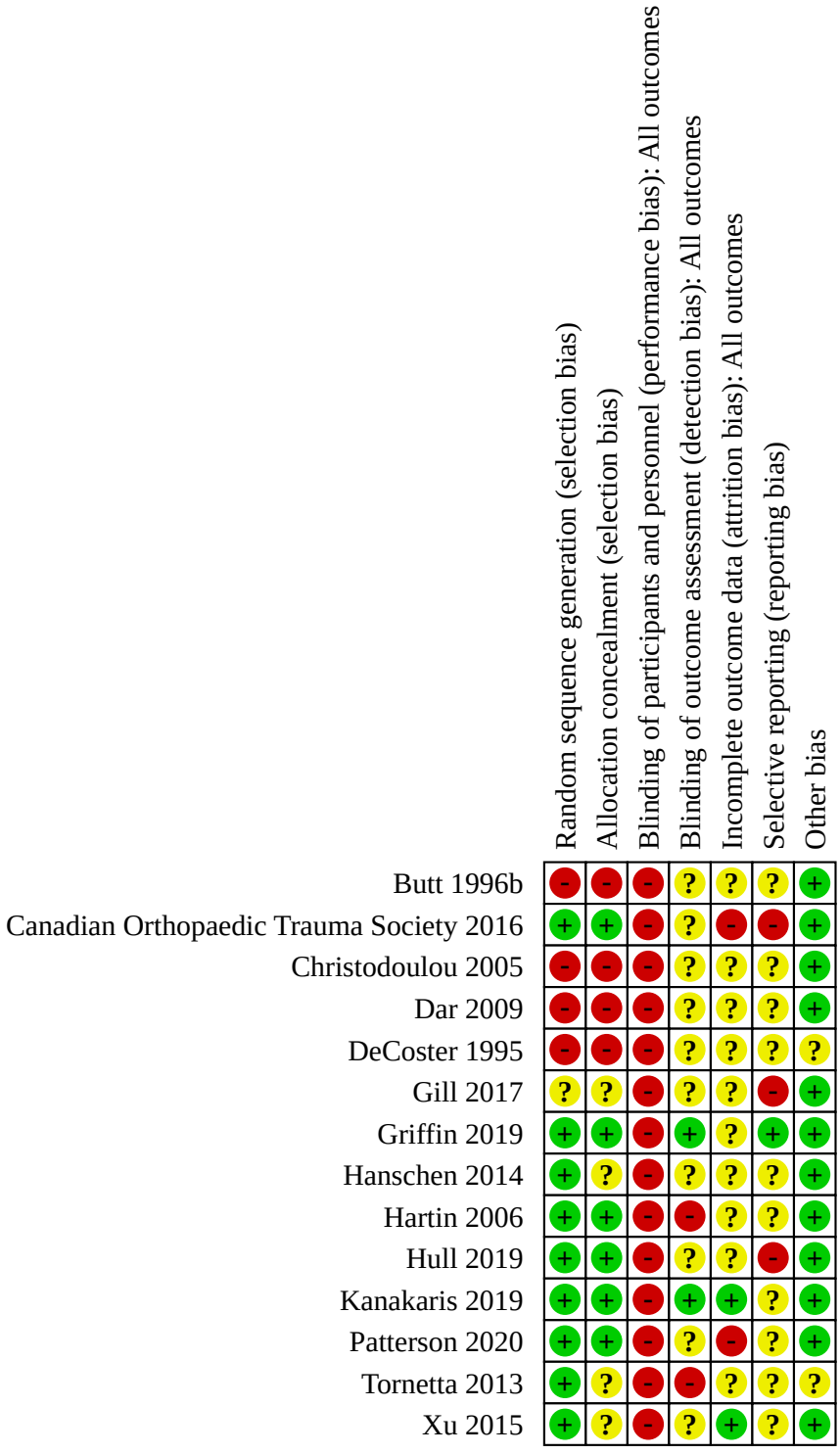
Full details of the five ongoing studies are presented in the Characteristics of ongoing studies table.

NCT01973712 will report a performance outcome (timed up and go test) following a comparison of the common contemporary interventions for periprosthetic femoral fractures – retrograde nails and locking plates. The estimated enrolment rate is 94 participants. Two studies will report functional and performance outcomes following the comparison of two different types of locking screw technology in anatomical angular-stable locking plates (ACTRN12617000493347; NCT01766648). ACTRN12617000493347 aims to recruit 100 participants aged 60 years or above and will also include periprosthetic fractures. NCT01766648 aims to recruit 130 participants aged 18 years or above with displaced distal femur fractures. NCT04076735 will report functional outcomes in terms of OKS for DFR versus surgical fixation in people aged 65 years or above and aims to recruit 140 participants. ACTRN12619001023145 will report radiographic union at eight months following comparison of titanium locking plate with long working length versus titanium locking plate with short working length in people aged 18 years or above and aims to recruit 76 participants.

Risk of bias in included studies

The quality of reporting of the studies varied but was generally fair to poor, with trial reports being limited to conference abstracts in two studies (DeCoster 1995; Tornetta 2013). A detailed description of the assessment of the risk of bias is given in the Characteristics of included studies table. Figure 2 presents a summary of the assessment of the risk of bias in each study.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

In terms of random sequence generation, nine studies were at low risk of bias (Canadian Orthopaedic Trauma Society 2016; Griffin 2019; Hanschen 2014; Hartin 2006; Hull 2019; Kanakaris 2019; Patterson 2020; Tornetta 2013; Xu 2015). One study was at unclear risk of bias (Gill 2017). Four studies were at high risk of bias (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995).

Six studies were at low risk of selection bias reflecting a valid method of allocation concealment (Canadian Orthopaedic Trauma Society 2016; Griffin 2019; Hartin 2006; Hull 2019; Kanakaris 2019; Patterson 2020). Four studies were at unclear risk of allocation concealment (Gill 2017; Hanschen 2014; Tornetta 2013; Xu 2015). Four studies were at high risk of bias of allocation concealment due to being quasi-randomised based on either date of admission (Butt 1996b) or alternation (Christodoulou 2005; Dar 2009; DeCoster 1995).

Both Griffin 2019 and Kanakaris 2019 informed participants at the end of the trial what implant they received if they requested this information.

Blinding

We made judgements according to the type of outcome: participant-reported measures or objectives measures.

Participants and personnel

The nature of the interventions being compared in the included studies meant that no blinding of treatment providers was possible. Therefore, all studies were at high risk of performance bias. Canadian Orthopaedic Trauma Society 2016 and Tornetta 2013 confirmed lack of blinding of trial participants.

Blinding of outcome assessment

Two studies were at low risk of detection bias as outcome assessors were blinded and independent (Griffin 2019; Kanakaris 2019). Ten studies did not mention blinding of outcome assessment and so were at unclear risk of detection bias (Butt 1996b; Canadian Orthopaedic Trauma Society 2016; Christodoulou 2005; Dar 2009; DeCoster 1995; Gill 2017; Hanschen 2014; Hull 2019; Patterson 2020; Xu 2015). Two studies were at high risk of detection bias (Hartin 2006; Tornetta 2013). Lack of blinding of outcome assessors was confirmed in Hartin 2006, where the clinical assessment was made by the operating surgeon, and in Tornetta 2013, which was described as an open-label trial in their trial registration document.

Incomplete outcome data

Two studies were at low risk of attrition bias (Kanakaris 2019; Xu 2015). Kanakaris 2019 reported three participant deaths prior to completing follow-up, but this did not cause imbalances between groups. Xu 2015 followed up all participants in their trial.

Two studies were at high risk of attrition bias (Canadian Orthopaedic Trauma Society 2016; Patterson 2020). Patterson 2020 was at high risk of attrition bias for reporting 55/79 functional assessments, whereas Canadian Orthopaedic Trauma Society 2016 was at high risk due to a larger than expected loss to follow-up of 27%.

Ten studies were at unclear risk of bias due to lack of information (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995; Gill 2017; Griffin 2019; Hanschen 2014; Hartin 2006; Hull 2019; Tornetta 2013). Three studies did not split numbers by treatment group (Christodoulou 2005; Dar 2009; Tornetta 2013). As well as loss to follow-up, the effect on outcome of the cross-over in Butt 1996b was unknown. The same uncertainty applied to the participants with bilateral fractures included in Hartin 2006. Griffin 2019 reported 39.1% loss to follow-up. Hull 2019 reported that 23% of participants withdrew after the operation, with four in the intervention group and one in the control group; it is unclear what effect this may have. It was not clear or explicitly stated how many participants were lost to follow-up in Gill 2017 or DeCoster 1995.

Selective reporting

Several included studies had published protocols allowing comparison, whereas five studies had poor quality of reporting of outcome measurement in the methods and results, which hampered the assessment of the risk of bias from selective reporting of outcomes, with protocols not available for comparison with the trial reports (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995; Hartin 2006).

One study was at low risk of bias as the primary and secondary outcome measures were consistent with the protocol (Griffin 2019). Three studies were at high risk of bias (Canadian Orthopaedic Trauma Society 2016; Gill 2017; Hull 2019). Hull 2019 omitted range of motion and radiographic outcome reporting as secondary outcome measures in the trial report. It was unclear if Gill 2017 registered a protocol for their trial, and primary or secondary outcomes were not explicitly stated. However, in the manuscript, Gill 2017 reported assessing pain using a VAS, but there were no data in the results. The protocol of Canadian Orthopaedic Trauma Society 2016 mentioned assessing SF-36, Lower Extremity Measure, and gait function and range of motion, but these were not in the trial reports (high risk). The remaining studies were at unclear risk of bias because of a lack of information provided (Butt 1996b; Christodoulou 2005; Dar 2009; DeCoster 1995; Hanschen 2014; Hartin 2006; Kanakaris 2019; Patterson 2020; Tornetta 2013; Xu 2015). Whilst Patterson 2020 registered their study, the outcome measures were not reported in the protocol, and, therefore, the risk of reporting bias was unclear.

Other potential sources of bias

Two studies were at unclear risk of other bias due to being presented as conference abstracts and, therefore, we could not be certain of other potential sources of bias (DeCoster 1995; Tornetta 2013). The remaining studies had low risk of other bias.

Effects of interventions

See: **Summary of findings 1** Retrograde intramedullary nail (RIMN) compared to locking plate for treating fractures of the distal femur in adults

Comparison of different methods of surgical treatment

Thirteen studies investigated different methods of surgical management (Canadian Orthopaedic Trauma Society 2016; Christodoulou 2005; Dar 2009; DeCoster 1995; Gill 2017; Griffin 2019; Hanschen 2014; Hartin 2006; Hull 2019; Kanakaris 2019; Patterson 2020; Tornetta 2013; Xu 2015). These trials were grouped into seven classes of comparison, determined by the groups in the Types of interventions.

Retrograde intramedullary nail versus locking plate

See Summary of findings 1. Three studies including 210 participants compared a RIMN versus a locking plate (Gill 2017; Griffin 2019; Tornetta 2013).

Tornetta 2013 reported incomplete one-year results in a conference abstract. Due to a combination of incompletely reported outcomes (no measures of variance reported) and a lack of details on the treatment group of the 30 participants loss to follow-up at one year, we were unable to report a 'completed-case' analysis. Rather, we have assumed data to have been missing at random and performed analyses using group size as 'per-allocation'.

Griffin 2019 reported Dementia quality of life measure, but at follow-up there were no data available for the plate group. This study also reported EQ-VAS in addition to EQ-5D, but to enable comparison with other studies, we chose to present EQ-5D.

Critical outcomes

Validated patient-reported functional outcomes of the knee

The three studies reported different PROMs and we used SMDs to pool the results. Griffin 2019 reported DRI at four months, a PROM whereby the participant rates their ability to complete a set of tasks on a VAS that is scored with 0 reflecting no disability and 100 reflecting total inability to complete the task. Tornetta 2013 reported functional outcome at one year using the SMFA, made up of two component standardised indices (dysfunction and bother indices), where higher scores represent worse function. Gill 2017 reported functional outcome at 18 months using the KSS, with scores ranging from 0 to 100, where higher scores indicate better function.

Short-term outcome data showed very-low certainty evidence of a difference in PROMs favouring RIMN (MD −21.90, 95% CI −38.16 to −5.64; 1 study, 12 participants; very-low certainty evidence; Analysis 1.1). We downgraded the certainty of the evidence two levels due to imprecision because of wide CI and a very small number of participants and one level due to study limitations due to high risk of performance bias.

Pooled long-term outcome data showed no evidence of improvement (SMD −0.22, 95% CI −0.50 to 0.06; 2 studies, 198 participants; low-certainty evidence; Analysis 1.2). Re-expressing the SMD to KSS showed an MD of −2.47 (95% CI −6.18 to 0.74). This is unlikely to be of clinical importance as previous studies reported a minimal clinically important difference (MCID) of at least nine points (Lizaur-Utrilla 2020). We downgraded the certainty of the evidence one level due to imprecision as the evidence was from two studies and one level for study limitations due to high risk of performance bias and because of some unknown risks of bias.

Direct adverse events

All three studies reported at least one direct adverse event. These were reoperation for removal of implant, loss of fixation, superficial infection, deep infection, haematoma formation and implant loosening. Tornetta 2013 also reported in the conference abstract no deaths and five venous thromboembolic events but did not categorise them by treatment group. There was little or no difference in adverse events between treatment groups (Analysis 1.3). We deemed reoperation for removal of the implant as the most clinically important, but this showed no evidence of a difference between the two implants (RR 1.48, 95% CI 0.55 to 4.00; 1 study, 114 participants; very low-certainty evidence). We downgraded the certainty of the evidence one level for study limitations due to high risk of performance bias and significant amounts of unknown bias in the studies and two levels for imprecision because there was a small number of participants for each adverse event and wide CI.

Participant-reported quality of life

Griffin 2019 and Tornetta 2013 used the EQ-5D score to report quality of life outcomes (Analysis 1.4). This widely used outcome tool comprises five questions that can be converted to a population-specific utility index where a score of 1.0 represents maximum quality of life. Griffin 2019 reported EQ-5D at four months and Tornetta 2013 at one year. Griffin 2019 also reported EQ-VAS at four months.

There was no evidence of a difference between the two treatments at each time point for the separate studies (Griffin 2019: MD 0.01, 95% CI −0.42 to 0.44; 14 participants; Tornetta 2013: MD 0.10, 95% CI −0.01 to 0.21; 156 participants). These were both very-low certainty evidence. We downgraded two levels for study limitations due to high risk of performance bias and one study being at risk of unknown bias, and two levels for imprecision due to a small number of participants and a wide CI.

Pain

There were no reported data for pain. One study reported in their methodology to have assessed pain using VAS, but this was not reported in the results section (Gill 2017).

Other important outcomes

Two studies reported indirect adverse events (Gill 2017; Griffin 2019). These were deep vein thrombosis, pneumonia, urinary tract infection, cerebrovascular accident, myocardial infarction, blood transfusion and anterior knee pain. There were no differences between the two implants for any of the indirect adverse events (Analysis 1.5). This was very-low certainty evidence. We downgraded two levels for study imprecision due to a low number of participants for each direct adverse event and for wide CI and one level due to study limitations because of high risk of performance bias and unknown biases in one study.

RIMN may be more likely to lead to varus/valgus deformity of greater than 5° in Griffin 2019 (5/12 with locking plate versus 10/11 with RIMN; RR 2.18, 95% CI 1.09 to 4.37; 1 study, 33 participants; low-certainty evidence; Analysis 1.6). We downgraded the certainty of the evidence one level due to study limitations of being a feasibility study with some substantial risk of bias, including performance bias and one level due to study imprecision with only 33 participants from one study available for pooling. There was no evidence of differences in other outcomes of union, including malunion, non-union, delayed union, loss of fixation, recurvatum greater than 10°, procurvatum greater than 10°, shortening greater than 1 cm, malalignment greater than 10° or malalignment of 5° to 10°.

Resource use was reported in terms of operating time (Gill 2017) and length of stay (Griffin 2019). There was evidence showing a small difference in operating time between the interventions favouring locking plate (MD 13.90 minutes, 95% CI 1.43 to 26.37; 1 study, 42 participants; very-low certainty evidence; Analysis 1.7). However, this is unlikely to be of clinical importance. We

downgraded the certainty of the evidence two levels for risk of bias from the study design with unclear risk of bias, and one level for study imprecision because of a low number of participant and broad CI. There was evidence of shorter length of stay favouring locking plate (MD 8.90 days, 95% CI −17.26 to 35.06; 1 study, 23 participants; very-low certainty evidence; Analysis 1.7). However, this difference is unlikely to be of clinical importance. We downgraded the certainty of the evidence by two levels due to study imprecision due to a broad CI and low number of participants, and by one level one due to study limitations of being a feasibility study with some substantial risk of bias, including performance bias. Griffin 2019 also reported resource use in terms of cost favouring RIMN, but this is unlikely to be of clinical importance due to the wide CI (MD GBP −1001.03, 95% CI −3783.56 to 5785.62; 1 study, 23 participants; very low-certainty evidence; Analysis 1.8). We downgraded the certainty of the evidence one level due to study limitations because of study design and risk of performance bias, and two levels for imprecision due to very wide CIs and low number of participants.

Retrograde intramedullary nail versus single fixed-angle device

Three studies, including 159 participants, compared RIMN fixation versus DCS or blade plate fixation (Christodoulou 2005; Dar 2009; Hartin 2006). The allocation of participants who were lost to follow-up was not reported and our attempts previously to contact the authors were unsuccessful. Therefore, we analysed the data only on an 'as reported' basis.

Critical outcomes

Validated patient-reported functional outcomes of the knee

No studies reported data for PROMs.

Direct adverse events

We pooled data for reoperation, death and individual adverse events where data were available from two or more studies. There was variability in the direct adverse events reported by the three studies, which included reoperation, death, infection, haematoma formation requiring aspiration, implant failure or nail protrusion. Effect estimates showed very-low certainty evidence of little or no difference between the two interventions (Analysis 2.1). Reoperation was deemed most clinically important and showed no difference between the operations (RR 1.85, 95% CI 0.62 to 5.57; 3 studies, 159 participants; very-low certainty evidence). We downgraded the certainty of the evidence two levels due to study limitations as two studies were at high risk of selection bias and performance bias and one level for imprecision as the total number of participants for pooling was small.

Participant-reported quality of life

One study reported both mental and physical quality of life using the SF-36 health-related quality of life outcome tool (Hartin 2006). The general health surveys were completed at approximately 20 months in both groups, representing long-term follow-up. There was very low-certainty evidence of no little to no difference in quality of life between groups in either the physical component (MD −0.30, 95% CI −11.84 to 11.24; 1 study, 16 participants; Analysis 2.2) or the mental component (MD −3.30, 95% CI −15.34 to 8.74; 1 study, 16 participants; Analysis 2.2). We downgraded the certainty of the evidence two levels for imprecision due to comparison with one study with very few participants and one level for study quality due to high risk of performance bias and detection bias.

Pain

No studies reported data for pain.

Other important outcomes

One study reported indirect adverse events in terms of pneumonia, urinary tract infection, acute renal failure and pressure sores (Hartin 2006). Effect estimates showed little or no difference between the two implants (Analysis 2.3).

There was little or no difference between the two implants in non-union (MD 1.10, 95% CI 0.33 to 3.71; 3 studies, 159 participants; very-low certainty of evidence; Analysis 2.4) and malunion (MD 1.84, 95% CI 0.28 to 11.97; 3 studies, 159 participants; very low-certainty evidence; Analysis 2.4). We downgraded the certainty of the evidence two levels for imprecision due to comparison with one study with a small number of participants and one level due to study limitations as two studies were at high risk of selection bias and performance bias.

Two studies reported length of hospital stay (Christodoulou 2005; Hartin 2006). Christodoulou 2005 reported a shorter hospital stay favouring RIMN (MD −2.80 days, 95% CI −3.40 to −2.20; 75 participants; very low-certainty evidence; Analysis 2.5). We downgraded the certainty of the evidence two levels for imprecision due to comparison with one study with a small number of participants and two levels due to study limitations as the study was at high risk of selection, performance and detection bias. Hartin 2006 found the mean length of hospital stay was 36 days in the RIMN group and 38 days in the fixed-angle device group; they did not report the SD precluding pooled analysis.

Retrograde intramedullary nail versus non-locking plate fixation

DeCoster 1995 compared RIMN versus buttress plate fixation in 18 participants with open distal femur fractures.

There was very low-certainty evidence. We downgraded two levels due to study limitations of being a quasi-randomised study and substantial risk of performance and detection bias and two levels due to serious imprecision as there was only one study with 18 participants.

Critical outcomes

Validated patient-reported functional outcomes of the knee

DeCoster 1995 did not report validated PROMs. Based on a categorical rating system that included clinical outcomes (knee range of motion and pain) and radiological outcomes (angulation and shortening), DeCoster 1995 reported there was no difference in functional outcome between the treatment groups (five participants in each group had excellent or good results).

Direct adverse events

DeCoster 1995 reported one infection in the RIMN group as a direct adverse event (RR 3.00, 95% CI 0.14 to 65.16; 18 participants; very low-certainty evidence; Analysis 3.1). Subsequent treatment for infection was not described.

Participant-reported quality of life

There were no data on participant-reported quality of life.

Pain

There were no data on pain.

Other important outcomes

All fractures healed, with delayed union occurring in one participant from each group (RR 1.00, 95% CI 0.07 to 13.64; 1 study, 18 participants, very low-certainty evidence; Analysis 3.2).

Locking plate versus single fixed-angle device

Two studies, including 130 participants, compared a locking plate (LISS or LCP) versus a single fixed-angle device (DCS or ABP). Canadian Orthopaedic Trauma Society 2016 compared a locking plate (LISS) versus a DCS in 53 participants with a supracondylar fracture of the distal femur; 27% of participants were lost to follow-up. Patterson 2020 compared an LCP with a 95° ABP in 78 participants with 79 distal femur fractures; 11 participants died prior to completion of follow-up.

Critical outcomes

Validated patient-reported functional outcomes of the knee

Both studies reported PROMs. However, pooled analysis could not be performed as neither study reported SDs. However, Canadian Orthopaedic Trauma Society 2016 reported functional outcomes in terms of the SMFA at six months and 12 months. The 12-month score was 37.6 in the LISS group versus 30.6 in the DCS group; the authors were unable to provide the SDs through correspondence. Patterson 2020 reported MFA at 12 months (41.4 with LISS versus 36.8 with DCS; SDs not reported).

Direct adverse events

Both studies reported data for direct adverse events (non-anatomical reduction, deep infection, revision required, failure of treatment, pain and implant prominence, superficial infection, implant removal, secondary procedures) but no subgroup analysis showed evidence favouring either intervention (Analysis 4.1). The secondary operations in the LISS group reported by Patterson 2020 were due to non-anatomical reduction, malunion, non-union, loss of reduction and failure of metal fixation non-union and early loss of reduction. We chose failure of treatment as the most clinically important and this showed little difference between the two implants (RR 2.29, 95% CI 0.68 to 7.66; 1 study, 52 participants; very-low certainty evidence). We downgraded the certainty of the evidence one level because of study limitations due to risk of performance bias of implants and high risk of attrition bias, and two levels due to imprecision due to the small number of participants available for pooling.

Participant-reported quality of life

There were no data for participant-reported quality of life.

Pain

There was no data for pain. Canadian Orthopaedic Trauma Society 2016 reported pain as a complication in two participants in the LISS group and one in the DCS group.

Other important outcomes

One study reported indirect adverse events and these were reported as deep vein thrombosis, pulmonary embolism and death (Canadian Orthopaedic Trauma Society 2016). The death was classified as indirect as the trial stated it was due to pneumonia and chronic obstructive pulmonary disease several months postoperatively, rather than as a direct result of the intervention. Effect estimates showed little or no difference between groups (Analysis 4.2). This was very low-certainty evidence. We downgraded two levels due to study imprecision because the number of participants was small from one study population and the CI were large and one level due study limitations because of high risk of performance bias and attrition bias.

Patterson 2020 defined non-union as a lack of persistent pain and incomplete cortical healing on at least three of four cortices on x-ray within six months. It was not possible to ascertain what Canadian Orthopaedic Trauma Society 2016 defined as non-union, but it was reported at 12 months. The pooled analysis for non-union did not favour either intervention (RR 3.56, 95% CI 0.62 to 20.41; 2 studies, 130 participants; very-low certainty evidence; Analysis 4.3). We downgraded the certainty of the evidence two levels due to imprecision with wide CIs and a small number of participants and one level due to study limitations because of high risk of performance bias and attrition bias.

Patterson 2020 also reported malunion defined as minor deformity, defined by greater than 5° in any plane, or major deformity by greater than 10° at six months. There was no evidence of a difference between groups (Analysis 4.3).

Internal fixation versus distal femoral replacement

One study compared internal fracture fixation versus DFR in 23 participants aged over 65 years (mean age 89.9 years) (Hull 2019).

The certainty of the evidence was very low. We downgraded one level due to study limitations of being a feasibility study with a high risk of performance bias and risk of reporting bias and two levels due to imprecision because of a low numbers of participants and wide CI.

Critical outcomes

Validated patient-reported functional outcomes of the knee

Hull 2019 reported PROMs as median with interquartile range (IQR), which could not be displayed in forest plots. The OKS is a 12-item questionnaire scored from 0 to 48, where higher scores represent better function. Hull 2019 reported higher median OKS in participants treated with DFR compared to those treated with internal fixation (OKS: median: 31, IQR 30 to 32 with DFR versus 26.5, IQR 20.8 to 33.3 with internal fixation). Similarly, DRI score at nine months was higher with DFR compared to internal fixation (median: 9, IQR 8.95 to 9.05 with DFR versus 5.15, IQR 4.88 to 5.43 with internal fixation).

Direct adverse events

There was no evidence of a difference in direct adverse events (superficial infection and additional procedures) between groups (Analysis 5.1). Additional procedures was deemed to be most clinically relevant and showed no difference between interventions (RR 0.40, 95% CI 0.02 to 8.78; 1 study, 20 participants).

Participant-reported quality of life

We were unable to source the mean and SDs of the EQ-5D tariff scores by correspondence with study authors.

Pain

There were no data on pain.

Other important outcomes

Indirect adverse events were hospital readmissions, late stress fracture, compartment syndrome and pulmonary embolism. There was no evidence of a difference between groups (Analysis 5.2).

Hull 2019 reported little or no difference in length of stay (MD 3.47 days, 95% CI −5.56 to 12.50; 22 participants; Analysis 5.3) or operating time (MD −14.00 minutes, 95% CI −55.62 to 27.62; 22 participants; Analysis 5.3).

Resource use in terms of cost of operating favoured internal fixation (MD GBP −6566.48, 95% CI −10,211.20 to −2921.76; 22 participants; Analysis 5.4). In terms of mean National Health Services and Personal Social Services costs following discharge, there was no evidence of a difference between groups (MD GBP −15,040.58, 95% CI −47,723.65 to 17,642.49; 8 participants; Analysis 5.4).

Mono-axial plate versus poly-axial plate

Two studies (67 participants) compared a mono-axial plate versus a poly-axial plate (Hanschen 2014; Kanakaris 2019).

Critical outcomes

Validated patient-reported functional outcomes of the knee

Hanschen 2014 used the Tegner activity scale on a range from 0 to 10, with a higher score indicating a higher level of activity participation. Mono-axial plate group mean Tegner score at sixth months was 0.7 (SD 0.3) versus 1.5 (SD 0.5) in the poly-axial group. This outcome was not included in the pooled analysis due to the presence of another functional outcome in the same study.

We chose to use the OKS, which both studies reported. Pooled analysis at six months favoured the poly-axial plate (MD 7.10, 95% CI 4.89 to 9.30; 2 studies, 67 participants; very low-certainty evidence; Analysis 6.1). We downgraded the certainty of the evidence two levels due to inconsistency with heterogeneity of I^2 statistic of 87% and one level due to imprecision with few participants available for analysis.

There were missing data for Hanschen 2014 in the LISS group at 12 months precluding pooled analysis at 12 months assessment. Therefore, data from Kanakaris 2019 showed no evidence of a difference at 12 months (MD −1.41, 95% CI −7.29 to 4.47; 40 participants; very low-certainty evidence; Analysis 6.2). We downgraded the certainty of the evidence two levels for study imprecision due to low number of participants available for pooling and wide CI and one level for study limitations due to one study having a number of unknown biases.

Hanschen 2014 reported radiological outcomes in the form of the Rasmussen score, which assesses articular depression, condylar widening, varus/valgus angulation and osteoarthrosis, with higher scores being better. This favoured the poly-axial plate (MD 6.30, 95% CI 5.14 to 7.46; 27 participants; low-certainty evidence; Analysis 6.3). An MCID has not been previously reported for this outcome score. We downgraded the certainty of the evidence two levels for study imprecision due to low number of participants from one study and one level for study limitations due to unknown study design biases.

Direct adverse events

Both studies reported at least one direct adverse event (superficial infection, secondary surgeries, hardware-related problems and mortality at three months). Effect estimates were imprecise and did not favour either intervention (Analysis 6.4). There was no evidence of a difference in secondary surgeries between groups (RR 2.76, 95% CI 0.61 to 12.61; 1 study, 40 participants; very low-certainty evidence). We downgraded the certainty of the evidence two levels due to imprecision with data only available for each adverse event from one study population only and each CI was wide and two levels due to study limitations due to unknown study design biases.

Participant-reported quality of life

It was not possible to extract EQ-5D scores in Kanakaris 2019, and we were unsuccessful in personal communication in acquiring these data.

One study reported no evidence of a difference in health-state VAS (MD 0.40 95% CI −0.56 to 1.36; 40 participants; low-certainty evidence; Analysis 6.5) (Kanakaris 2019). We downgraded the certainty of the evidence two levels for study imprecision due to low number of participants from one study and the CI crossing the line of no effect.

Pain

One study reported no evidence of a difference in knee pain measured using VAS (MD 0.00, 95% CI −0.59 to 0.59; 40 participants; low-certainty evidence; Analysis 6.6) (Kanakaris 2019). We downgraded the certainty of the evidence two levels for study imprecision due to low number of participants from one study and the CI crossing the line of no effect.

Other important outcomes

Hanschen 2014 reported indirect adverse events in peroneal lesions and compartment syndrome, but did not report any cases of these events (Analysis 6.7). This was deemed to be low-certainty evidence. We downgraded two levels for study imprecision due to low number of participants from one study available for analysis.

Kanakaris 2019 reported one malunion in both the poly-axial plate and mono-axial plate group (RR 1.11, 95% CI 0.07 to 16.47; 40 participants; low-certainty evidence; Analysis 6.8). We downgraded the certainty of the evidence two levels for study imprecision due to low number of participants from one study and wide CI.

It was not possible to perform pooled analysis of resource use as the SD was not reported and could not be obtained by correspondence. However, Kanakaris 2019 reported a length of stay of 20.5 days (range 10 to 43 days) in the poly-axial plate group versus 20.6 days (range 4 to 42 days) in the mono-axial plate group. Hanschen 2014 reported an operating time of 141.9 minutes in the poly-axial plate group versus 134.1 minutes in the mono-axial plate; SDs were not reported and hence not included in our analysis.

Mono-axial plate versus condylar buttress plate

One study compared a mono-axial plate (LISS) versus a condylar buttress plate in 78 participants aged over 18 years (mean age 55.6, SD 4.2 years in the LISS group versus 54.9, SD 4.0 years in the condylar plate group) (Xu 2015).

We downgraded the certainty of the evidence one level for study limitations due to unknown study design biases and two levels for imprecision due to low number of participants available for pooling and wide CI.

Critical outcomes

Validated patient-reported functional outcomes of the knee

Xu 2015 reported the Evanich score, which is similar to the modified Hospital for Special Surgery Knee score examining pain, function, range of motion, muscle strength and flexion deformity, to give a maximum score of 100, with higher scores showing better function. The Evanich was reported at 12 months showing a higher score in the LISS group versus the condylar buttress plate (MD −11.70, 95% CI −17.52 to −5.88; 78 participants; Analysis 7.1).

Direct adverse events

Xu 2015 reported superficial infection, haematoma formation and implant loosening as direct adverse events. There was no evidence of a difference between interventions (Analysis 7.2). Implant loosening was deemed to be most clinically relevant and showed no evidence of a difference (RR 0.14, 95% CI 0.01 to 2.68; 78 participants).

Participant-reported quality of life

There were no data participant-reported quality of life.

Pain

There were no data for pain.

Other important outcomes

Analysis of resource use showed a shorter length of stay favouring the mono-axial plate (MD −3.20 days, 95% CI −5.00 to −1.40; 1 study, 78 participants; low-certainty evidence; Analysis 7.3). This may be of importance to healthcare economics in terms of reducing costs of admission. Analysis of resource use in terms of operating time showed a quicker operating time in the mono-axial plate group (MD −2.80 minutes, 95% CI −6.55 to 0.95; favours mono-axial plate; 1 study, 78 participants; low-certainty evidence; Analysis 7.3). However, this small effect size is unlikely to be clinically important difference.

Different methods of non-surgical treatment

None of the studies reported comparisons of different methods of non-surgical treatment.

Surgical versus non-surgical treatment

One study compared surgical and non-surgical treatment. Butt 1996b compared DCS fixation versus skeletal traction followed by bracing in 42 people over 60 years of age (mean age 79 years) with displaced fractures of the distal femur. Two people, one of whom died in hospital, in the traction group were excluded because they should have been judged unfit for surgery. Moreover, one person in the surgery group was crossed over to the traction group when the person's family refused permission for surgery. Since our attempts to contact the authors were unsuccessful, the data presented below were based on 'treatment received' and not intention-to-treat.

The evidence was very low certainty. We downgraded two level due to imprecision (one level for low participant number and one level as the CI indicated benefit and harm) and one level for study limitations as the risk of bias was substantial due to high risk of selection bias in quasi-randomised study.

Critical outcomes

Validated patient-reported functional outcomes of the knee

Butt 1996b did not report PROMs.

Direct adverse events

There was no evidence of a difference in between-group differences in clinically relevant adverse events. We presented death as the most important clinical adverse event, which showed no evidence of a difference between the two interventions (RR 2.0, 95% CI 0.20 to 20.33; 1 study, 40 participants; Analysis 8.1).

Participant-reported quality of life

Butt 1996b did not report participants-reported quality of life.

Pain

Butt 1996b did not report pain.

Other important outcomes

There was no evidence of a difference in adverse events indirectly related to the procedure (Analysis 8.2). Of note, however, was that the complications, such as pressure sores, more associated with immobilisation and longer hospital stays occurred in greater numbers in the traction group.

Based on a categorical rating system that included clinical and radiological outcomes (extension, flexion, valgus/varus/rotational deformity, pain, joint congruency), Butt 1996b found greater numbers with excellent or good treatment outcomes with surgery (9/17 in surgical group versus 6/19 in non-surgical group). As this was not a validated PROM, analysis was not performed in this review. There was no difference between the two groups in delayed union (1/17 in surgical group versus 2/19 in non-surgical group) or malunion (1/17 in surgical group versus 3/19 in non-surgical group) (Analysis 8.3). Mean hospital stay was on average 33 days shorter in the surgery group (39 days, range 20 to 79 in surgical group versus 62 days, range 40 to 120 in non-surgical group). However, no statistical analysis was performed to compare the two means and no SD was given to allow for an effect estimate.

DISCUSSION

Summary of main results

We found 14 studies (eight RCTs, two randomised feasibility trials and four quasi-RCTs). Seven studies were new since the previous version of this review. They involved 753 participants (755 fractures). The studies included 18 to 156 participants. We also identified five ongoing studies.

There are eight main comparisons in this review. We present the main findings below between RIMN versus locking plate.

Three studies (210 participants) compared RIMN versus locking plate fixation (Gill 2017; Griffin 2019; Tornetta 2013). The evidence for this comparison is summarised in Summary of findings 1. There was very low-certainty evidence of little difference in short-term PROMs. There was low-certainty evidence of little or no difference in long-term PROMs, with re-expressing the SMD showing no MCID. We found very low-certainty evidence of little or no difference between the two implants in direct adverse events. There was very low-certainty of evidence of little or no improvement in quality of life at short- and long-term follow-up. No studies reported pain.

The seven other comparisons were RIMN versus single fixed-angle device (three studies, 159 participants), RIMN versus non-locking (buttress) plate (one study, 18 participants), locking plate versus single fixed-angle device (two studies, 130 participants), internal fixation versus DFR (one study, 23 participants), mono-axial plate versus poly-axial plate (two studies, 67 participants), mono-axial plate versus condylar buttress plate (one study, 78 participants) and surgical versus non-surgical management (one study, 42 participants). The certainty of the evidence for outcomes in these comparisons was low to very low with effect estimates being too imprecise to make any meaningful conclusions.

Overall completeness and applicability of evidence

Only limited data were available for single comparisons, ranging from eight to 198 participants with distal femur fractures. Although the studies were small, the studies' eligibility criteria were comparatively broad, reflecting the population sustaining this injury. They were performed in several centres in eight different countries (Australia, Canada, China, Germany, Greece, India, the UK and the USA). Studies included participants aged between 16 and 98.8 years, including both males and females. Most studies included participants with both open and closed fractures of the distal femur. However, only four studies included periprosthetic fractures and only represented a few participants (Hanschen 2014; Hartin 2006; Kanakaris 2019; Tornetta 2013). While Kanakaris 2019 reported a pilot RCT, we are currently unable to inform clinical practice in people with this complex injury with numbers being too low to include subgroup analysis for this review.

There was limited reporting of PROMs with only 7/14 studies reporting complete PROMS with mean and SDs that could be included for analysis (Gill 2017; Griffin 2019; Hanschen 2014; Hartin 2006; Kanakaris 2019; Tornetta 2013; Xu 2015). These PROMs were heterogeneous, with no consistency of the appropriate PROM to use. Of the PROMs included, few utilised health economics measurements and few presented data regarding health-related quality of life. Such tools are increasingly accepted as the principal means of determining the clinical and cost-effectiveness of treatments and would therefore influence the availability of these treatments in some healthcare systems. A core outcome set containing PROMs would optimise the reporting in future studies on people with fractures of the distal femur.

Some studies were not representative in the intervention that is used in current practice. For example, one study investigated non-surgical interventions (Butt 1996b). However, with the push to reduce prolonged stays in hospital, is no longer in favour. Additionally, some studies investigated DCS, which is now not in frequent use, with more recent studies investigating locking plate technology. While our review found little difference between DCS and locking plates, locking plate technology has become widespread around the world, with more-recent studies in this review comparing mono-axial plates with poly-axial plates or condylar buttress plates. While two studies compared mono-axial plates to poly-axial plates, the number of participants was low. Furthermore, there was very low- to low-certainty evidence with which to make a definitive conclusion as to the superior plate.

More contemporary analysis of current clinical practice is RIMN or plate technology. Only three studies reported this comparison (Gill 2017; Griffin 2019; Tornetta 2013). However, one was a feasibility study (Griffin 2019), with another that reported results from a conference abstract (Tornetta 2013), and another at high risk of bias (Gill 2017). While at the 5% significance level the pooled 95% CI for the difference in PROMs crossed the line of no effect, it was notable that nearly all CIs favoured RIMN. Therefore, it is possible that even a small future trial on this question may move the result in favour of RIMN and reveal an important difference that the relatively low number of small studies has failed to detect.

Quality of the evidence

We used GRADE to assess the certainty of the evidence for the main comparisons for the critical outcomes in the review. The certainty of the evidence for most outcomes in each comparison was low. For study limitations, the risk of bias of the studies was substantial (Figure 2), reflecting the high risk of selection bias in the four quasi-RCTs, as well as the high risks of performance and detection biases from the difficulty of blinding implants from operators. Only 3/14 studies were at low risk of attrition bias (Hull 2019; Kanakaris 2019; Xu 2015). Most studies were small, reporting imprecise estimates, and likely to be at high risk of imprecision and type II error. Even for the comparison where pooling was possible, the total number of participants available for pooling was small (286 participants). We did not find a reason to downgrade due to risk of publication bias or indirectness.

Potential biases in the review process

The study authors utilised robust Cochrane methodology to search for eligible studies, extract data, assess the risk of bias and conduct GRADE assessments independently. Where data were missing from included studies, we contacted authors to request these data. Any changes to the protocol are stated in the Differences between protocol and review.

One review author (XG) is the lead author of one of the included trials and is also the Co-ordinating Editor of the Cochrane Bone, Joint and Muscle Trauma group. XG did not complete data extraction or risk of bias assessments for this study and he was not involved in the editorial evaluation of the review.

Agreements and disagreements with other studies or reviews

We identified four systematic reviews comparing interventions in the treatment of distal femoral fractures. The most recent systematic review and meta-analysis investigated distal femur replacement and open reduction and internal fixation of periprosthetic distal femur fractures (Wadhwa 2022). The review found no difference in complications or functional outcomes. Another review investigated geriatric fractures in studies with mean age of more than 55 years treated with distal femur replacement or surgical fixation (Salazar 2021). The review was inconclusive highlighting further trials are required to definitively

determine superior management for geriatric fractures. Another review aimed to evaluate early complications and reoperation rates in periprosthetic fractures, comparing open reduction and internal fixation, intramedullary nail and DFR (Quinzi 2021). The review was inconclusive showing no differences in major complications or reoperating rates. One review compared locking compression plates and RIMN to identify any differences in non-union rates requiring reoperation (Yoon 2021). Meta-analysis showed no difference in non-union rates.

One review concerned the treatment of fractures of the distal femur around a native knee (Zlowodzki 2006). This was mainly a review of case series and only included one quasi-RCT (Butt 1996b). They found no significant difference in outcome between interventions, in line with the results of this review. Another review concerned the treatment of fractures of the distal femur around a total knee replacement (Herrera 2008). This was a review of case series only. They found reduced RRs for developing non-union and revision surgery when comparing retrograde nail versus a traditional non-locked plate and also when comparing retrograde nail or locked plates versus non-operative treatment. However, there was substantial diversity amongst the included studies and the non-randomised nature of treatment allocation allows for the introduction of substantial bias. The review found no RCTs investigating exclusively periprosthetic fractures to compare with these conclusions.

AUTHORS' CONCLUSIONS

Implications for practice

This review highlights the serious limitations of the available evidence concerning current treatment of fractures of the distal femur in adults. The currently available evidence is incomplete and insufficient to inform current clinical practice.

Implications for research

In order to determine the effectiveness of contemporary treatments in the management of fractures of the distal femur, well-conducted, adequately powered randomised controlled trials are needed. Current studies are small or at high risk of bias, and thus it is still not possible with current evidence to inform clinical practice. We suggest that the eligibility criteria of trials should be broad to include as representative a sample of participants as possible. The trial design needs to allow for the technical difficulties of fixing some types of fracture, for example, severely comminuted Arbeitsgemeinschaft für Osteosynthesefragen/Association of the Study of Internal Fixation (AO/ASIF) C3 fractures or those about a knee arthroplasty where the separation of condylar elements precludes nail introduction. Fully pragmatic eligibility criteria where the details of this decision are left with the treating surgeon may be able to overcome these difficulties whilst still reporting outcomes for the full spectrum of this injury. Ideally, future trials would include a separate subgroup of people who sustain fractures about a knee arthroplasty, or investigate exclusively this population group. This review has highlighted additionally that poly-axial plates may help in periprosthetic or osteoporotic fractures, and future research should compare mono-axial and poly-axial plates in these fracture types. One current ongoing study may provide some answers to retrograde nail versus locking plate (NCT01973712). However, the registered outcomes are a timed-up and go test, rates of reoperation and rates of malunion. There is no intention to report on patient-reported outcome measures (PROMs), quality of life or cost-effectiveness. Moreover, only 94 participants are estimated to be enrolled, which may not give adequate power to detect differences between groups. The remaining ongoing studies are investigating different locking screws (ACTRN12617000493347; NCT01766648), different locking plates (ACTRN12619001023145), and DFR to surgical fixation (either plates/screws or retrograde nail) (NCT04076735).

We strongly recommend that future trials report primarily on validated disease/region-specific patient-reported functional outcome measures and patient-reported quality-of-life measures, such as the EuroQol 5 Dimensions (EQ-5D). To better enable comparisons, there should be consistency in the PROMs reported with an agreed core outcome set. Furthermore, measures of cost-effectiveness are key to enabling the widespread uptake of clinically effective technologies. At a minimum, follow-up should be reported at one and two years. All trials should be reported in full using the CONSORT guidelines.

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- Sign-off Editor (final editorial decision); Toby Lasserson, Deputy Editor-in-Chief, Cochrane;
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Joanne Elliott, Bone, Joint and Muscle Trauma Group;
- Methodological Editor (advised on methodology and review content): Toby Lasserson, Deputy Editor-in-Chief, Cochrane;
- Copy Editor (copy-editing and production): Anne Lawson, Central Production Service, Cochrane;
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REFERENCES

References to studies included in this review

Butt 1996b *{published data only (unpublished sought but not used)}*

* Butt MS, Krikler SJ, Ali MS. Displaced fractures of the distal femur in elderly patients. Operative versus non-operative treatment. *Journal Bone and Joint Surgery. British Volume* 1996;**78**(1):110-4.

Witt JD. Displaced fractures of the distal femur in elderly patients [letter, comment]. *Journal of Bone and Joint Surgery. British Volume* 1996;**78**:998.

Canadian Orthopaedic Trauma Society 2016 *{published data only (unpublished sought but not used)}*

* Canadian Orthopaedic Trauma Society. Are locking constructs in distal femoral fractures always best? A prospective multicenter randomized controlled trial comparing the Less Invasive Stabilization System with the minimally invasive dynamic condylar screw system. *Journal of Orthopaedic Trauma* 2016;**30**(1):e1-6.

Hawsawi H, Leighton R, Presis A, Barron L, Trask K, Stephen D, et al. A prospective randomised multicentre trial comparing the Less Invasive Stabilisation System (LISS) to the mini invasive dynamic condylar system (DCS) for distal femur fractures. *Journal of Bone Joint Surgery. British Volume* 2012;**94**(Supp XXI):66.

Leighton R, Dunbar M, Petrie D, Deluzio K, O'Brien P, Buckley R, et al. A prospective randomised multicentre trial comparing the Less Invasive Stabilisation System (LISS) to the mini invasive dynamic condylar system (DCS) for distal femur fractures. *Journal of Bone Joint Surgery. British Volume* 2011;**93**(Supp IV):305.

NCT00552331. Prospective randomized clinical study to evaluate the effects of Less Invasive Stabilization System (LISS) plating techniques in distal femoral fractures. clinicaltrials.gov/ct2/show/NCT00552331 (first received 1 November 2007).

Christodoulou 2005 *{published data only (unpublished sought but not used)}*

Christodoulou A, Terzidis I, Ploumis A, Metsovitis S, Koukoulidis A, Toptsis C. Supracondylar femoral fractures in elderly patients treated with the dynamic condylar screw and the retrograde intramedullary nail: a comparative study of the two methods. *Archives of Orthopaedic Trauma Surgery* 2005;**125**(2):73-9.

Dar 2009 *{published data only (unpublished sought but not used)}*

Dar GN, Tak SR, Kangoo KA, Halwai MA. Bridge plate osteosynthesis using dynamic condylar screw (DCS) or retrograde intramedullary supracondylar nail (RIMSN) in the treatment of distal femoral fractures: comparison of two methods in a prospective randomized study. *Turkish Journal of Trauma & Emergency Surgery* 2009;**15**(2):148-53.

DeCoster 1995 *{published data only (unpublished sought but not used)}*

DeCoster TA, Behzadi K, Naraghi F, Moneim MS, Jabczenski F. Clinical comparison of retrograde nail versus plate fixation for severe open distal femur fractures [abstract]. *Orthopaedic Transactions* 1995;**19**(2):343.

Gill 2017 *{published data only}*

Gill S, Mittal A, Raj M, Singh P, Singh J, Kumar S. Extra articular supracondylar femur fractures managed with locked distal femoral plate or supracondylar nailing: a comparative outcome study. *Journal of Clinical and Diagnostic Research* 2017;**11**(5):RC19-23.

Griffin 2019 *{published data only}*

Griffin XL, Costa ML, Phelps E, Drtsaki M, Png M, Achten J, et al. Retrograde intramedullary nail fixation compared with fixed-angle plate fixation for fracture of the distal femur: the TrAFFix feasibility RCT. *Health Technology Assessment* 2019;**23**(51):1-132.

* Griffin XL, Costa ML, Phelps E, Parsons N, Dritsaki M, Achten J, et al. Intramedullary nails versus distal locking plates for fracture of the distal femur: results from the Trial of Acute Femoral Fracture Fixation (TrAFFix) randomised feasibility study and process evaluation. *BMJ Open* 2019;**9**(5):e026810.

ISRCTN92089567. Trial of acute femoral fracture fixation. isrctn.com/ISRCTN92089567 (first received 26 May 2016).

Hanschen 2014 *{published data only}*

Hanschen M, Aschenbrenner IM, Fehske K, Kirchhoff S, Keil L, Holzapfel BM, et al. Mono- versus polyaxial locking plates in distal femur fractures: a prospective randomized multicentre clinical trial. *International Orthopaedics (SICOT)* 2014;**38**:857-63.

Hartin 2006 *{published data only (unpublished sought but not used)}*

Hartin NL, Harris I, Hazratwala K. Retrograde nailing versus fixed-angle blade plating for supracondylar femoral fractures: a randomized controlled trial. *ANZ Journal of Surgery* 2006;**76**(5):290-4.

Hull 2019 *{published data only}*

Hull P, Chou D, Lewis S, Carrothers AD, Queally JM, Allison A, et al. Knee Fix or Replace Trial (KFORT): a randomized controlled feasibility study. OTA Annual Meeting; 2019 Sept 25-28; Denver (CO).

* Hull PD, Chou DT, Lewis S, Carrothers AD, Queally JM, Allison A, et al. Knee Fix or Replace Trial (KFORT): a randomized controlled feasibility study. *Bone & Joint Journal* 2019;**101**(B):1408-15.

ISRCTN16109266. KFORT: Knee fix or replacement trial. www.isrctn.com/ISRCTN16109266 (first received 5 November 2015).

Kanakaris 2019 *{published data only}*

Kanakaris NK, Obakponovwe O, Krkovic M, Costa ML, Shaw D, Mohanty KR, et al. Fixation of periprosthetic or osteoporotic distal femoral fractures with locking plates: a pilot randomised controlled trial. *International Orthopaedics* 2019;**43**:1193-204.

Patterson 2020 *{unpublished data only}*

NCT00644397. Plate fixation of distal femur fractures: a protocol for a study of two plate options. clinicaltrials.gov/ct2/show/NCT00644397 (first received 26 March 2008).

Patterson BM, Breslin MA, Wadenpfuhl L, Vallier HA. New versus old: a prospective, randomized controlled trial comparing the 95° angled blade plate with the locking condylar plate for distal femur fractures. OTA Annual Meeting 2017; 2017 Oct 11-14; Vancouver (BC).

* Patterson BM, Breslin MA, Wadenpfuhl LK, Vallier HA. New versus old: 95 degree angled blade plate versus distal femoral locking plate. A randomized clinical trial. *Injury* 2020;**S0020-1383**(20):30985-2.

Tornetta 2013 *{published data only (unpublished sought but not used)}*

NCT00429663. A multicenter randomized trial comparing IM nails and plate fixation in distal femur fractures. clinicaltrials.gov/show/NCT00429663 (first received 9 February 2017).

* Tornetta P III, Egol KA, Jones CB, Ertl JP, Mullis B, Perez E, et al. Locked plating versus retrograde nailing for distal femur fractures: a multicenter randomized trial. Orthopaedic Trauma Association; 2013 Oct 9-12; Phoenix (AZ).

Xu 2015 *{published data only}*

* Xu L. LISS plate versus condylar plate internal fixation for the treatment of distal femoral fractures: difference in bone healing and knee joint functional prognosis [Chinese]. *Chinese Journal of Tissue Engineering Research* 2015;**19**(4):562-7.

References to studies excluded from this review

Firoozabadi 2012 *{published data only}*

Firoozabadi R, McDonald E, Nguyen TQ, Buckley JM, Kandemir U. Does plugging unused combination screw holes improve the fatigue life of fixation with locking plates in comminuted supracondylar fractures of the femur? *Journal of Bone & Joint Surgery. British Volume* 2012;**94**(2):241-8.

Gao 2013 *{published data only}*

Gao K, Gao W, Huang J, Li H, Li F, Tao J, et al. Retrograde nailing versus locked plating of extra-articular distal femoral fractures: comparison of 36 cases. *Medical Principles & Practice* 2013;**22**(2):161-6.

Han 2011 *{published data only}*

Han HS, Kim DH, Kang SB. The use of a ti-ni shape memory alloy ring bone fixator during the retrograde nailing of supracondylar femoral fractures. *Knee Surgery Related Research* 2011;**23**(4):231-5.

Horneff 2013 *{published data only}*

Horneff JG 3rd, Scolaro JA, Jafari SM, Mirza A, Parvizi J, Mehta S. Intramedullary nailing versus locked plate for treating supracondylar periprosthetic femur fractures. *Orthopaedics* 2013;**36**(5):561-6.

Liu 2014 *{published data only}*

* Liu Y, Li H, Zhang Y. Mono versus polyaxial locking plates in distal femur fractures: a prospective randomized multicentre clinical trial. International Orthopaedics 2014;**38**(7):1543.

Markmiller 2004 *{published data only}*

Markmiller M, Konrad G, Sudkamp N. Femur-LISS and distal femoral nail for fixation of distal femoral fractures: are there differences in outcome and complications? *Clinical Orthopaedics Related Research* 2004;**426**:252-7.

NCT00578019 *{published data only}*

NCT00578019. Comparison between LISS plating and intramedullary (IM) nailing for supracondylar femur fractures (LISS). clinicaltrials.gov/ct2/show/NCT00578019 (first received 20 December 2017).

NCT01553630 *{published data only}*

NCT01553630. Reamed locked plating – metaphyseal fractures of the distal femur and tibia. clinicaltrials.gov/show/NCT01553630 (first received 14 March 2012).

NCT01693367 *{published data only}*

NCT01693367. Dynamic locking screws 5.0 vs. standard locking screws in fracture of distal femur treated with locked plate fixation. clinicaltrials.gov/ct2/show/NCT01693367 (first received 4 January 2016).

Petsatodis 2010 *{published data only}*

Petsatodis G, Chatzisymeon A, Antonarakos P, Givissis P, Papadopoulos P, Christodoulou A. Condylar buttress plate versus fixed-angle condylar blade plate versus dynamic condylar screw for supracondylar intra-articular distal femoral fractures. *Journal of Orthopaedic Surgery (Hong Kong)* 2010;**18**:35-8.

Thomas 1981 *{published data only}*

Thomas TL, Meggitt BF. A comparative study of methods for treating fractures of the distal half of the femur. *Journal of Bone and Joint Surgery. British Volume* 1981;**63**:3-6.

Tornetta 2000 *{published data only}*

Tornetta P III, Tiburzi D. Reamed versus nonreamed antegrade femoral nailing. *Journal Orthopaedic Trauma* 2000;**14**(1):15-9.

Vallier 2012 *{published data only}*

Vallier HA, Immler W. Comparison of the 95-degree angled blade plate and the locking condylar plate for the treatment of distal femoral fractures. *Journal of Orthopaedic Trauma* 2012;**26**(6):327-32.

References to studies awaiting assessment

Mahar 2021 *{published data only}*

* Mahar S, Aziz S, Ahmed S, Kumar J, Ali S. Outcome of extra-articular fractures of distal femur: Less Invasive Stabilization on System (LISS) plating versus closed retrograde intramedullary interlocking nail. *Pakistan Journal of Medical & Health Sciences* 2021;**15**(5):1144-7.

References to ongoing studies

ACTRN12617000493347 *{published data only}*

ACTRN12617000493347. Does far cortical locking improve fracture healing in elderly patients distal femur fractures: a randomised, controlled, prospective, multi-centre study. anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12617000493347 (first received 23 January 2017).

ACTRN12619001023145 *{published data only}*

ACTRN12619001023145. A comparative study of distal femoral locking plates for the fixation of distal femoral fractures: long working length versus short working length titanium locking plates. anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12619001023145 (first received 26 May 2019).

NCT01766648 *{published data only}*

NCT01766648. Far cortical locking versus standard constructs for distal femur fractures (FCL). clinicaltrials.gov/show/NCT01766648 (first received 11 January 2013).

NCT01973712 *{published data only}*

NCT01973712. Periprosthetic distal femur fracture. clinicaltrials.gov/ct2/show/NCT01973712 (first received 31 October 2013).

NCT04076735 *{published data only}*

NCT04076735. DIFFIR: geriatric distal femur fixation versus replacement – a randomized controlled trial of acute open reduction internal fixation (ORIF) versus distal femoral replacement (DFR). clinicaltrials.gov/ct2/show/NCT04076735 (first received 3 September 2019).

Additional references

Arneson 1988

Arneson TJ, Melton LJ 3rd, Lewallen DG, O'Fallon WM. Epidemiology of diaphyseal and distal femoral fractures in Rochester, Minnesota, 1965–1984. *Clinical Orthopaedics and Related Research* 1988;**234**:188-94.

Butt 1996a

Butt MS, Krikler SJ, Ali MS. Displaced fractures of the distal femur in elderly patients. Operative versus non-operative treatment. *Journal of Bone & Joint Surgery. British Volume* 1996;**78**(1):110-4. [PMID: 8898139]

Court-Brown 2006

Court-Brown CM, Caesar B. Epidemiology of adult fractures: a review. *Injury* 2006;**37**(8):691-7.

Crist 2008

Crist BC, Della Rocca GJ, Murtha YM. Treatment of acute distal femur fractures. *Orthopedics* 2008;**31**(7):681-90. [PMID: 18705562]

Deeks 2011

Deeks JJ, Higgins JP, Altman DG. Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook/archive/v5.1/.

Foster 2006

Foster MC, Komarsamy B, Davison JN. Distal femoral fractures: a review of fixation methods. *Injury* 2006;**37**(2):97-108. [PMID: 16439229]

GRADEpro GDT [Computer program]

GRADEpro GDT. Version accessed 25 October 2021. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015. Available at gradepro.org.

Gustilo 1976

Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *Journal of Bone and Joint Surgery. American Volume* 1976;**58**(4):453-8.

Hake 2019

Hake ME, Davis ME, Perdue AM, Goulet JA. Modern implant options for the treatment of distal femur fractures. *Journal of the American Academy of Orthopaedic Surgeons* 2019;**27**(19):e867-75.

Hemmann 2021

Hemmann P, Friederich M, Körner D, Klopfer T, Bahrs C. Changing epidemiology of lower extremity fractures in adults over a 15-year period – a National Hospital Discharge Registry study. *BMC Musculoskeletal Disorders* 2021;**22**(456):1-24.

Herrera 2008

Herrera DA, Kregor PJ, Cole PA, Levy BA, Jonsson A, Zlowodzki M. Treatment of acute distal femur fractures above a total knee arthroplasty: systematic review of 415 cases (1981–2006). *Acta Orthopaedica* 2008;**79**(1):22-7.

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557-60.

Higgins 2011

Higgins JP, Altman DG, Sterne JA. Chapter 8: Assessing risk of bias in included studies Table 8.5a. Chapter 8: Assessing risk of bias in included studies. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook/archive/v5.1/.

Hoskins 2016

Hoskins W, Sheehy R, Edwards ER, Hau RC, Bucknill A, Parsons N, et al. Nails or plates for fracture of the distal femur? *Bone and Joint Journal* 2016;**98-B**(6):846-50.

Kolmert 1982

Kolmert L, Wulff K. Epidemiology and treatment of distal femoral fractures in adults. *Acta Orthopaedica Scandinavica* 1982;**53**(6):957-62. [PMID: 7180408]

Lefebvre 2021

Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I. Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (updated February 2021). Cochrane, 2021. Available from training.cochrane.org/handbook/archive/v6.2.

Lizaur-Utrilla 2020

Lizaur-Utrilla A, Gonzalez-Parreño S, Martinez-Mendez D, Miralles-Muñoz FA, Lopez-Prats FA. Minimal clinically important differences and substantial clinical benefits for Knee Society Scores. *Knee Surgery, Sports Traumatology, Arthroscopy* 2020;**28**(5):1473-8.

Marsh 2007

Marsh JL, Slongo TF, Agel J, Broderick JS, Creevey W, DeCoster TA, et al. Fracture and dislocation classification compendium – 2007: Orthopaedic Trauma Association classification, database and outcomes committee. *Journal of Orthopaedic Trauma* 2007;**21**(Suppl 10):S1-133.

Martinet 2000

Martinet O, Cordey J, Harder Y, Maier A, Bühler M, Barraud GE. The epidemiology of fractures of the distal femur. *Injury* 2000;**31**(Suppl 3):C62-3. [PMID: 11052383]

Meek 2011

Meek RM, Norwood T, Smith R, Brenkel IJ, Howie CR. The risk of peri-prosthetic fracture after primary and revision total hip and knee replacement. *Journal of Bone and Joint Surgery. British Volume* 2011;**93**(1):96-101. [PMID: 21196551]

Müller 1990

Müller ME, Nazarian S, Koch P, Schatzker J. The comprehensive classification of fractures of long bones. 1st edition. Berlin (Germany): Springer Berlin Heidelberg, 1990.

Pitta 2018

Pitta M, Esposito CI, Li Z, Lee YY, Wright TM, Padgett DE. Failure after modern total knee arthroplasty: a prospective study of 18,065 knees. *Journal of Arthroplasty* 2018;**33**(2):407-14.

Quinzi 2021

Quinzi DA, Ramirez G, Kaplan NB, Myers TG, Thirukumaran CP, Ricciardi BF. Early complications and reoperation rates are similar amongst open reduction internal fixation, intramedullary nail, and distal femoral replacement for periprosthetic distal femur fractures: a systematic review and `meta-analysis`. *Archives of Orthopaedic and Trauma Surgery* 2021;**141**:997-1006.

Rasmussen 1973

Rasmussen PS. Tibial condylar fractures. Impairment of knee joint stability as an indication for surgical treatment. *Journal of Bone and Joint Surgery (America)* 1973;**55**:1331-50.

Review Manager 2014 [Computer program]

Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Rosen 2004

Rosen AL, Strauss E. Primary total knee arthroplasty for complex distal femur fractures in elderly patients. *Clinical Orthopaedics and Related Research* 2004;**425**:101-5. [PMID: 15292794]

Salazar 2021

Salazar BP, Babian AR, DeBaun MR, Githens MF, Chavez GA, Goodnough LH, et al. Distal femur replacement versus surgical fixation for the treatment of geriatric distal femur fractures: a systematic review. *Journal of Orthopaedic Trauma* 2021;**35**(1):2-9.

Schatzker 1979

Schatzker J, Lambert DC. Supracondylar fractures of the femur. *Clinical Orthopaedics* 1979;**138**:77-83.

Schünemann 2011

Schünemann HJ, Oxman AD, Vist GE, Higgins JP, Deeks JJ, Glaziou P, et al. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S, editor(s), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook/archive/v5.1/.

Sterne 2017

Sterne JA, Egger M, Moher D, Boutron I. Chapter 10: Addressing reporting biases. In: Higgins JP, Churchill R, Chandler J, Cumpston MS, editor(s), Cochrane Handbook for Systematic Reviews of Interventions Version 5.2.0 (updated June 2017), Cochrane, 2017. Available from training.cochrane.org/handbook/archive/v5.2.

Tsai 2021

Tsai SS, Lin TY, Tischler EH, Hung KH, Chen CH, Osgood GM, et al. Distal femur fractures have a higher mortality rate compared to hip fractures among the elderly: insights from the National Trauma Data Bank. *Injury* 2021;**52**(7):1903-7.

Wadhwa 2022

Wadhwa H, Salazar B, Goodnough LH, van Rysselberghe NL, DeBaun MR, Wong H, et al. Distal femur replacement versus open reduction and internal fixation for treatment of periprosthetic distal femur fractures: systematic review and meta-analysis. Journal of Orthopaedic Trauma 2022;**36**(1):1-6. [DOI: 10.1097/BOT.0000000000002141]

Wall 2012

Wall EJ, May MM. Growth plate fractures of the distal femur. *Journal of Paediatric Orthopaedics* 2012;**32**(Suppl 1):S40-6.

Yoo 2015

Yoo JD, Kim NK. Periprosthetic fractures following total knee arthroplasty. *Knee Surgery & Related Research* 2015;**27**(1):1-9.

Yoon 2021

Yoon B, Park IK, Kim Y, Oh H, Choo SK, Sung Y. Incidence of nonunion after surgery of distal femoral fractures using contemporary fixation device: a meta-analysis. *Archives of Orthopaedic and Trauma Surgery* 2021;**141**(2):225-33.

Zlowodzki 2006

Zlowodzki M, Bhandari M, Marek DJ, Cole PA, Kregor PJ. Operative treatment of acute distal femur fractures: systematic review of 2 comparative studies and 45 case series (1989 to 2005). *Journal of Orthopaedic Trauma* 2006;**20**(5):366-71.

References to other published versions of this review

Griffin 2015

Griffin XL, Parsons N, Zbaeda MM, McArthur J. Interventions for treating fractures of the distal femur in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 8. Art. No: CD010606. [DOI: 10.1002/14651858.CD010606.pub2]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Butt 1996b

Study characteristics	
Methods	Quasi-RCT: allocation according to treatment preference of consultant on-call at time of admission. 4 consultants involved in study, 2 opted for surgical treatment and 2 opted for non-surgical treatment.
Participants	Setting: Russell's Hall Hospital, Dudley, UK Size: 42 participants; 20 in surgical group, 22 in non-surgical group Recruitment period: January 1988 to March 1991 Baseline characteristics: surgical group: 20 participants, mean age 77.6 years; non-surgical group: 22 participants, mean age 80.5 years; sex and fracture type not reported Inclusion criteria: aged > 60 years with displaced fractures of the distal femur Exclusion criteria: people who were physiologically unfit for surgery
Interventions	All participants received low-dose warfarin as thromboprophylaxis. Participants were then allocated to either: • **surgical treatment:** fracture was fixed with a DCS applied laterally, supplemented with bone graft if medial cortex was deficient. Continuous passive mobilisation prescribed for 48 hours postoperatively. Functional cast brace then applied when wound was healed, and person was mobilised with a walking frame. Intravenous antibiotics given preoperatively and 24 hours postoperatively; • **non-surgical treatment:** skeletal traction applied using a Denham pin and the limb placed in a Thomas splint with a Pearson knee flexion attachment. Splints removed at 3–4 weeks and Perkin's exercises were started. A functional cast brace applied at 6–8 weeks.
Outcomes	Schedule: not formally reported but until "union had been achieved". Outcomes: Schatzker and Lambert criteria (full extension, loss of flexion, valgus/varus/rotational deformity, pain, joint congruency), length of hospital stay, deep vein thrombosis, urinary tract infection, pneumonia, wound and pin tract infection, pressure sores, delayed union, malunion, loosening of implant or traction pin, death
Notes	Funding/sponsor/declarations of interest: authors reported no declaration of interest. No information provided on funding/sponsor. Attempt at personal communication unsuccessful

Butt 1996b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quotes: "randomised controlled trial"; "prospective study"; "Each of the four consultants remained on call for a week at a time; two opted for operative treatment and the others treated all patients by traction". Comment: quasi-randomised study.
Allocation concealment (selection bias)	High risk	Predictable allocation – allocation based on treatment preference of on-call consultant.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study compared surgical vs non-surgical treatment and so it was not possible to blind either participants or personnel. Each intervention carried out by a consultant surgeon: 2 consultants performed operative treatment and 2 consultants supervised non-operative treatment. However, details of providers of the specific intervention not specified.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding of outcome assessment. Additionally, outcome assessment was poorly reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	20 participants allocated to surgical treatment and 22 to non-surgical treatment. 1 participant crossed over from surgical to non-surgical group and 2 participants were excluded after allocation from the non-surgical group. In the final per-protocol analysis, 17 participants analysed in surgical group and 19 in non-surgical group. Overall attrition 6/44, but the cross-over gave rise to concern.
Selective reporting (reporting bias)	Unclear risk	No protocol available. Timing of outcome assessment not given.
Other bias	Low risk	We identified no other sources of bias.

Canadian Orthopaedic Trauma Society 2016

Study characteristics	
Methods	RCT
Participants	Settings: 7 academic centres, Canada Size: 52 participants; 28 in LISS (locking plate) group and 24 in DCS fixation group Recruitment period: 2003–2008 Baseline characteristics: 18 men, 35 women; mean age 54 years in DCS group, 65 years in LISS group; fractures included were AO/OTA type A1 (7 fractures), A2 (5 fractures), A3 (12 fractures), B3 (1 fracture), C1 (11 fractures), C3 (16 fractures) Inclusion criteria: aged ≥ 16 years with fracture of distal femur; injury occurred in last 14 days, only fractures classified as AO/OTA 33A1–33C2 Exclusion criteria: C3 fractures (complete articular fractures), fractures older than 14 days, polytrauma, infection, neurological disorder, vascular disorder, metabolic disorders, history of malignancy, immunosuppressant medication including steroids.

Canadian Orthopaedic Trauma Society 2016 *(Continued)*

Interventions	Participants were allocated to either: • **LISS:** plate inserted under vastus lateralis, with plate centred on central proximal femoral shaft. Distal screws placed in arthrotomy incision, whilst proximal placed through small incisions; • **DCS:** DCS screw inserted after guidewire insertion and reaming over it. DCS plate inserted over DCS screw. Proximal screws inserted using a small incision, with the remaining screws inserted percutaneously. Antibiotic prophylaxis (first-generation cephalosporin) given to all participants.
Outcomes	Schedule: 6 and 12 months Outcomes: overall complications, number of revisions, orthopaedic complications, deaths, deep vein thrombosis, pulmonary embolism, failure of treatment, SMFA, SF-36, time to union, non-anatomical reduction, non-union, malunion, loss of reduction, failure of metal fixation, pain and implant prominence, range of motion and gait analysis
Notes	Communication with authors to request SD unsuccessful. Funding/sponsor/declarations of interest: study authors received financial support from industry, and are also members of editorial boards. Funding provided by 2 companies: AO Research Fund and a grant from Synthes.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Computer software was used to generate a random list of assignments, and this was put into consecutively numbered sealed envelopes that were sent to each site".
Allocation concealment (selection bias)	Low risk	Quote: "Computer software was used to generate a random list of assignments, and this was put into consecutively numbered sealed envelopes that were sent to each site".
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that operating surgeons were not blinded. No details relating to participant blinding. All surgeries performed by experienced orthopaedic trauma surgeons.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	Loss to follow-up 27%.
Selective reporting (reporting bias)	High risk	Trial registration mentions SF-36, lower extremity measure and gait analysis as outcomes, but no data reported.
Other bias	Low risk	We identified no other sources of bias.

Christodoulou 2005

Study characteristics

Christodoulou 2005 *(Continued)*

Methods	Quasi-RCT: allocation alternated between interventions after stratification by fracture type
Participants	Setting: Hippokratio General Hospital, Thessaloniki, Greece Size: 80 participants; 35 in nail group, 37 in plate group (allocation not reported in 8 participants, 5 died and 3 lost to follow-up) Recruitment period: January 1994 to June 1999 (2000 in abstract) Baseline characteristics: 25 men, 47 women; median age 73.2 years (range 60–88 years); all fractures were closed without substantial soft tissue damage; fracture types in the nail group were AO/ASIF A1 34%, A2 40%, A3 14%, C1 9%, C2 3%; and in the plate group were A1 35%, A2 35%, A3 16%, C1 8%, C2 6%. Age, sex and other variables not reported Inclusion criteria: supracondylar fracture of femur Exclusion criteria: not reported
Interventions	Participants were allocated to either: • **RIMN via an intercondylar notch approach**. Nails were 20–25 cm long and locked with 2 proximal screws and 2 or 3 distal screws; • **DCS with 95° angle plate**. Primary autologous bone grafting of the medial cortex used in 3 participants. A tourniquet and wound drainage used for all participants. Prophylactic perioperative antibiotics and postoperative anticoagulants used in all participants. Continuous passive motion started on the 2nd or 3rd postoperative day and mobilisation with partial weight-bearing on 4th or 5th day.
Outcomes	Schedule: 6, 12, 24 and 52 weeks and annually thereafter. Mean follow-up 28 months (range 18–42 months) Outcomes: Schatzker and Lambert criteria (full extension, loss of flexion, valgus/varus/rotational deformity, pain and joint congruency), length of hospital stay, operation time, blood loss, radiological union, clinical union, complications, death
Notes	Funding/sponsor/declarations of interest: not reported Attempt at personal communication unsuccessful

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "allocation alternated between each intervention after stratification by AO fracture classification". Comment: quasi-randomised.
Allocation concealment (selection bias)	High risk	The next intervention for each fracture type was known.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The nature of the interventions meant that the operating surgeons were not blinded. No details relating to participant blinding. Providers of interventions not stated.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention made of blinding of outcome assessment. Additionally, outcome assessment poorly reported.

Christodoulou 2005 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only 10% participants were lost to follow-up: 5 died and 3 changed address. Allocation of these participants not reported and they were not included in final analysis.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Low risk	We identified no other sources of bias.

Dar 2009

Study characteristics	
Methods	Quasi-RCT: allocation alternated between interventions
Participants	Setting: Government Medical College Srinagar, Kashmir, India Size: 73 participants, 37 in nail group, 31 in plate group (5 participants lost to follow-up) Recruitment period: September 2002 to December 2004 Baseline characteristics: 41 men, 27 women; mean age 48 years (range 21–75 years); fracture types in nail group were AO/ASIF A1 6, A2 11, A3 16, C1 2, C2 2; in plate group were A1 4, A2 9, A3 12, C1 3, C2 3 Inclusion criteria: not reported Exclusion criteria: not reported
Interventions	Participants were allocated to either: • **intramedullary supracondylar nail** inserted retrograde through a patella tendon splitting approach. Intramedullary canal reamed in all participants and statically locked at both ends; • **DCS fixation** through a small lateral incision. The guidewire was inserted 1.5–2 mm proximal to joint line and at junction of the anterior one-third and posterior two-thirds of the lateral condyle parallel to anterior and inferior planes of condyles. Intercondylar fractures fixed with 6.5 mm cancellous bone screws. Condylar complex and femoral shaft reduced indirectly without opening fracture site. Plate inserted retrograde beneath the vastus lateralis muscle and fixed to the femoral shaft by cortical screws through a limited proximal incision. Primary bone grafting was not used in any participants. Active- and passive-assisted exercises of the knee joint started on second day postoperatively and participants were mobilised on third postoperative day with help of crutches. Full weight-bearing permitted only after clinical and radiological union of fracture.
Outcomes	Schedule: weekly for 3 months, monthly for 12 months, and then every 3 months for a mean 30 months (range 24–36 months) Outcomes: operation time, blood loss, time to union, union risk, range of motion, deep vein thrombosis, shortening and malalignment, postoperative infection, implant failure, hardware prominence, nonunion, delayed union and stiffness
Notes	Funding/sponsor/declarations of interest: not reported Attempt at personal communication unsuccessful
Risk of bias	
Bias	**Authors' judgement** **Support for judgement**

Dar 2009 *(Continued)*

Random sequence generation (selection bias)	High risk	Quote: "the patients were allocated to two groups randomly one after the other". Comment: we interpreted this as meaning that allocation was alternated. Hence, it was quasi-randomised.
Allocation concealment (selection bias)	High risk	Allocation was predictable as it alternated between interventions.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that operating surgeons were not blinded. No details relating to participant blinding. Providers of interventions not stated.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding of outcome assessment. Additionally, method of outcome assessment not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only 5/73 participants were lost to follow-up although allocation of these participants not reported. (If randomised by alternation, then is it possible that all 5 participants were in the DCS group.) Thus, at unclear risk of bias.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Low risk	We identified no other sources of bias.

DeCoster 1995

Study characteristics	
Methods	Quasi-RCT: allocation alternated between interventions
Participants	Setting: University of New Mexico, Albuquerque, USA Size: 18 participants Recruitment period: not reported Baseline characteristics: mean age 35 years (range 19–45 years); sex not reported; fractures included were AO/ASIF type A3 (5 fractures), C1 (1 fracture), C2 (7 fractures), C3 (5 fractures) Inclusion criteria: severe open, Gustilo grade 3A or 3B, distal femur fractures; all injuries caused by high-energy trauma Exclusion criteria: not reported
Interventions	All participants initially treated with debridement and irrigation of wound and fracture. Articular fragments reduced and held with lag screws. Articular component of fracture then reduced and fixed to diaphysis of the femur using either: • **RIMN fixation**; • **indirect reduction and (buttress) plate fixation**. Range of motion exercises commenced immediately postoperatively and weight-bearing allowed after appearance of callus on x-rays.

DeCoster 1995 *(Continued)*

Outcomes	Schedule: not specifically reported but mean participant follow-up was variably reported as 28 months (range 18–46 years) and 26 months (range 17–50 years) in abstract. Outcomes: operative time, blood loss, time to union, functional outcome (rating scale based on clinical and radiological measures) and complications
Notes	Only an abstract available. Therefore, we are unaware of any funding/sponsor/declaration of interests. Attempt at personal communication unsuccessful.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "were alternately treated with either retrograde nail or plate". Comment: quasi-randomised.
Allocation concealment (selection bias)	High risk	Allocation was predictable as it alternated between interventions.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that operating surgeons were not blinded. No details relating to participant blinding. Providers of interventions not stated.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding of outcome assessment. Additionally, methods of outcome assessment not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers lost to follow-up not reported.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Unclear risk	Study report only available as an abstract. With limited information, uncertain if there were other risks of bias.

Gill 2017

Study characteristics

Methods	RCT
Participants	Setting: Uttar Pradesh Rural Institute of Medical Sciences & Research Size: 42 participants; 22 participants in locking plate group, 20 participants in retrograde nail group Recruitment period: July 2011 to January 2014 Baseline characteristics: 29 male, 13 female; mean age 38.7 (SD 15.6) years in locking plate group, 36.0 (SD 14.1) years in nail group; fractures included were AO/OTA type A1 (16 fractures), A2 (18 fractures), A3 (8 fractures); 12 open fractures, 30 closed fractures

Gill 2017 *(Continued)*

	Inclusion criteria: aged > 18 years; supracondylar femur fractures and supracondylar fractures with fracture line extending to distal third of femoral shaft; people with polytrauma without ipsilateral lower limb fractures. Exclusion criteria: follow-up < 18 months, fractures with intra-articular extensions, associated knee ligament tears, old fractures (> 3 weeks), Gustilo grade 3b and 3c open fractures, associated neurovascular injury, pre-existing significant ipsilateral limb joint arthritis or comorbidities hampering rehabilitation, periprosthetic supracondylar femur fractures
Interventions	Participants were allocated to either: • **locking plate (LISS technique):** locked screws inserted in proximal part of bone through plate, and reduction and hardware checked with fluoroscopy; • **RIMN:** guidewire inserted, fracture reduced and guidewire extended to proximal fragment up to a level proximal to lesser trochanter with sequential reaming in 1 mm increments.
Outcomes	Schedule: 2 weeks, 4 weeks, and then monthly until 6 months, thereafter 3-monthly Outcomes: mean operating time, intraoperative blood loss, union rate, mean time to union, range of motion, KSS, VAS, union disturbance rate, delayed union, non-union, malalignment > 10°, malalignment 5–10°, superficial infection, deep infection, haematoma formation, anterior knee pain, implant loosening
Notes	Funding/sponsor/declarations of interest: authors reported no declaration of interest. No information provided on funding or sponsors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention of allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions means that operating surgeons were not blinded. No details relating to participant blinding. Surgeries performed by same team of orthopaedic surgeons.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding in manuscript.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated. Patients were excluded if their follow-up was < 18 months and data were not reported for them.
Selective reporting (reporting bias)	High risk	No mention of prospective registration of trial. Quote: "Pain was assessed on Visual Analogue Scale (VAS)". However, no data reported in paper.
Other bias	Low risk	We identified no other sources of bias.

Griffin 2019

Study characteristics	
Methods	Randomised controlled feasibility trial
Participants	Setting: 7 NHS hospitals in England Size: 23 participants; 11 in retrograde intramedullary group, 12 in anatomical locking plate group Recruitment period: October 2016 to August 2017 Baseline characteristics: 16 female, 7 male; mean age 78.7 (SD 24.9) years in anatomical locking plate group, 70.1 (SD 13.6) years in RIMN group; fractures included were AO/OTA type A1 (12 fractures), A2 (5 fractures), A3 (1 fracture), B1 (1 fracture), C2 (2 fractures), C3 (3 fractures) Inclusion criteria: aged ≥ 18 years with fracture of distal femur, which treating surgeon believed would benefit from internal fixation Exclusion criteria: loose knee or hip arthroplasty requiring revision, or an arthroplasty or pre-existing femoral deformity that precluded nail fixation
Interventions	Participants were randomised to either: • **anatomical locking plate:** anatomical distal femoral locking plate and screws, with ≥ 1 fixed-angle locking screw; • **RIMN:** fixation achieved with proximally and distally locked nail. All participants received anaesthesia, analgesia and prophylactic antibiotics.
Outcomes	Schedule: 6 weeks and 4 months Outcomes: recruitment rate, EQ-5D-5L, EQ-VAS, Demential Quality of Life, DRI, rate of weight-bearing, rate of discharge, grip strength (kg), loss of fixation, varus/valgus > 5%, recurvatum > 10°, procurvatum > 10°, shortening > 1 cm, wound infection, venous thromboembolism, pneumonia, urinary tract infection, cerebrovascular accident, myocardial infarction, blood transfusion, malunion, failure of fixation, cost of surgery, length of stay
Notes	Funding/sponsor/declarations of interest: 1 co-author was a member of the board of the organisation that provided funding. Funding was provided by National Institute for Health Research Health Technology Assessment.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation using an online randomisation system.
Allocation concealment (selection bias)	Low risk	Participants not informed of their allocation during trial. Only informed at end of trial.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants not informed of their allocation during the trial but were able to request to be informed of their allocation at end of study. Nature of interventions means that operating surgeons were not blinded. Operations broken down into various grades of operating surgeons, which were "well-matched".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Radiographs reviewed by independent assessors; however, due to presence of implants they were also not blinded.

Griffin 2019 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Completeness of EQ-5D data reduced with time in follow-up. Participants may have been lost to follow-up in systematic manner. However, low attrition bias for other outcome measures.
Selective reporting (reporting bias)	Low risk	Trial prospectively registered and fully reported.
Other bias	Low risk	We identified no other sources of bias.

Hanschen 2014

Study characteristics	
Methods	Prospective RCT
Participants	Setting: 4 university trauma centres in South Germany Size: 27 participants; 12 to LISS group, 15 to NCB group) Recruitment period: 2008–2011 Baseline characteristics: 8 males, 19 females; mean age 63.9 years in LISS group, 73.1 years in NCB group; fractures included were AO/OTA type A (11 fractures), B (3 fractures), C (7 fractures); 6 periprosthetic fractures and 5 open fractures. Inclusion criteria: fractures of distal femur; all type 33-A (11), 33-B (3) and 33-C (7) fractures were included, as well as periprosthetic fractures of the distal femur. Exclusion criteria: none listed
Interventions	Either a standardised antero-lateral or additional medial approach used to reduce fragments. Temporary fixation achieved using K-wires, screws or clamps. Locking plate then applied with temporary K-wire fixation. Plate then fixed. Participants randomised to: • **LISS**; • **NCB**. All participants received prophylactic antibiotics. Physiotherapy commenced postoperatively with range of motion exercises. Participants instructed to be non-weight-bearing for 6–8 weeks.
Outcomes	Schedule: 1 and 6 weeks; 3, 6, 9 and 12 months Outcomes: mean operating time, mean intraoperative x-ray time, mean skin cut length, need for skin cut extension, mean size of implant, intraoperative arthroscopy, surgical complication (wound infection, peroneal lesions, compartment syndrome), range of motion, cruciate ligament stability, collateral ligament stability, VAS, OKS, Rasmussen score, Lysholm score, Tegner score
Notes	Funding/sponsor/declarations of interest: study author instructor for a course provided by 1 of the companies producing implants. No information provided on funding or sponsors.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomised according to a randomisation plan (Randlist). To ensure balanced randomisation in all 4 trauma centres, randomisation performed blockwise.

Hanschen 2014 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No mention of allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that the operating surgeons were not blinded. No details relating to participant blinding. All surgeons described as experienced.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers of participants with data for each variable not reported, though no reporting of missing data.
Selective reporting (reporting bias)	Unclear risk	No study prospectively published protocol or registration exists.
Other bias	Low risk	We identified no other sources of bias.

Hartin 2006

Study characteristics	
Methods	RCT
Participants	Settings: 2 regional trauma centres in New South Wales, Australia Size: 22 participants with 23 supracondylar fractures of the femur, 12 in nail group, 11 in plate group Recruitment period: August 2001 to October 2003 Baseline characteristics: 7 men, 16 women; mean age 68 years Inclusion criteria: all AO/ASIF type 33-A and 33-C type fractures Exclusion criteria: AO/ASIF type 33A1.1 (avulsion fractures); skeletally immature people; concurrent ipsilateral proximal or mid-shaft fractures of femur
Interventions	Surgery performed in a manner consistent with AO principles is all cases. Participants allocated to either: • **intramedullary nail** fixation inserted retrograde without anatomical reduction of metaphysis; • **95° fixed-angle condylar blade plate** fixation achieved open with anatomical reduction and interfragmentary compression where possible. Postoperatively, all participants received intravenous antibiotics for 36 hours. Active range of motion exercises permitted immediately and participants not permitted to weight-bear for 12 weeks or until evidence of callus formation seen on x-rays
Outcomes	Schedule: not specifically reported but a minimum of 12 months (mean follow-up 20 months, range 12–36 months) Outcomes: operation time, blood transfusion requirement, length of hospital stay, wound infection, complications, death, union, malalignment and shortening, infection, knee flexion and extension loss, SF-36 and reoperation

Hartin 2006 *(Continued)*

Notes	3 participants in blade plate group had their procedure augmented; 1 received a DCS and 2 received additional buttress plates or interfragmentary screws. Attempt at personal communication unsuccessful. Funding/sponsor/declarations of interest: not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was carried out by a remote source, contactable by telephone, using odd and even numbers from a random number table in blocks of 10". Comment: appropriate method of sequence generation.
Allocation concealment (selection bias)	Low risk	Quote: "randomization was carried out by a remote source, contactable by telephone, using odd and even numbers from a random number table in blocks of 10". Comment: distant randomisation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant operating surgeons were not blinded. No details relating to participant blinding. Providers of interventions not stated.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "clinical assessment was made at follow up by the relevant operating surgeon". Comment: thus, there was no blinding of outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	4/22 participants not available for complete follow-up: 3 died and 1 lost to follow-up. Only data from 16 participants available for the quality-of-life assessment. 1 person had a bilateral fracture; group was not identified.
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration document available.
Other bias	Low risk	We identified no other sources of bias.

Hull 2019

Study characteristics

Methods	Randomised controlled feasibility trial
Participants	Setting: 7 centres in the UK Size: 23 participants; 12 in internal fracture fixation group, 11 in distal femoral replacement group Recruitment: 23 October 2015 to 15 August 2017 Baseline characteristics: 23 women; mean age 89.9 years in internal fracture fixation group and 87.9 years in distal femur replacement group; no breakdown of fracture classifications in manuscript.

Hull 2019 *(Continued)*

	Inclusion criteria: aged > 65 years with a distal femoral fracture; treating surgeon considered them suitable for either internal fracture fixation or DFR Exclusion criteria: ipsilateral total knee arthroplasty, open fracture, unfit for anaesthesia, immobile prior to the injury
Interventions	Participants were randomised to either: • **internal fracture fixation:** treated either a lateral locking plate or locked retrograde femoral nail; • **distal femoral replacement:** using an implant chosen by surgeon. Rehabilitation programme according to treating surgeon, which was documented as well as weight-bearing status and frequency of physiotherapy treatments.
Outcomes	Schedule: 6 weeks, 6 months and 9 months Outcomes: EQ-5D-5L, OKS, DRI, adverse events (additional procedure, superficial infection, late stress fracture, compartment syndrome, pulmonary embolus), knee range of motion for knee extension and flexion, health economic data (time in theatre, length of hospital stay, additional procedures, hospital readmissions, resource use, readmission length of stay, mean hospital cost, mean NHS and PSS cost following discharge), walking with or without aids prior to discharge, residence at baseline and at each follow-up.
Notes	Authors contacted to request mean and SD of the EQ-5D tariff scores, but unsuccessful. Funding/sponsor/declarations of interest: funding provided from National Institute for Health Research. Authors reported no conflict of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation sequence generated by Cambridge Clinical Trials Unit through a secure web-based randomisation service.
Allocation concealment (selection bias)	Low risk	Randomisation performed by professional Clinical Trials Unit online through secure-service.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that operating surgeons were not blinded. No details relating to participant blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No mention of blinding in manuscript.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	23% of participants withdrew after their operation, of whom 4 were in the intervention group and 2 were in the control group. It is unclear what effect this would have on the data.
Selective reporting (reporting bias)	High risk	Not all study's prespecified primary outcomes reported (radiographic findings and knee ROM) www.isrctn.com/ISRCTN16109266.
Other bias	Low risk	We identified no other sources of bias.

Kanakaris 2019

Study characteristics	
Methods	Pilot RCT
Participants	Setting: 4 UK centres Size: 40 participants; 21 in poly-axial plating system group, 19 in LISS group Recruitment period: December 2010 to December 2013 Baseline characteristics: 34 women, 6 men; median age 77 years in both groups; 33 A2/3/B/C 19 fractures, 17 periprosthetic fractures Inclusion criteria: aged > 60 years with displaced distal femoral fracture (AO/OTA 33-A1 to C3 fractures) of a participant with diagnosed osteoporosis to his/her medical history or a Singh index grade < 4 or a displaced distal femoral fracture above or below a femoral component of total knee or total hip arthroplasty (Rorabeck type 1–2 or Vancouver type C fracture Exclusion criteria: major organic pathologies (dementia, severe cardiovascular, hepatic, pulmonary, neurological, renal or known neoplastic disease scoring > 2 in the Charlson Comorbidity Index), pre-injury impaired mobility (household or non-functional ambulatory patients), associated trauma influencing ambulation or rehabilitation (or both), loose femoral components (as evaluated preoperatively based on x-rays CT-scans and intra-operative screening), fractures as a result of infection or metastatic disease (based on the medical history of patient)
Interventions	Participants were randomised to either: • **poly-axial plating system**; • **LISS system**. Standardised local antibiotic and venous thromboembolism prophylaxis guidelines were applied to all participants.
Outcomes	Schedule: 1, 3, 6, 9 and 12 months Outcomes: intraoperative blood loss, length of incision, duration of surgery, length of stay, OKS, VAS, health-state VAS, EQ-5D, union rate, delayed union, non-union, malunion, secondary surgeries, hardware-related problems, mortality
Notes	Authors contacted by e-mail to seek ED-5D tariff scores, but this could not be provided. Funding/sponsor/declarations of interest: authors reported no declaration of interest. Funding provided by DePuy International Limited, a company that provided LISS plates.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was performed using a ballot system of 40 sealed envelopes containing either a card of a POLYAX or LISS plating systems at a 1:1 ratio. A single sealed envelope was opened post the patient's signed informed consent and enrolment to the study from one of the investigators".
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was performed using a ballot system of 40 sealed envelopes containing either a card of a POLYAX or LISS plating systems at a 1:1 ratio. A single sealed envelope was opened post the patient's signed informed consent and enrolment to the study from one of the investigators".
Blinding of participants and personnel (performance bias)	High risk	Quote: "All patients were blinded to the treatment assignment until completion of follow-up".

Kanakaris 2019 *(Continued)*

All outcomes		However, nature of interventions means that operating surgeons were not blinded. Surgical fixations performed by 6 specialist trauma surgeons. Familiarity of each surgeon with either system not strictly controlled or matched during phases of trial. Thus, learning curve of each surgeon with either system may have affected recorded outcomes.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All patients were blinded to the treatment assignment until completion of follow-up as well as the outcome assessors".
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 participants died before completing follow-up, no other loss to follow-up (CONSORT flow chart at link.springer.com/article/10.1007%2Fs00264-018-4061-1).
Selective reporting (reporting bias)	Unclear risk	Trial did not appear to have been registered.
Other bias	Low risk	We identified no other sources of bias.

Patterson 2020

Study characteristics	
Methods	RCT
Participants	Setting: level I trauma centre, USA Size: 78 participants; 34 in ABP group, 44 in LCP group Recruitment: 2007–2016 Baseline characteristics: 31 male, 47 female; mean age 60 years (range 21–96 years); fractures were AO/OTA type A1 (9 fractures), A2 (11 fractures), A3 (18 fractures), C1 (12 fractures), C2 (29 fractures); 6 periprosthetic fractures and 5 open fractures; 17 fractures were open fractures. Inclusion criteria: skeletally mature patients with distal femur fracture requiring surgical management Exclusion criteria: AO/OTA 33C3.3 fractures with coronal plane fracture within medial or lateral (or both) condyle. Insufficient lateral cortex for blade insertion Gustilo and Anderson type IIIC open fractures, periprosthetic fractures, ipsilateral proximal femur fractures, pre-existing fracture devices
Interventions	All participants underwent reduction and fixation via a lateral approach. Surgeon discretion was utilised as to the technique of reduction and fixation. Participants were randomised to either: • **95° angled blade plate**; • **LCP**.
Outcomes	Schedule: 6 and 12 months (mean follow-up period 25 months) Outcomes: non-union, malunion ≥ 5°, malunion ≥ 10°, superficial and deep infections, implant removal, any secondary procedure, MFA
Notes	Funding/sponsor/declarations of interest: authors reported no declaration of interest or funding.
Risk of bias	
Bias	**Authors' judgement** **Support for judgement**

Patterson 2020 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Randomization was by sealed envelope in computer-generated random blocks of ten".
Allocation concealment (selection bias)	Low risk	Sealed envelope.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The nature of the interventions means that the operating surgeons were not blinded. There were no details relating to participant blinding. All experienced surgeons – "experienced and proficient with both devices".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Independent interviewer for PROMs, but no other mention of blinding for other outcome assessments.
Incomplete outcome data (attrition bias) All outcomes	High risk	Functional outcome reported for 55/79 participants and no reasons for missing data provided.
Selective reporting (reporting bias)	Unclear risk	Trial registered, but outcomes not assessed.
Other bias	Low risk	We identified no other sources of bias.

Tornetta 2013

Study characteristics	
Methods	RCT
Participants	Setting: multicentre study (22 listed in trial registration document) in USA Size: 156 participants, 80 in locking plate group, 76 in intramedullary nail group Recruitment period: February 2007 to (estimated) December 2012, expected date of completion December 2013 Baseline characteristics: 71 men, 55 women (of the 126 completing follow-up); mean age 51 years (range 16–90 years); mean Injury Severity Score 12.6 (range 9 to 43); 34% open fractures Inclusion criteria: skeletally mature; fracture of the metaphyseal distal femur with or without intra-articular extension and with or without a total knee arthroplasty; fracture requiring operative treatment amenable to either intramedullary nail or plate; informed consent obtained; English speaking Exclusion criteria: fracture of the metaphyseal distal femur with intra-articular comminution; fracture with vascular injury (Gustillo Type IIIC injury) requiring repair; pathological fracture; known metabolic bone disease; contralateral distal femur fractures (bilateral injury) or ipsilateral lower extremity injury that would compromise function of the knee; retained hardware or existing deformity in the affected limb that would complicate intramedullary nailing or plating; symptomatic knee arthritis; soft tissue injuries compromising either treatment method with nail or plate; surgical delay > 3 weeks for closed fractures or 24 hours for open fractures; immunocompromised; unable to comply with postoperative rehabilitation protocols or instructions (i.e. head injured or mentally impaired); current or impending incarceration; unlikely to follow-up in surgeon's estimation
Interventions	Participants were allocated to either: • **RIMN**;

Tornetta 2013 *(Continued)*

- **ORIF with locking plate**.

Outcomes	Schedule: 3, 6 and 12 months; 12-month follow-up reported to date; planned to be up to 24 months Outcomes: patient-reported functional and quality of life scores (SF-12 Version 2, EQ-5D, SMFA, KSS, clinical assessment, reoperation, non-union, malunion, infection, compartment syndrome, knee range of motion
Notes	Funding/sponsor/declarations of interest: no data provided on funding or sponsors. Authors reported affiliation with industry. Communication with authors unsuccessful.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization scheme was with permutated blocks for open and closed fractures using a HIPAA [Health Insurance Portability and Accountability Act]-compliant computer-based system". Comment: appropriate sequence generation.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "masking: open label" (trial registration). Comment: nature of interventions means that operating surgeons were not blinded. This also confirms that there was no participant blinding. Providers of interventions not stated.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "masking: open label" (trial registration). This confirms that there was no blinding of outcome assessors. Additionally, outcome assessment was poorly reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "156 patients were randomized … 126 patients were followed". Comment: 81% follow-up but allocations of those participants who were lost were not reported.
Selective reporting (reporting bias)	Unclear risk	Most outcomes described in trial registry entry were reported in conference abstract. However, no data reported beyond 1-year stage despite follow-up planned out to 2 years.
Other bias	Unclear risk	Study data were only reported as an abstract. With limited information, it was uncertain if other risks of bias were present.

Xu 2015

Study characteristics

Methods	RCT
Participants	Setting: Department of Orthopedics, Central People's Hospital of Huizhou City, China

Xu 2015 *(Continued)*

	Size: 78 participants; 39 in LISS group, 39 in condylar plate group Recruitment period: March 2009 to January 2013 Baseline characteristics: 54 male, 24 female; mean age: 55.6 (SD 4.2) years in LISS group, 54.9 (SD 4.0) years in condylar plate group; fractures included were AO type C1 (36 fractures), C2 (26 fractures), C3 (16 fractures) Inclusion criteria: aged ≥ 18 years; LISS plate or condylar plate selected for internal fixation; fresh fractures; informed consent signed, which was approved by the hospital ethics committee. Exclusion criteria: diseases of the heart, liver, kidney and other important organs; osteoporosis; autoimmune diseases; congenital malformation or disability of both lower limbs; contraindications for internal fixation
Interventions	Participant were randomised to: • **LISS**; • **condylar plate method**.
Outcomes	Schedule: mean follow-up 12.2 (SD 2.9) months in LISS group, mean follow-up 12.5 (SD 3.1) months in condylar plate method group Outcomes: mean operating time, length of stay, incision length, Evanich score, superficial infection, haematoma formation and implant loosening
Notes	Paper was translated to English to enable data extraction and review. Funding/sponsor/declarations of interest: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation by random number table.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Nature of interventions meant that operating surgeons were not blinded. No details relating to participant blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed follow-up, all included in the results analysis, and no dropouts.
Selective reporting (reporting bias)	Unclear risk	No protocol registered.
Other bias	Low risk	No other sources of bias.

AO: Arbeitsgemeinschaft für Osteosynthesefragen; ASIF: Association of the Study of Internal Fixation; CT: computer tomography; DCS: dynamic condylar screw; DRI: Disability Rating Index; EQ-5D: EuroQol-5 Dimensions; EQ-VAS: EuroQol-Visual Analogue Scale; KSS: Knee

Society Score; LCP: locking condylar plate; LISS: Less Invasive Stabilization System; MFA: Musculoskeletal Function Assessment; NCB: non-contact bridging; NHS: National Health Service; OKS: Oxford Knee Score; ORIF: open reduction and internal fixation; OTA: Orthopaedic Trauma Association; PSS: Personal Social Services; RCT: randomised controlled trial; RIMN: retrograde intramedullary nail; SD: standard deviation; SF-12: 12-item Short Form; SF-36: 36-item Short Form; SMFA: Short Musculoskeletal Function Assessment; VAS: Visual Analogue Scale.

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

Study	Reason for exclusion
Firoozabadi 2012	Not an RCT or quasi-RCT
Gao 2013	Not an RCT or quasi-RCT
Han 2011	Not an RCT or quasi-RCT
Horneff 2013	Not an RCT or quasi-RCT
Liu 2014	Not an RCT or quasi-RCT
Markmiller 2004	Not an RCT or quasi-RCT
NCT00578019	Trial abandoned due to the Primary Investigator moving institutions
NCT01553630	Study abandoned due to low enrolment
NCT01693367	Email communication 13 January 2020 stating 1 of the interventions (distal locking screw) removed from market. No data available.
Petsatodis 2010	Not an RCT or quasi-RCT
Thomas 1981	Not an RCT or quasi-RCT
Tornetta 2000	Participants were "all patients with femoral shaft fractures", excluding fractures within 3 cm from knee joint. It was not possible to extract the data specific to distal femoral fractures.
Vallier 2012	Not an RCT or quasi-RCT

RCT: randomised controlled trial.

Characteristics of studies awaiting classification *[ordered by study ID]*

Mahar 2021

Methods	Randomised controlled trial: no methods of randomisation described
Participants	Setting: Department of Orthopaedic Surgery, Ghulam Muhammad Mahar Medical College Sukkur Size: 100 participants; 50 in LISS group and 50 in RIMN group Recruitment period: 1 July 2019 to 31 December 2020 Baseline characteristics: 65 men, 35 women; 70 participants aged 20–40 years, 30 participants aged 40–60 years; OTA classification A1 64, A2 22, A3 14 Inclusion criteria: aged 20–60 years; fit for surgery with closed fractures AO33A; poly-trauma without ipsilateral lower limb fractures

Mahar 2021 *(Continued)*

	Exclusion criteria: intra-articular extensions; old fracture (> 3 weeks); open fractures; associated neurovascular injury; periprosthetic supracondylar femur fracture and any associated ipsilateral fracture of lower limb
Interventions	Participants were allocated to either: • **LISS plating** (operative details not stated); • **RIMN** (operative details not stated).
Outcomes	Schedule: not stated Outcomes: not stated explicitly, but mean time to union, NEERs classification and complications (presence of shoulder pain, superficial infection, delayed union, non-union, shoulder stiffness and elbow stiffness) presented in manuscript.
Notes	Contacted authors for a protocol or ethical approval form to confirm randomisation process. Authors were unable to provide this at this stage.

AO: Arbeitsgemeinschaft für Osteosynthesefragen; LISS: Less Invasive Stabilization System; OTA: Orthopaedic Trauma Association; RIMN: retrograde intramedullary nail.

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

ACTRN12617000493347

Study name	Distal femur fracture healing in the elderly using far cortical locking screws
Methods	Randomised, prospective, controlled, double-blind (patient and investigator), multicentre trial
Participants	Target 100 participants Inclusion criteria: age ≥ 60 years; men and women; capable of providing prospective informed consent; acute distal femur fractures; hip periprosthetic fractures and knee periprosthetic fractures; all fractures suitable for distal femur locking plate fixation; informed patient consent available from patient or legal guardian. Exclusion criteria: Glasgow Coma Scale score < 15 at time of informed consent; age < 60 years; limited life expectancy (likely unable to complete follow-up programme); anticipated treatment plan for fracture within first 12 weeks after surgical fixation includes procedures to promote fracture healing (e.g. use of autogenous bone graft, allograft, bone graft substitute, use of ultrasound, magnetic field or electrical stimulation); persistent compartment syndrome or compartment syndrome with clinically significant neurovascular residua in the fractured limb under study; femoral fracture is pathological (except if due to idiopathic osteoporosis); history of heterotopic ossification at any site; history of malignancy, radiotherapy or chemotherapy for malignancy within past 2 years except for basal cell carcinoma of skin; unwilling to return for required follow-up visits; unable to comply with rehabilitation and follow-up programme; premorbid non-ambulatory patients; open fracture patterns (Gustilo grade III open fractures); periprosthetic fractures Vancouver Type B1, B2 and B3 at the hip joint and Rorabeck type 3; other condition that, in judgement of Investigator, would prohibit patient from participating.
Interventions	Participants were allocated to either: • **far cortical locking screws**; • **standard locking screw**.
Outcomes	Primary outcome • CT-based radiological fracture healing at 3 months postsurgery with bridging callus on ≥ 2 cortices on ≥ 2 CT slices on a sagittal and coronal reconstruction

ACTRN12617000493347 *(Continued)*

	Secondary outcomes • Radiological healing using RUST score at 6, 12, 18, 26 and 52 weeks • Assurance of fracture healing (defined as by the absence of screw or plate failure and delayed or non-union) assessed using radiographs and CT scans at 6, 12, 18, 26 and 52 weeks • Volume of callus formation based on CT and radiographs at 6, 12, 18, 26 and 52 weeks • Patient clinical satisfaction assessed using VAS pain at 6, 12, 18, 26 and 52 weeks
Starting date	29 October 2016
Contact information	Dr Humza Khan; PO Box 541, Floreat, WA, 6014 (Royal Perth Hospital); humza.khan@health.wa.gov.au
Notes	

ACTRN12619001023145

Study name	A comparative study of distal femoral locking plates for the fixation of distal femoral fractures: long working length versus short working length titanium locking plates
Methods	Randomised controlled trial. Participants will be assigned to a single group
Participants	Targeted enrolment: 76 participants Inclusion criteria: men or women aged ≥ 18 years; fractures with AO classification 33-A1, 33-A2 and 33-A3 received within 1 week after sustaining the fracture Exclusion criteria: open fractures; polytrauma patients with other fractures such as ipsilateral tibia or proximal femur fractures; pathological fractures; previously surgically treated fractures; neurovascular injury/deep vein thrombosis; periprosthetic fractures
Interventions	Participants were allocated to either: • **titanium locking plate with long working length**; • **titanium locking plate with short working length**.
Outcomes	Primary outcome • Radiographic union at 8 months Secondary outcomes • Infection (composite secondary outcome) assessed clinically by recording pain using VAS • Swelling thigh measured with a tape and compared with the other normal thigh • Discharge from wound site assessed visually and collecting the discharge with a swab on stick • Fever recorded with a thermometer • Biochemically elevated white cell count, raised ESR, raised CRP.
Starting date	August 2019
Contact information	Dr Faaiz Ali Shah; Department of Orthopaedics & Traumatology Lady Reading Hospital, Peshawar, Khyber Pakhtunkhwa, Pakistan; faaizalisha@yahoo.com
Notes	

NCT01766648

Study name	Multicentre, randomized trial of far cortical locking versus standard constructs for acute, displaced fractures of the distal femur treated with locked plate fixation
Methods	Interventional, randomised, efficacy study. Participants will be assigned to a single group
Participants	Estimated enrolment: 130 participants Inclusion criteria: men or women aged ≥ 18 years; displaced distal femur fracture (OTA 33A or 33C) as seen in x-rays; planned treatment using a distal femur locking plate; fractures < 14 days' postinjury; provision of informed consent Exclusion criteria: open distal femur fracture; vascular injury present at the site of the fracture; planned fixation strategy includes interfragmentary lag fixation of non-articular fractures; history of previous femur infection; limited life expectancy due to significant medical comorbidity or medical contraindication to surgery; inability to comply with rehabilitation or form completion; likely problems, in the judgement of the investigators, with maintaining follow-up (i.e. people with no fixed address, people not mentally competent to give consent, etc.)
Interventions	Participants were allocated to either: • **far cortical locking screw fixation** (experimental); • **standard locking screw fixation** (active comparator).
Outcomes	Primary outcome • Fracture healing at 3 months: radiographic and clinical assessment of fracture healing defined as bridging of ≥ 2 cortices. Clinical healing assessed with FIX-IT Secondary outcomes: • Participant-reported quality of life and CT quantification of fracture callus volume (at 6 weeks, and 3, 6 and 12 months) • Participant-reported quality of life using 36-item Short Form at 4 follow-up intervals and CT scan at 3 months only
Starting date	December 2013
Contact information	Benita Okocha; Division of Orthopaedic Trauma, Vancouver General Hospital, Canada; benita.okocha@vch.ca
Notes	

NCT01973712

Study name	Treatment of periprosthetic distal femur fractures: a randomized controlled trial of locking plate osteosynthesis versus retrograde nailing
Methods	Allocation: randomised Intervention model: parallel assignment Masking: single blind (outcomes assessor)
Participants	Inclusion criteria: aged ≥ 18 years displaced periprosthetic fracture of the distal femur; fracture amenable to both treatment groups, in the opinion of the investigator; knee prosthesis is well-fixed and non-stemmed; open box femoral component; provision of written informed consent

NCT01973712 *(Continued)*

	Exclusion criteria: presence of an active infection around the fracture (soft tissue or bone); open fracture; Injury Severity Score > 15 or any associated major injuries of the lower extremities; medical contraindication to surgery; pregnant women; likely problems, in the judgement of the investigators, with maintaining follow-up
Interventions	Participants were allocated to either: • **locked compression plate:** a direct lateral approach to distal femur will be employed utilising minimally invasive and indirect reduction techniques. After fracture reduction is achieved with the use of intraoperative fluoroscopy, a locking plate will be provisionally implanted. Following confirmation of placement, definitive fixation will follow with multiple locking screws in the distal fragment and bicortical screw fixation proximally. A standard layered closure will follow; • **retrograde intramedullary nail:** the previous mid-line knee incision will be employed to access to the knee joint, allowing exposure of the femoral start point via the open box in the femoral component. Following reaming of the canal, an appropriately sized retrograde nail will be inserted. Intraoperative fluoroscopy will be used to confirm reduction. Both proximal and distal locking screws will be used to transfix the nail. A standard layered closure will follow.
Outcomes	Primary outcome • Timed Up and Go test at 3 months Secondary outcomes • Rates of reoperation at 12 months • Rates of malunion at 12 months
Starting date	May 2014
Contact information	Contact: Milena Vicente; vicentem@smh.ca Contact: Melanie MacNevin; macnevinm@smh.ca St Michael's Hospital, Toronto, Canada
Notes	Estimated enrolment 94 participants

NCT04076735

Study name	DIFFIR: geriatric distal femur fixation versus replacement – a randomized controlled trial of acute open reduction internal fixation (ORIF) versus distal femoral replacement (DFR)
Methods	Prospective, randomised controlled trial, involving multiple centres across North America
Participants	Estimated 140 participants Inclusion criteria: men and women age ≥ 65 years; isolated fracture of distal femur (Classification 33); fracture is amenable to both treatments; fracture is acute (within 2 weeks from time of injury); ambulatory (with or without walking aids) prior to injury; independent or moderately frail with score of 3–6 on Clinical Frailty Scale; able to read and understand English, French or Spanish; participant or substitute decision maker is able to provide written informed consent to participate in study. Exclusion criteria: active or previous infection around fracture (soft tissue or bone); open fracture; bilateral femur fractures; major vascular injuries requiring intervention, compartment syndrome and major neurological injuries; pathological fracture excluding osteoporosis; previous surgical fixation or total knee replacement of the distal femur or proximal tibia; previous surgical fixation or hemi/total replacement of hip; current or previous extensor mechanism (patellar tendon, quadriceps tendon or patella fracture) disruption or repair; polytrauma (Injury Severity Score > 15) or any

NCT04076735 *(Continued)*	associated major injuries of the lower extremities; previous medical diagnosis of dementia; medical or surgical contraindication to surgery.
Interventions	Participants were allocated to either: • **distal femoral replacement**; • **open reduction internal fixation**.
Outcomes	Primary outcome • OKS at 3, 6, 9 and 12 months postsurgery to detect a 5-point improvement on the OKS with 0.5 correlation between assessments Secondary outcomes • Daily morphine equivalent usage while in hospital (will be assessed daily from the day of the surgery until the patient gets discharge from the hospital (24 hours up to 7 days)) • VAS assessed immediately after surgery at 24 hours, 48 hours, and at each follow-up visit at 3, 6, 9, 12 and 24 months postsurgery • Health status and quality of life – EQ-5D questionnaire at 3, 6, 9, 12 and 24 months postsurgery • Knee range of movement at 3, 6, 12 and 24 months postsurgery • Timed Up and Go test at 3, 6, 12 and 24 months postsurgery • Knee extension lag at 3, 6, 12 and 24 months postsurgery
Starting date	16 March 2020
Contact information	Amir Khoshbin, MD & Jesse Wolfstadt, MD St Michael's Hospital - Unity Health Toronto, ON, Canada
Notes	

AO: Arbeitsgemeinschaft für Osteosynthesefragen; CRP: C-reactive protein; CT: computed tomography; EQ-5D: EuroQol 5 Dimensions; ESR: erythrocyte sedimentation rate; OKS: Oxford Knee Score; OTA: Orthopaedic Trauma Association; RUST: radiographic union score for tibial; VAS: Visual Analogue Scale.

DATA AND ANALYSES

Comparison 1. Retrograde intramedullary nail (RIMN) versus locking plate

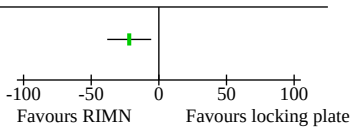
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Patient-reported functional outcomes (short term)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2 Patient-reported functional outcomes (long term)	2	198	Std. Mean Difference (IV, Fixed, 95% CI)	-0.22 [-0.50, 0.06]
1.3 Direct adverse events	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.3.1 Reoperation for removal of implant	1	114	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.55, 4.00]
1.3.2 Loss of fixation	1	23	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.02, 8.04]
1.3.3 Superficial infection	2	65	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.11, 2.69]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3.4 Deep infection	1	42	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.07, 16.45]
1.3.5 Haematoma formation	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.14, 3.95]
1.3.6 Implant loosening	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.02, 8.48]
1.4 Quality of life	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4.1 Short term	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.4.2 Long term	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.5 Indirect adverse events	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.5.1 Deep vein thrombosis	1	23	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
1.5.2 Pneumonia	1	23	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.15, 72.36]
1.5.3 Urinary tract infection	1	23	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.15, 72.36]
1.5.4 Cerebrovascular accident	1	23	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
1.5.5 Myocardial infarction	1	23	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.15, 72.36]
1.5.6 Blood transfusion	1	23	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.18, 6.48]
1.5.7 Anterior knee pain	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.03, 2.26]
1.6 Failure of union	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.6.1 Malunion	2	179	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.42, 1.22]
1.6.2 Non-union	2	198	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.29, 2.22]
1.6.3 Delayed union	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.03, 1.73]
1.6.4 Loss of fixation	1	23	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.08, 15.41]
1.6.5 Varus/valgus > 5°	1	23	Risk Ratio (M-H, Fixed, 95% CI)	2.18 [1.09, 4.37]
1.6.6 Recurvatum > 10°	1	23	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.15, 72.36]
1.6.7 Procurvatum > 10°	1	23	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.15, 72.36]
1.6.8 Shortening > 1 cm	1	23	Risk Ratio (M-H, Fixed, 95% CI)	5.42 [0.29, 101.77]
1.6.9 Malalignment > 10°	1	42	Risk Ratio (M-H, Fixed, 95% CI)	2.20 [0.22, 22.45]
1.6.10 Malalignment 5–10°	1	42	Risk Ratio (M-H, Fixed, 95% CI)	2.20 [0.45, 10.74]
1.7 Resource use – operating time and length of stay	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.7.1 Operating time (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.7.2 Length of stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.8 Resource use – cost (GBP)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.8.1 Cost (GBP)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 1: Patient-reported functional outcomes (short term)

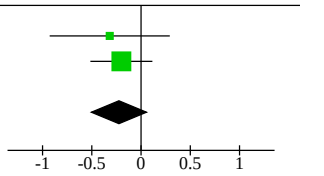
	RIMN			Locking plate			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Griffin 2019	60.9	23.1	8	82.8	2.9	4	-21.90 [-38.16 , -5.64]	



Analysis 1.2. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 2: Patient-reported functional outcomes (long term)

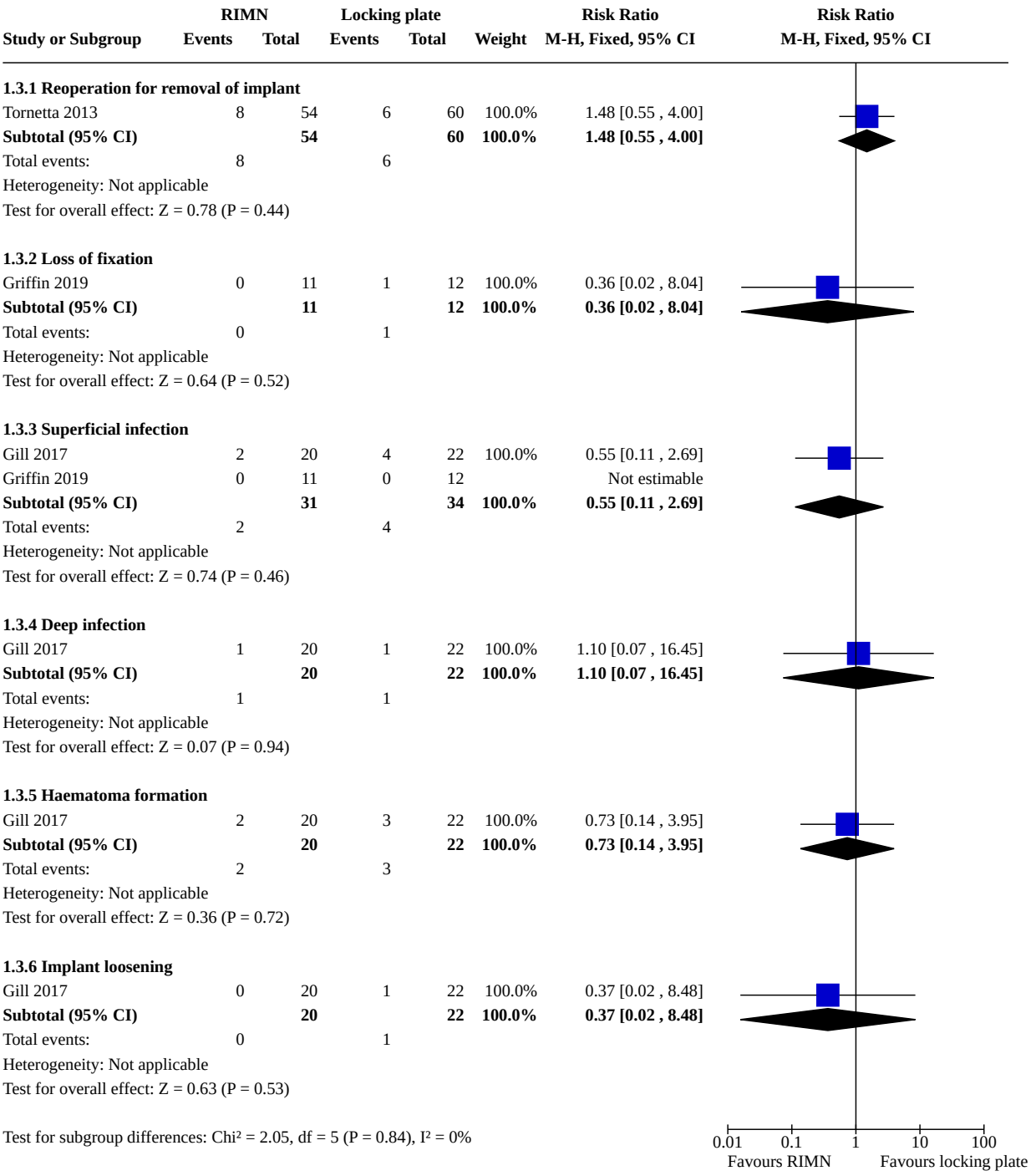
	RIMN			Locking plate				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gill 2017	-77.6	8.6	20	-74.4	10.9	22	21.0%	-0.32 [-0.93 , 0.29]	
Tornetta 2013 (1)	21.5	29.4	76	27.4	29.4	80	79.0%	-0.20 [-0.51 , 0.12]	
Total (95% CI)			**96**			**102**	**100.0%**	**-0.22 [-0.50 , 0.06]**	

Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 1.57 (P = 0.12)
Test for subgroup differences: Not applicable



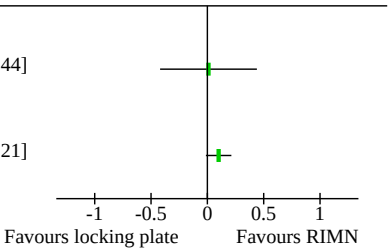
Footnotes
(1) Pooled SD derived from reported P values and means.

Analysis 1.3. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 3: Direct adverse events



Analysis 1.4. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 4: Quality of life

Study or Subgroup	RIMN Mean	RIMN SD	RIMN Total	Locking plate Mean	Locking plate SD	Locking plate Total	Mean Difference IV, Fixed, 95% CI
1.4.1 Short term							
Griffin 2019	0.38	0.36	9	0.37	0.41	5	0.01 [-0.42 , 0.44]
1.4.2 Long term							
Tornetta 2013 (1)	0.78	0.36	76	0.68	0.36	80	0.10 [-0.01 , 0.21]

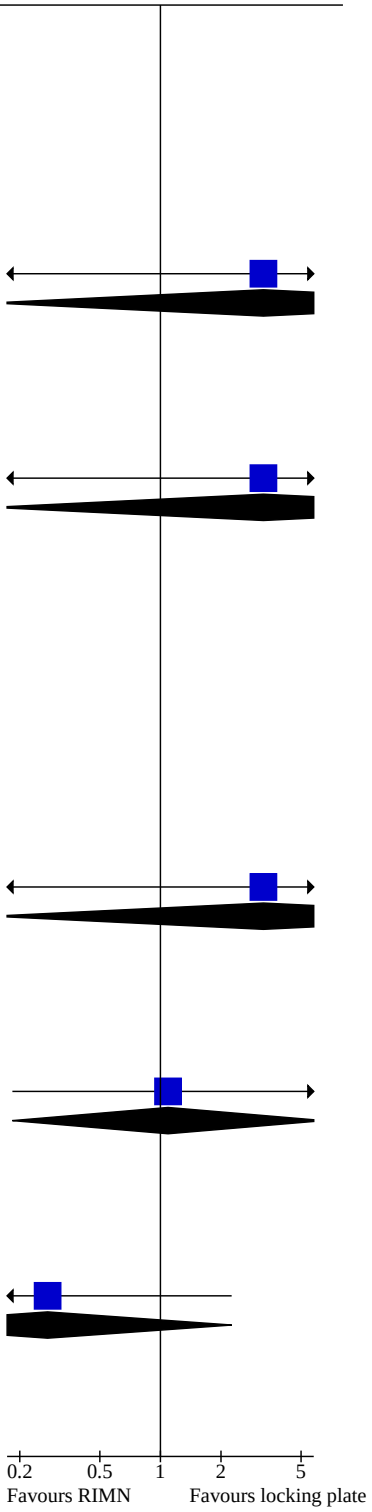


Footnotes

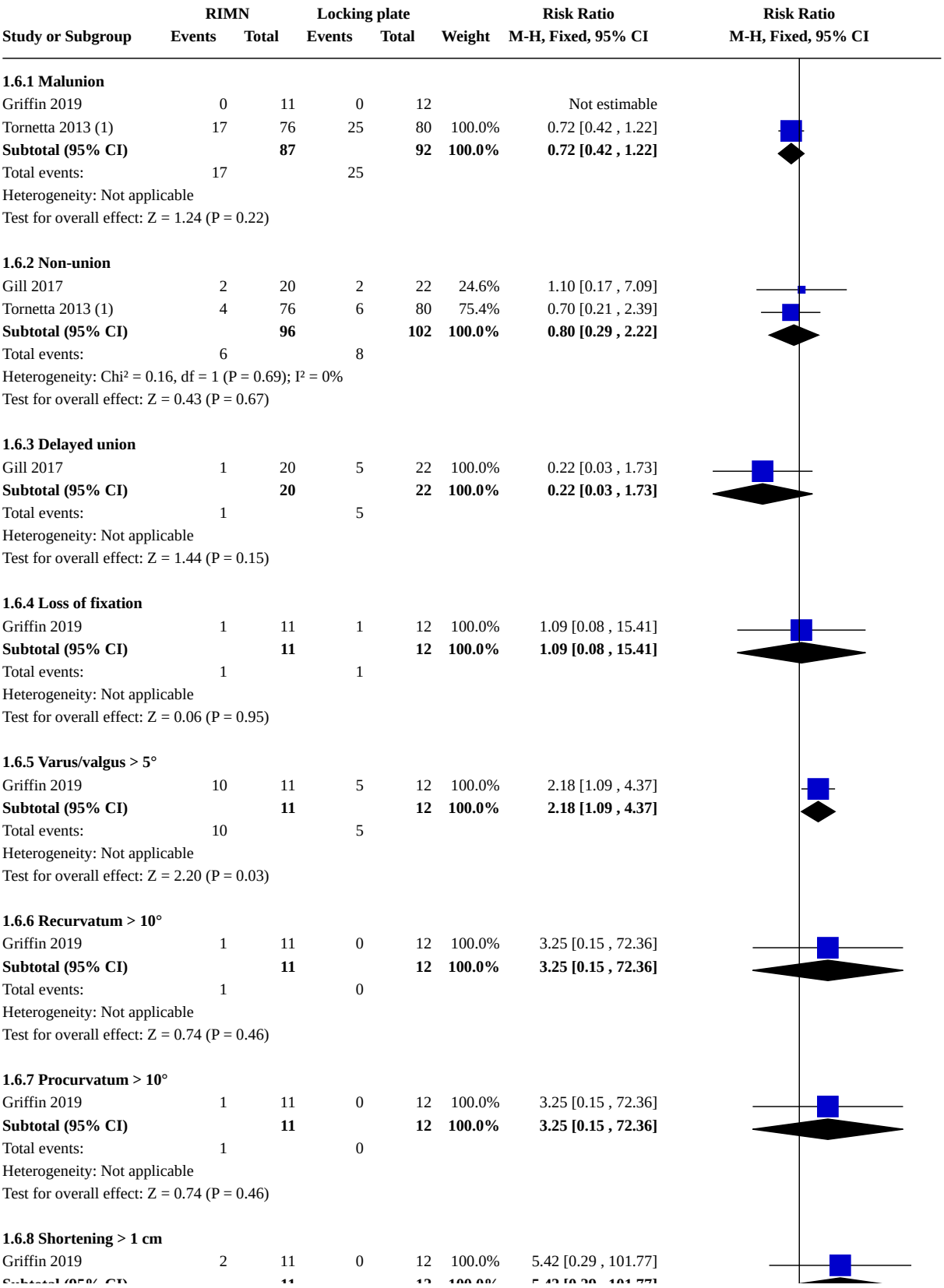
(1) Pooled SD derived from reported P values and means.

Analysis 1.5. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 5: Indirect adverse events

Study or Subgroup	RIMN Events	RIMN Total	Locking plate Events	Locking plate Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Deep vein thrombosis						
Griffin 2019	0	11	0	12		Not estimable
Subtotal (95% CI)		**11**		**12**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.2 Pneumonia						
Griffin 2019	1	11	0	12	100.0%	3.25 [0.15 , 72.36]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**3.25 [0.15 , 72.36]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
1.5.3 Urinary tract infection						
Griffin 2019	1	11	0	12	100.0%	3.25 [0.15 , 72.36]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**3.25 [0.15 , 72.36]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
1.5.4 Cerebrovascular accident						
Griffin 2019	0	11	0	12		Not estimable
Subtotal (95% CI)		**11**		**12**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.5 Myocardial infarction						
Griffin 2019	1	11	0	12	100.0%	3.25 [0.15 , 72.36]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**3.25 [0.15 , 72.36]**
Total events:	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
1.5.6 Blood transfusion						
Griffin 2019	2	11	2	12	100.0%	1.09 [0.18 , 6.48]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**1.09 [0.18 , 6.48]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.10 (P = 0.92)						
1.5.7 Anterior knee pain						
Gill 2017	1	20	4	22	100.0%	0.28 [0.03 , 2.26]
Subtotal (95% CI)		**20**		**22**	**100.0%**	**0.28 [0.03 , 2.26]**
Total events:	1		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						
Test for subgroup differences: Chi^2 = 3.07, df = 4 (P = 0.55), I^2 = 0%						

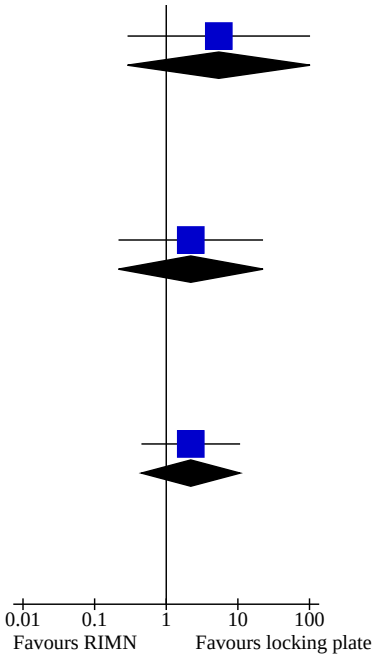


Analysis 1.6. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 6: Failure of union



Analysis 1.6. (Continued)

Griffin 2019	2	11	0	12	100.0%	5.42 [0.29 , 101.77]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**5.42 [0.29 , 101.77]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						
1.6.9 Malalignment > 10°						
Gill 2017	2	20	1	22	100.0%	2.20 [0.22 , 22.45]
Subtotal (95% CI)		**20**		**22**	**100.0%**	**2.20 [0.22 , 22.45]**
Total events:	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.51)						
1.6.10 Malalignment 5–10°						
Gill 2017	4	20	2	22	100.0%	2.20 [0.45 , 10.74]
Subtotal (95% CI)		**20**		**22**	**100.0%**	**2.20 [0.45 , 10.74]**
Total events:	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						

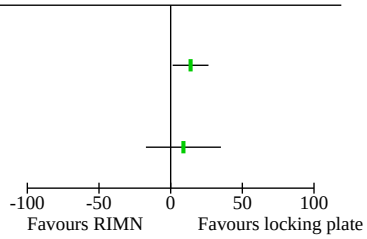


Footnotes

(1) Event number derived from reported percentages.

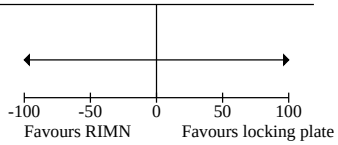
Analysis 1.7. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 7: Resource use – operating time and length of stay

	RIMN			Locking plate			Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
1.7.1 Operating time (minutes)								
Gill 2017	102.3	20.6	20	88.4	20.6	22	13.90 [1.43 , 26.37]	
1.7.2 Length of stay (days)								
Griffin 2019	28.3	45.2	12	19.4	9.3	11	8.90 [-17.26 , 35.06]	



Analysis 1.8. Comparison 1: Retrograde intramedullary nail (RIMN) versus locking plate, Outcome 8: Resource use – cost (GBP)

	RIMN			Locking plate			Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
1.8.1 Cost (GBP)								
Griffin 2019	33374.89	8287.41	12	32373.86	1610.69	11	1001.03 [-3783.56 , 5785.62]	

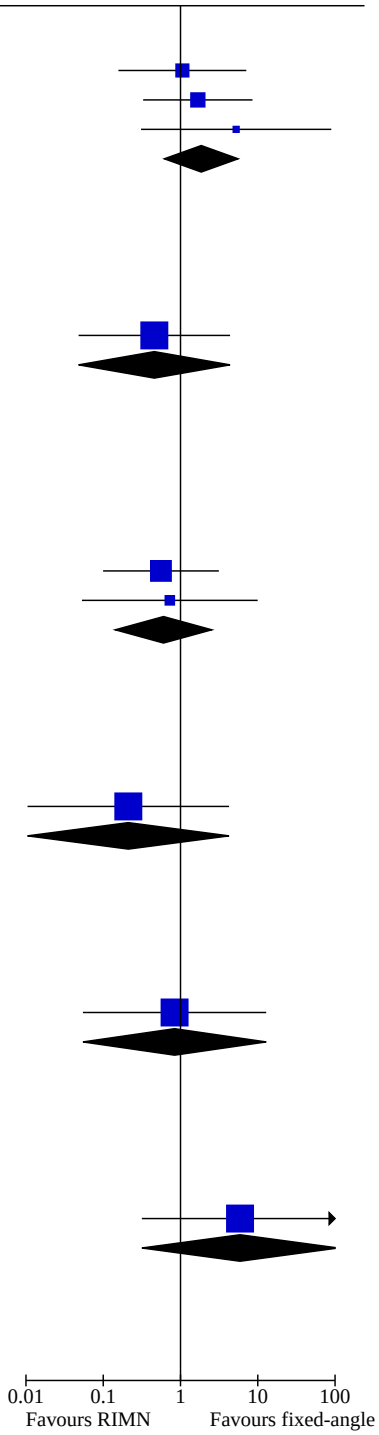


Comparison 2. Retrograde intramedullary nail (RIMN) versus single fixed-angle device

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Direct adverse events	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1.1 Reoperation	3	159	Risk Ratio (M-H, Fixed, 95% CI)	1.85 [0.62, 5.57]
2.1.2 Death	1	23	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.05, 4.38]
2.1.3 Infection	3	159	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.14, 2.54]
2.1.4 Haematoma requiring aspiration	1	72	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.01, 4.25]
2.1.5 Implant failure	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.05, 12.85]
2.1.6 Nail protrusion	1	68	Risk Ratio (M-H, Fixed, 95% CI)	5.89 [0.32, 109.91]
2.2 36-item Short Form (SF-36; higher scores = better quality of life)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.2.1 Physical component (0–100)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.2.2 Mental component (0–100)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.3 Indirect adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.3.1 Pneumonia	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.3.2 Urinary tract infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.3.3 Acute renal failure	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.3.4 Pressure sores	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.4 Failure of union	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.4.1 Non-union	3	159	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.33, 3.71]
2.4.2 Malunion	3	159	Risk Ratio (M-H, Fixed, 95% CI)	1.84 [0.28, 11.97]
2.5 Resource use: length of hospital stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2: Retrograde intramedullary nail (RIMN) versus single fixed-angle device, Outcome 1: Direct adverse events

Study or Subgroup	RIMN Events	RIMN Total	Fixed-angle Events	Fixed-angle Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Reoperation						
Christodoulou 2005 (1)	2	35	2	37	41.4%	1.06 [0.16 , 7.10]
Dar 2009 (2)	4	37	2	31	46.4%	1.68 [0.33 , 8.54]
Hartin 2006 (3)	3	11	0	8	12.2%	5.25 [0.31 , 89.35]
Subtotal (95% CI)		**83**		**76**	**100.0%**	**1.85 [0.62 , 5.57]**
Total events:	9		4			
Heterogeneity: Chi² = 0.87, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.10 (P = 0.27)						
2.1.2 Death						
Hartin 2006	1	12	2	11	100.0%	0.46 [0.05 , 4.38]
Subtotal (95% CI)		**12**		**11**	**100.0%**	**0.46 [0.05 , 4.38]**
Total events:	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
2.1.3 Infection						
Christodoulou 2005	0	35	0	37		Not estimable
Dar 2009	2	37	3	31	73.8%	0.56 [0.10 , 3.13]
Hartin 2006	1	11	1	8	26.2%	0.73 [0.05 , 9.97]
Subtotal (95% CI)		**83**		**76**	**100.0%**	**0.60 [0.14 , 2.54]**
Total events:	3		4			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.69 (P = 0.49)						
2.1.4 Haematoma requiring aspiration						
Christodoulou 2005	0	35	2	37	100.0%	0.21 [0.01 , 4.25]
Subtotal (95% CI)		**35**		**37**	**100.0%**	**0.21 [0.01 , 4.25]**
Total events:	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
2.1.5 Implant failure						
Dar 2009 (4)	1	37	1	31	100.0%	0.84 [0.05 , 12.85]
Subtotal (95% CI)		**37**		**31**	**100.0%**	**0.84 [0.05 , 12.85]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						
2.1.6 Nail protrusion						
Dar 2009 (5)	3	37	0	31	100.0%	5.89 [0.32 , 109.91]
Subtotal (95% CI)		**37**		**31**	**100.0%**	**5.89 [0.32 , 109.91]**
Total events:	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.23)						
Test for subgroup differences: Chi² = 4.58, df = 5 (P = 0.47), I² = 0%						



Footnotes

(1) All reoperations for non-union.

(2) 2 versus 2 for non-union (+ implant failure/infection); 2 in RIMN: nail protrusion.

(3) 1 was for valgus collapse + nail protrusion, 2 for persistent knee pain.

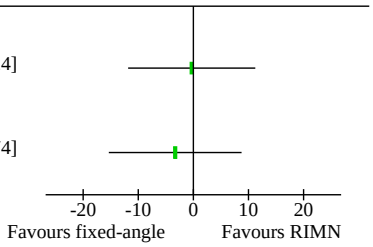
(4) Both had non-union.

Analysis 2.1. (Continued)

(3) 1 was for valgus collapse + nail protrusion, 2 for persistent knee pain.
(4) Both had non-union.
(5) In 2 cases, nail was unlocked and countersunk, in 1 case, reoperation refused with subsequent restricted range of motion.

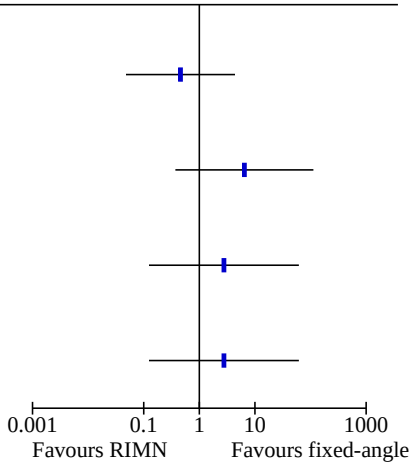
Analysis 2.2. Comparison 2: Retrograde intramedullary nail (RIMN) versus single fixed-angle device, Outcome 2: 36-item Short Form (SF-36; higher scores = better quality of life)

Study or Subgroup	RIMN Mean	RIMN SD	RIMN Total	Fixed-angle Mean	Fixed-angle SD	Fixed-angle Total	Mean Difference IV, Fixed, 95% CI
2.2.1 Physical component (0–100)							
Hartin 2006	33.7	11.4	10	34	11.4	6	-0.30 [-11.84 , 11.24]
2.2.2 Mental component (0–100)							
Hartin 2006	51.4	11.9	10	54.7	11.9	6	-3.30 [-15.34 , 8.74]



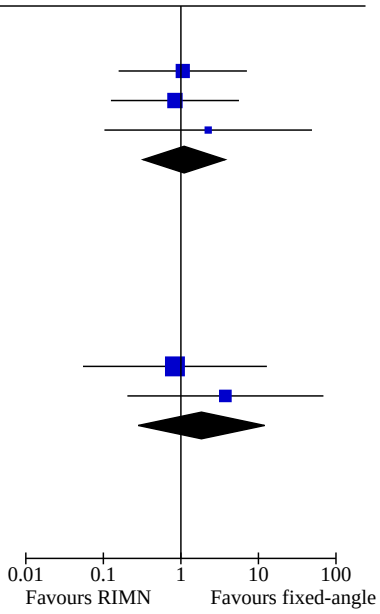
Analysis 2.3. Comparison 2: Retrograde intramedullary nail (RIMN) versus single fixed-angle device, Outcome 3: Indirect adverse events

Study or Subgroup	RIMN Events	RIMN Total	Fixed-angle Events	Fixed-angle Total	Risk Ratio M-H, Fixed, 95% CI
2.3.1 Pneumonia					
Hartin 2006	1	12	2	11	0.46 [0.05 , 4.38]
2.3.2 Urinary tract infection					
Hartin 2006	3	12	0	11	6.46 [0.37 , 112.54]
2.3.3 Acute renal failure					
Hartin 2006	1	12	0	11	2.77 [0.12 , 61.65]
2.3.4 Pressure sores					
Hartin 2006	1	12	0	11	2.77 [0.12 , 61.65]



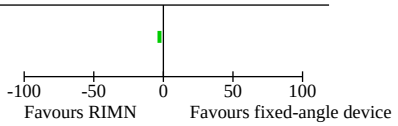
Analysis 2.4. Comparison 2: Retrograde intramedullary nail (RIMN) versus single fixed-angle device, Outcome 4: Failure of union

Study or Subgroup	RIMN Events	RIMN Total	Fixed-angle Events	Fixed-angle Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 Non-union						
Christodoulou 2005	2	35	2	37	41.4%	1.06 [0.16 , 7.10]
Dar 2009	2	37	2	31	46.4%	0.84 [0.13 , 5.61]
Hartin 2006	1	11	0	8	12.2%	2.25 [0.10 , 49.04]
Subtotal (95% CI)		**83**		**76**	**100.0%**	**1.10 [0.33 , 3.71]**
Total events:	5		4			
Heterogeneity: Chi² = 0.29, df = 2 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.15 (P = 0.88)						
2.4.2 Malunion						
Christodoulou 2005	0	35	0	37		Not estimable
Dar 2009	1	37	1	31	65.6%	0.84 [0.05 , 12.85]
Hartin 2006	2	11	0	8	34.4%	3.75 [0.20 , 68.89]
Subtotal (95% CI)		**83**		**76**	**100.0%**	**1.84 [0.28 , 11.97]**
Total events:	3		1			
Heterogeneity: Chi² = 0.55, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 0.64 (P = 0.52)						



Analysis 2.5. Comparison 2: Retrograde intramedullary nail (RIMN) versus single fixed-angle device, Outcome 5: Resource use: length of hospital stay (days)

Study or Subgroup	RIMN Mean	RIMN SD	RIMN Total	Fixed-angle device Mean	Fixed-angle device SD	Fixed-angle device Total	Mean Difference IV, Fixed, 95% CI
Christodoulou 2005	16.4	0.9	35	19.2	1.6	37	-2.80 [-3.40 , -2.20]

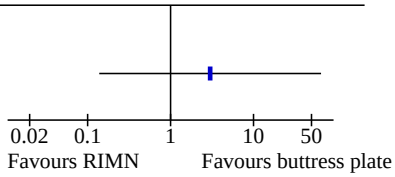


Comparison 3. Retrograde intramedullary nail (RIMN) versus non-locking (buttress) plate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Direct adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1.1 Infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.2 Delayed union	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

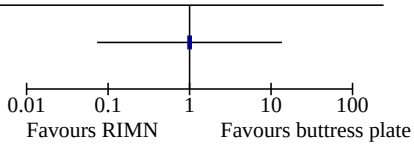
Analysis 3.1. Comparison 3: Retrograde intramedullary nail (RIMN) versus non-locking (buttress) plate, Outcome 1: Direct adverse events

Study or Subgroup	RIMN Events	RIMN Total	Buttress plate Events	Buttress plate Total	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Infection					
DeCoster 1995	1	9	0	9	3.00 [0.14 , 65.16]



Analysis 3.2. Comparison 3: Retrograde intramedullary nail (RIMN) versus non-locking (buttress) plate, Outcome 2: Delayed union

Study or Subgroup	RIMN Events	RIMN Total	Buttress plate Events	Buttress plate Total	Risk Ratio M-H, Fixed, 95% CI
DeCoster 1995	1	9	1	9	1.00 [0.07 , 13.64]

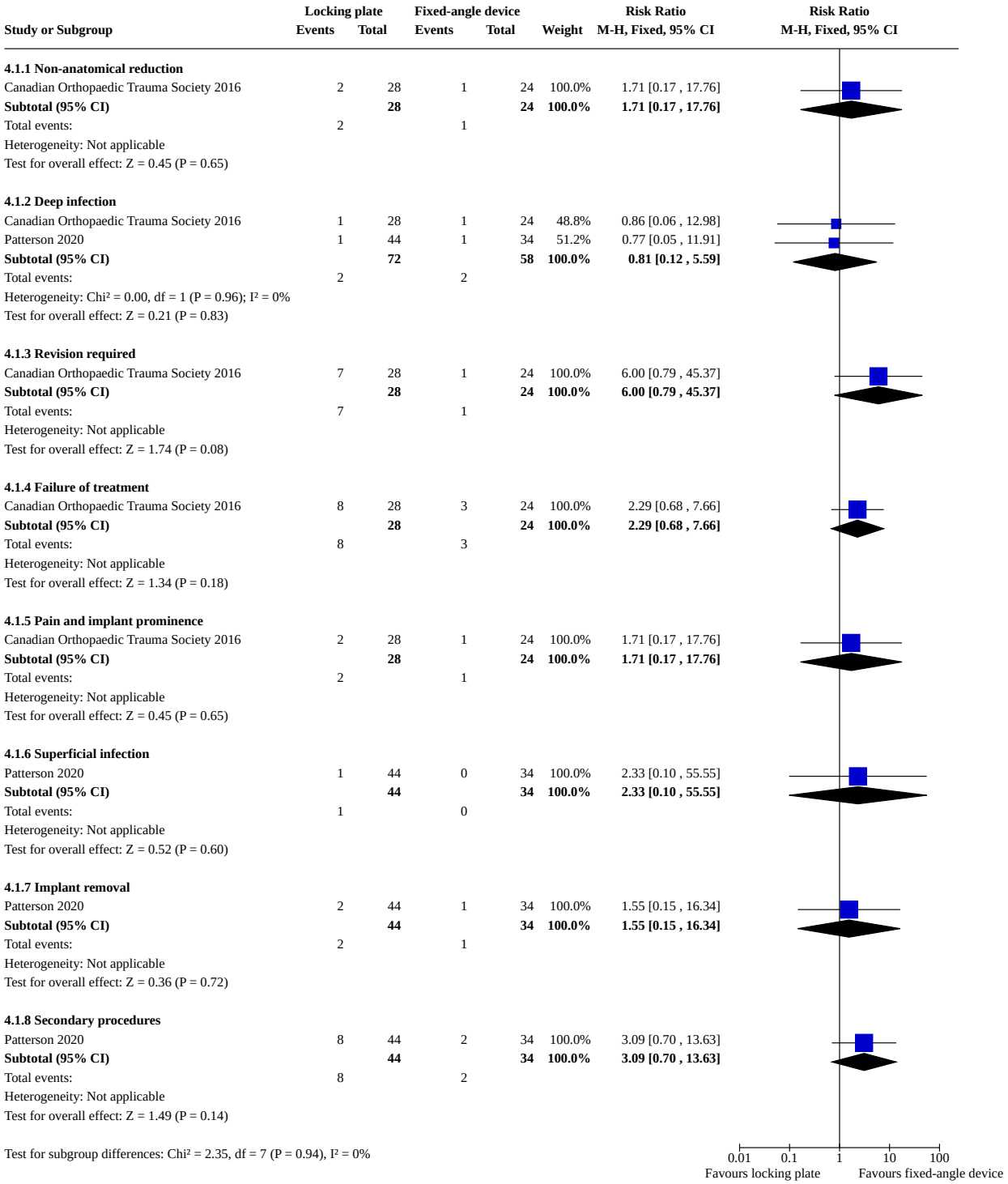


Comparison 4. Locking plate versus single fixed-angle device

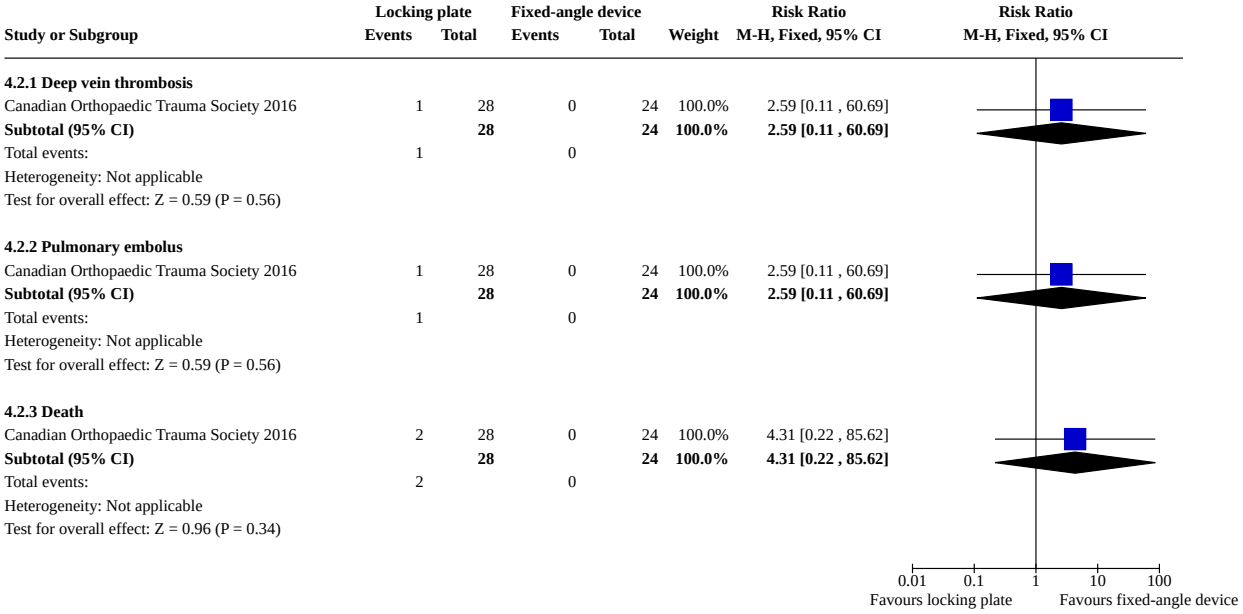
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Direct adverse events	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1.1 Non-anatomical reduction	1	52	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.17, 17.76]
4.1.2 Deep infection	2	130	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.12, 5.59]
4.1.3 Revision required	1	52	Risk Ratio (M-H, Fixed, 95% CI)	6.00 [0.79, 45.37]
4.1.4 Failure of treatment	1	52	Risk Ratio (M-H, Fixed, 95% CI)	2.29 [0.68, 7.66]
4.1.5 Pain and implant prominence	1	52	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.17, 17.76]
4.1.6 Superficial infection	1	78	Risk Ratio (M-H, Fixed, 95% CI)	2.33 [0.10, 55.55]
4.1.7 Implant removal	1	78	Risk Ratio (M-H, Fixed, 95% CI)	1.55 [0.15, 16.34]
4.1.8 Secondary procedures	1	78	Risk Ratio (M-H, Fixed, 95% CI)	3.09 [0.70, 13.63]
4.2 Indirect adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.2.1 Deep vein thrombosis	1	52	Risk Ratio (M-H, Fixed, 95% CI)	2.59 [0.11, 60.69]
4.2.2 Pulmonary embolus	1	52	Risk Ratio (M-H, Fixed, 95% CI)	2.59 [0.11, 60.69]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2.3 Death	1	52	Risk Ratio (M-H, Fixed, 95% CI)	4.31 [0.22, 85.62]
4.3 Failure of union	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.3.1 Non-union	2	130	Risk Ratio (M-H, Fixed, 95% CI)	3.56 [0.62, 20.41]
4.3.2 Malunion ≥ 5°	1	78	Risk Ratio (M-H, Fixed, 95% CI)	1.39 [0.51, 3.77]
4.3.3 Malunion ≥ 10°	1	78	Risk Ratio (M-H, Fixed, 95% CI)	1.55 [0.15, 16.34]

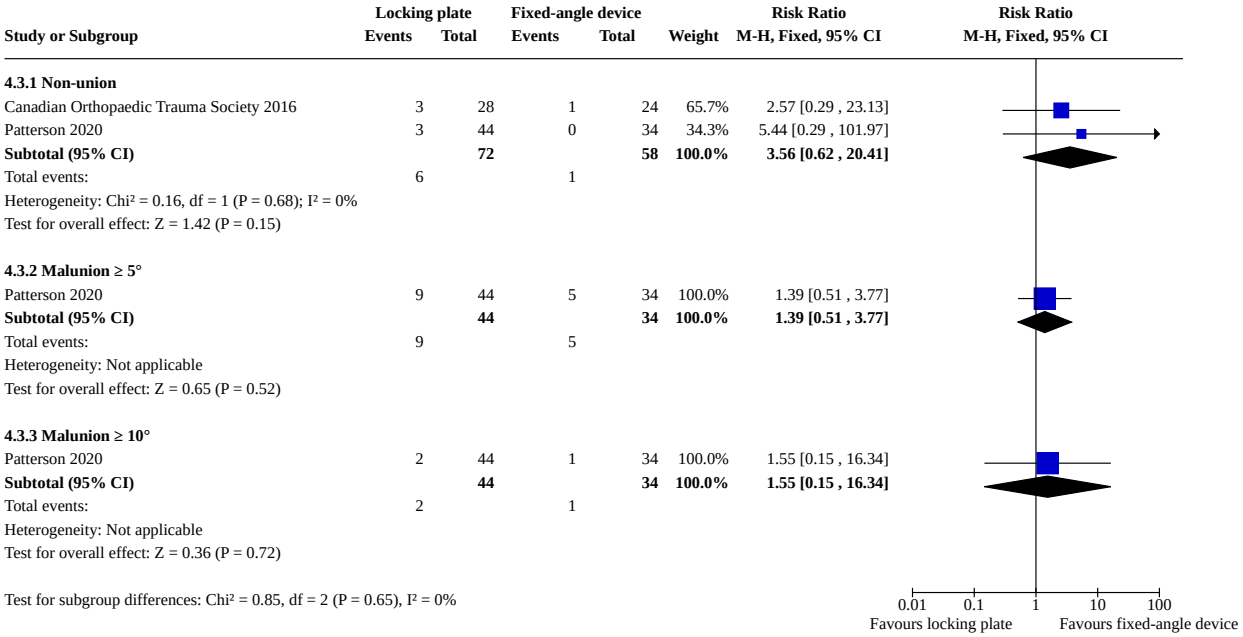
Analysis 4.1. Comparison 4: Locking plate versus single fixed-angle device, Outcome 1: Direct adverse events



Analysis 4.2. Comparison 4: Locking plate versus single fixed-angle device, Outcome 2: Indirect adverse events



Analysis 4.3. Comparison 4: Locking plate versus single fixed-angle device, Outcome 3: Failure of union

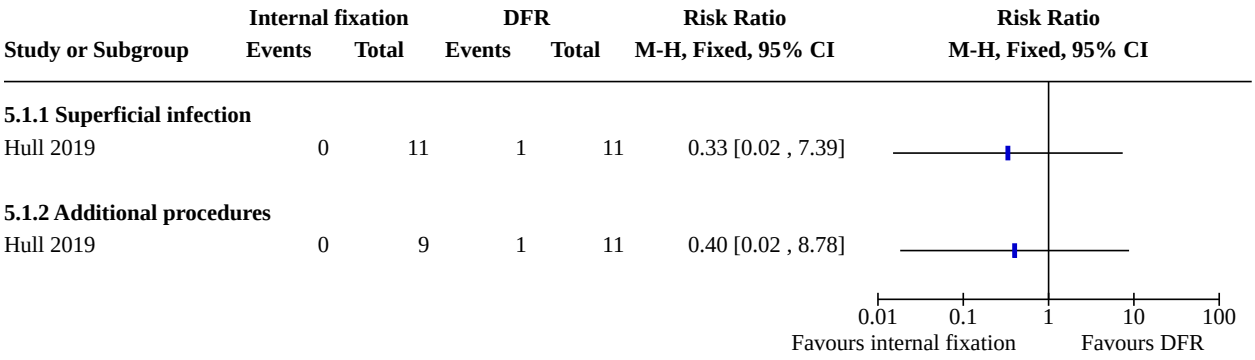


Comparison 5. Internal fixation versus distal femoral replacement (DFR)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Direct adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.1.1 Superficial infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

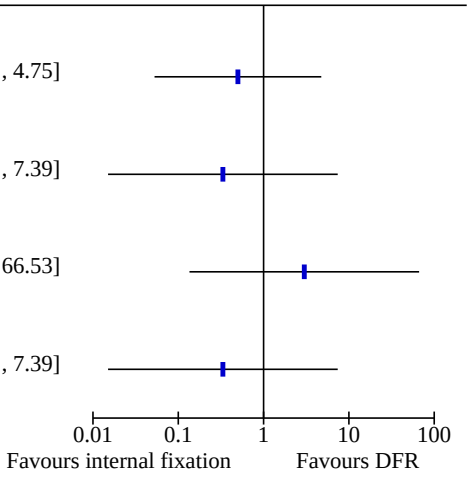
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1.2 Additional procedures	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2 Indirect adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2.1 Hospital readmissions	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2.2 Late stress fracture	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2.3 Compartment syndrome	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2.4 Pulmonary embolus	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.3 Resource use – length of stay and readmission	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.3.1 Length of stays (days)	1	22	Mean Difference (IV, Fixed, 95% CI)	3.47 [-5.56, 12.50]
5.3.2 Operating time (minutes)	1	22	Mean Difference (IV, Fixed, 95% CI)	-14.00 [-55.62, 27.62]
5.4 Resource use	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.4.1 Operation cost (GBP)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.4.2 Mean National Health Service and Personal Social Services cost following discharge (GBP)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5: Internal fixation versus distal femoral replacement (DFR), Outcome 1: Direct adverse events



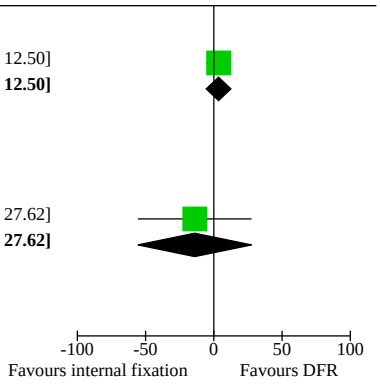
Analysis 5.2. Comparison 5: Internal fixation versus distal femoral replacement (DFR), Outcome 2: Indirect adverse events

Study or Subgroup	Internal fixation Events	Total	DFR Events	Total	Risk Ratio M-H, Fixed, 95% CI
5.2.1 Hospital readmissions					
Hull 2019	1	11	2	11	0.50 [0.05 , 4.75]
5.2.2 Late stress fracture					
Hull 2019	0	11	1	11	0.33 [0.02 , 7.39]
5.2.3 Compartment syndrome					
Hull 2019	1	11	0	11	3.00 [0.14 , 66.53]
5.2.4 Pulmonary embolus					
Hull 2019	0	11	1	11	0.33 [0.02 , 7.39]



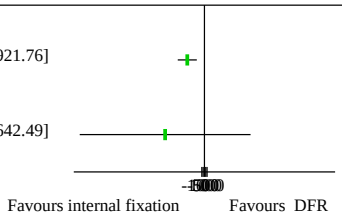
Analysis 5.3. Comparison 5: Internal fixation versus distal femoral replacement (DFR), Outcome 3: Resource use – length of stay and readmission

Study or Subgroup	Internal fixation Mean	SD	Total	DFR Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.3.1 Length of stays (days)								
Hull 2019	26.27	10.03	11	22.8	11.52	11	100.0%	3.47 [-5.56 , 12.50]
Subtotal (95% CI)			**11**			**11**	**100.0%**	**3.47 [-5.56 , 12.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.75 (P = 0.45)								
5.3.2 Operating time (minutes)								
Hull 2019	137	44	11	151	55	11	100.0%	-14.00 [-55.62 , 27.62]
Subtotal (95% CI)			**11**			**11**	**100.0%**	**-14.00 [-55.62 , 27.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.66 (P = 0.51)								
Test for subgroup differences: Chi² = 0.65, df = 1 (P = 0.42), I² = 0%								



Analysis 5.4. Comparison 5: Internal fixation versus distal femoral replacement (DFR), Outcome 4: Resource use

Study or Subgroup	Internal fixation Mean	SD	Total	DFR Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
5.4.1 Operation cost (GBP)							
Hull 2019	13241.05	3244.56	11	19807.53	5245.14	11	-6566.48 [-10211.20 , -2921.76]
5.4.2 Mean National Health Service and Personal Social Services cost following discharge (GBP)							
Hull 2019	28007.2	23986.79	5	43047.78	22112.92	3	-15040.58 [-47723.65 , 17642.49]

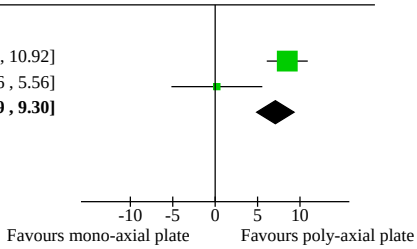


Comparison 6. Mono-axial plate versus poly-axial plate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Patient-reported functional outcome measures at 6 months	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1.1 Oxford Knee Score at 6 months	2	67	Mean Difference (IV, Fixed, 95% CI)	7.10 [4.89, 9.30]
6.2 Patient-reported functional outcome measures at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.3 Rasmussen score at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.4 Direct adverse event	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.4.1 Superficial infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.4.2 Secondary surgeries	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.4.3 Hardware-related problems	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.4.4 Mortality at 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.5 Quality of life	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.5.1 Health-state visual analogue scale score at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.6 Pain	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.6.1 Knee pain visual analogue scale score at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.7 Indirect adverse event	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.7.1 Peroneal lesions	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.7.2 Compartment syndrome	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.8 Failure of union	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.8.1 Malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

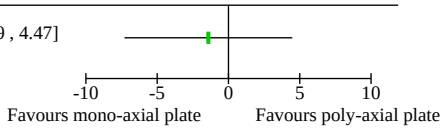
Analysis 6.1. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 1: Patient-reported functional outcome measures at 6 months

Study or Subgroup	Mono-axial plate Mean	SD	Total	Poly-axial plate Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.1.1 Oxford Knee Score at 6 months								
Hanschen 2014	-23.3	2.7	12	-31.8	3.7	15	83.1%	8.50 [6.08 , 10.92]
Kanakaris 2019	-33.2	9.4	19	-33.4	7.7	21	16.9%	0.20 [-5.16 , 5.56]
Subtotal (95% CI)			**31**			**36**	**100.0%**	**7.10 [4.89 , 9.30]**
Heterogeneity: Chi² = 7.66, df = 1 (P = 0.006); I² = 87%								
Test for overall effect: Z = 6.31 (P < 0.00001)								



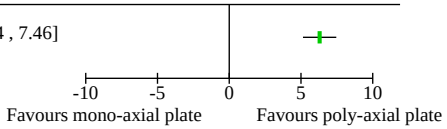
Analysis 6.2. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 2: Patient-reported functional outcome measures at 12 months

Study or Subgroup	Mono-axial plate Mean	SD	Total	Poly-axial plate Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Kanakaris 2019	-29.91	10.5	19	-28.5	8.2	21	-1.41 [-7.29 , 4.47]



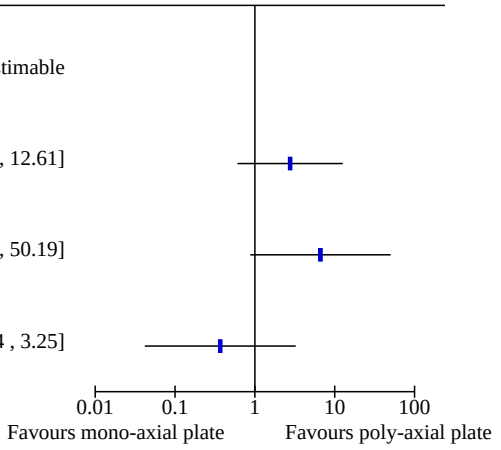
Analysis 6.3. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 3: Rasmussen score at 6 months

Study or Subgroup	Mono-axial plate Mean	SD	Total	Poly-axial plate Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Hanschen 2014	-18.7	1.8	12	-25	1.1	15	6.30 [5.14 , 7.46]



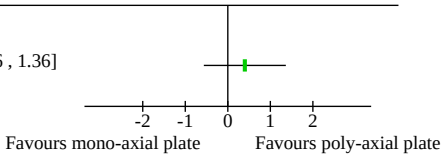
Analysis 6.4. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 4: Direct adverse event

Study or Subgroup	Mono-axial plate Events	Total	Poly-axial plate Events	Total	Risk Ratio M-H, Fixed, 95% CI
6.4.1 Superficial infection					
Hanschen 2014	0	12	0	15	Not estimable
6.4.2 Secondary surgeries					
Kanakaris 2019	5	19	2	21	2.76 [0.61 , 12.61]
6.4.3 Hardware-related problems					
Kanakaris 2019	6	19	1	21	6.63 [0.88 , 50.19]
6.4.4 Mortality at 3 months					
Kanakaris 2019	1	19	3	21	0.37 [0.04 , 3.25]



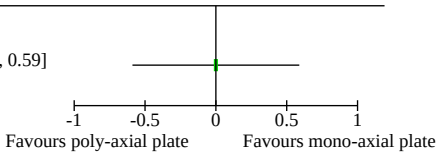
Analysis 6.5. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 5: Quality of life

Study or Subgroup	Mono-axial plate Mean	SD	Total	Poly-axial plate Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
6.5.1 Health-state visual analogue scale score at 12 months							
Kanakaris 2019	7.1	1.6	19	6.7	1.5	21	0.40 [-0.56 , 1.36]



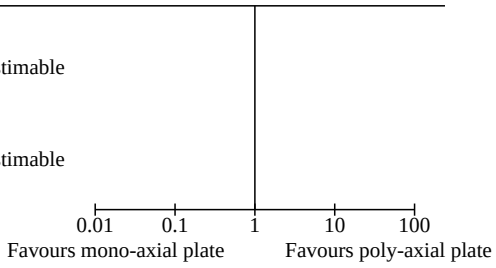
Analysis 6.6. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 6: Pain

Study or Subgroup	Mono-axial plate Mean	SD	Total	Poly-axial plate Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
6.6.1 Knee pain visual analogue scale score at 12 months							
Kanakaris 2019	1.4	0.9	19	1.4	1	21	0.00 [-0.59 , 0.59]



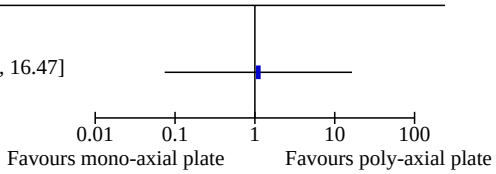
Analysis 6.7. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 7: Indirect adverse event

Study or Subgroup	Mono-axial plate Events	Total	Poly-axial plate Events	Total	Risk Ratio M-H, Fixed, 95% CI
6.7.1 Peroneal lesions					
Hanschen 2014	0	12	0	15	Not estimable
6.7.2 Compartment syndrome					
Hanschen 2014	0	12	0	15	Not estimable



Analysis 6.8. Comparison 6: Mono-axial plate versus poly-axial plate, Outcome 8: Failure of union

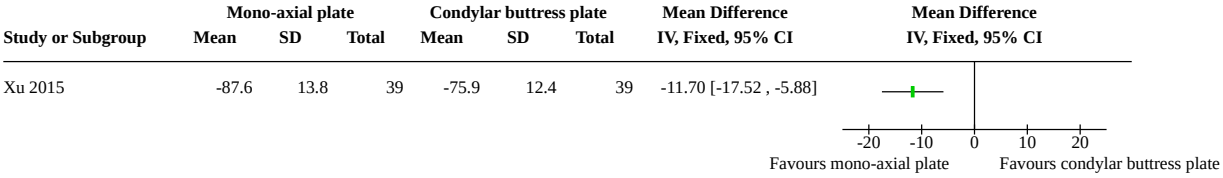
Study or Subgroup	Mono-axial plate Events	Total	Poly-axial plate Events	Total	Risk Ratio M-H, Fixed, 95% CI
6.8.1 Malunion					
Kanakaris 2019	1	19	1	21	1.11 [0.07 , 16.47]



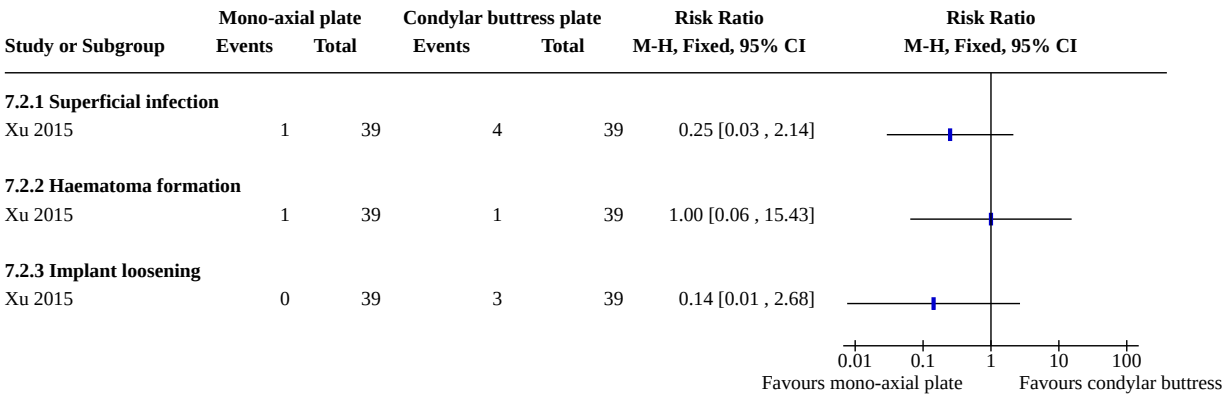
Comparison 7. Mono-axial plate versus condylar buttress plate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Evanich score at 12 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.2 Direct adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.2.1 Superficial infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.2.2 Haematoma formation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.2.3 Implant loosening	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.3 Resource use – hospital stay and operation length	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.3.1 Operation time (minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.3.2 Length of stay (days)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

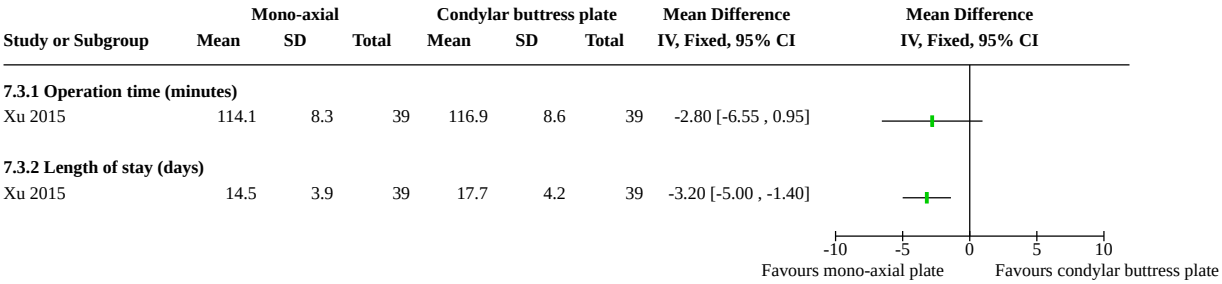
Analysis 7.1. Comparison 7: Mono-axial plate versus condylar buttress plate, Outcome 1: Evanich score at 12 months



Analysis 7.2. Comparison 7: Mono-axial plate versus condylar buttress plate, Outcome 2: Direct adverse events



Analysis 7.3. Comparison 7: Mono-axial plate versus condylar buttress plate, Outcome 3: Resource use – hospital stay and operation length

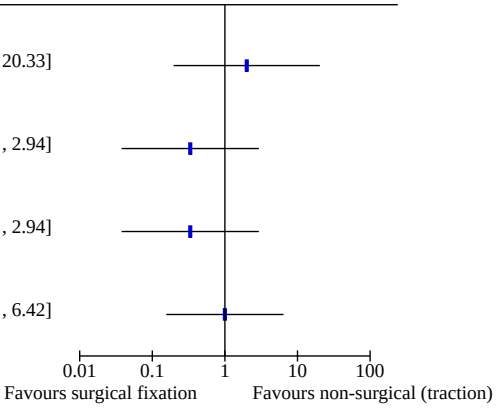


Comparison 8. Surgical versus non-surgical management

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Direct adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1.1 Death	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1.2 Reoperation or repeat procedure	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1.3 Implant or traction loosening	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1.4 Superficial or pin-tract infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.2 Indirect adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.2.1 Deep vein thrombosis	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.2.2 Urinary tract infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.2.3 Pneumonia	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.2.4 Pressure sore	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.3 Failure of union	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.3.1 Delayed union	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.3.2 Malunion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8: Surgical versus non-surgical management, Outcome 1: Direct adverse events

Study or Subgroup	Surgical fixation Events	Total	Non-surgical (traction) Events	Total	Risk Ratio M-H, Fixed, 95% CI
8.1.1 Death					
Butt 1996b (1)	2	20	1	20	2.00 [0.20 , 20.33]
8.1.2 Reoperation or repeat procedure					
Butt 1996b (2)	1	20	3	20	0.33 [0.04 , 2.94]
8.1.3 Implant or traction loosening					
Butt 1996b	1	20	3	20	0.33 [0.04 , 2.94]
8.1.4 Superficial or pin-tract infection					
Butt 1996b	2	20	2	20	1.00 [0.16 , 6.42]



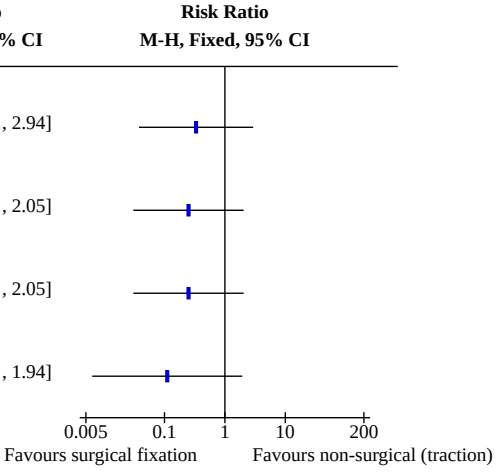
Footnotes

(1) Surgery: 1 myocardial infarction, 1 pulmonary embolism; non-surgery: 1 pneumonia.

(2) All for implant or traction pin loosening.

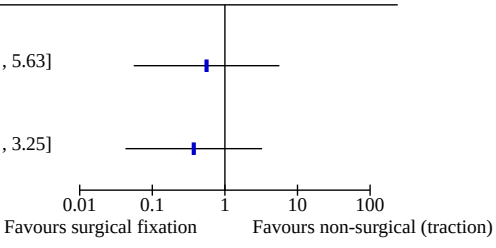
Analysis 8.2. Comparison 8: Surgical versus non-surgical management, Outcome 2: Indirect adverse events

Study or Subgroup	Surgical fixation Events	Total	Non-surgical (traction) Events	Total	Risk Ratio M-H, Fixed, 95% CI
8.2.1 Deep vein thrombosis					
Butt 1996b	1	20	3	20	0.33 [0.04 , 2.94]
8.2.2 Urinary tract infection					
Butt 1996b	1	20	4	20	0.25 [0.03 , 2.05]
8.2.3 Pneumonia					
Butt 1996b	1	20	4	20	0.25 [0.03 , 2.05]
8.2.4 Pressure sore					
Butt 1996b	0	20	4	20	0.11 [0.01 , 1.94]



Analysis 8.3. Comparison 8: Surgical versus non-surgical management, Outcome 3: Failure of union

Study or Subgroup	Surgical fixation Events	Total	Non-surgical (traction) Events	Total	Risk Ratio M-H, Fixed, 95% CI
8.3.1 Delayed union					
Butt 1996b	1	17	2	19	0.56 [0.06 , 5.63]
8.3.2 Malunion					
Butt 1996b	1	17	3	19	0.37 [0.04 , 3.25]



APPENDICES

Appendix 1. Search strategies for this update (2014 to October 2021)

The Cochrane Library (CENTRAL, CRS-Web)

The CENTRAL search was run in three stages: the first search was run in October 2019, top-up searches were run in October 2020 and 2021.

Search 1

1 MESH DESCRIPTOR Femur AND CENTRAL:TARGET (776)
2 MESH DESCRIPTOR Fractures, Bone AND CENTRAL:TARGET (1899)
3 MESH DESCRIPTOR Fracture Fixation EXPLODE ALL AND CENTRAL: TARGET (1613)
4 MESH DESCRIPTOR Fracture Healing AND CENTRAL:TARGET (510)
5 #2 or #3 or #4 (3408)
6 #1 and #5 (48)
7 MESH DESCRIPTOR Femoral Fractures AND CENTRAL:TARGET (293)
8 (femur* or femoral*) near3 fractur*: AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL: TARGET (3060)
9 #6 OR #7 OR #8 (3071)
10 distal* or condyl* or supracondyl* or epicondyl* or transcondyl* or intercondyl* or bicondyl* or transchondral* or periprosth*: AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL: TARGET (14862)
11 #9 and #10 (314)
12 01/08/2014_TO_10/10/2019:CRSCREATED AND CENTRAL:TARGET (792646)
13 #11 and 12 (200)

Search 2 (top-up search)

#12 10/10/2019_TO_20/10/2020:CRSCREATED AND CENTRAL:TARGET (176929)
#13 #11 AND #12 (33)

Search 3 (top-up search)

#12 20/10/2020_TO_26/10/2021:CRSCREATED AND CENTRAL:TARGET (120864)
#13 #11 AND #12 (32)

MEDLINE (Ovid)

The MEDLINE search was run in three stages: the first search was run in October 2019, top-up searches were run in October 2020 and 2021

Search 1

1 Femur/ (40195)
2 Fractures, Bone/ (62707)
3 exp Fracture Fixation/ (59488)
4 Fracture Healing/ (12860)
5 2 or 3 or 4 (113398)
6 1 and 5 (3827)
7 Femoral Fractures/ (16020)
8 ((femur* or femoral*) adj3 fractur*).tw. (21533)
9 6 or 7 or 8 (31039)
10 (distal* or condyl* or supracondyl* or epicondyl* or transcondyl* or intercondyl* or bicondyl* or transchondral* or periprosth*).tw. (265573)
11 9 and 10 (4927)
12 Randomized controlled trial.pt. (491154)
13 Controlled clinical trial.pt. (93310)
14 randomized.ab. (456510)
15 placebo.ab. (201348)
16 Drug therapy.fs. (2146171)
17 randomly.ab. (319304)
18 trial.ab. (478827)
19 groups.ab. (1961041)
20 or/12-19 (4539365)
21 exp animals/ not humans.sh. (4626413)
22 20 not 21 (3930130)
23 11 and 22 (597)

24 (201409* or 201410* or 201411* or 201412* or 2015* or 2016* or 2017* or 2018* or 2019*).ed,dt. (6819159)
25 23 and 24 (275)

Search 2 (top-up search)

24 (201910* or 201911* or 201912* or 2020*).ed,dt. (2150741)
25 23 and 24 (123)

Search 3 (top-up search)

24 (202010* or 202011* or 202012* or 2021*).ed,dt. (2384288)
25 23 and 24 (136)

Embase (Ovid)

The Embase search was run in 3 stages: the first search was run in October 2019, top-up searches were run in October 2020 and 2021.

Search 1

1 Femur Condyle/ or Femur/ (50509)
2 exp Fracture/ (264787)
3 exp Fracture Fixation/ (77984)
4 2 or 3 (288106)
5 1 and 4 (8512)
6 Femur Fracture/ (17558)
7 ((femur* or femoral*) adj3 fractur*).tw. (24486)
8 5 or 6 or 7 (37901)
9 (distal* or condyl* or supracondyl* or epicondyl* or transcondyl* or intercondyl* or bicondyl* or transchondral* or periprosth*).tw. (336729)
10 8 and 9 (6743)
11 exp Randomized Controlled Trial/ or exp Single Blind Procedure/ or exp Double Blind Procedure/ or Crossover Procedure/ (638909)
12 (random* or RCT or placebo or allocat* or crossover* or 'cross over' or trial or (doubl* adj1 blind*) or (singl* adj1 blind*)).ti,ab. (2025665)
13 11 or 12 (2116107)
14 (exp Animal/ or Animal.hw. or Nonhuman/) not (exp Human/ or Human Cell/ or (human or humans).ti.) (5836378)
15 13 not 14 (1872771)
16 10 and 15 (313)
17 (2014* or 2015* of 2016* or 2017* or 2018* or 2019*).dc,yr. (6952146)
18 16 and 17 (111)

Search 2 (top-up search)

17 (2019* or 2020*).dc,yr. (3649452)
18 16 and 17 (53)

Search 3 (top-up search)

17 (2020* or 2021*).dc,yr. (3820810)
18 16 and 17 (52)

Bone & Joint Journal Orthopaedic Proceedings

www.boneandjoint.org.uk/search/advanced

Advanced search

Title: femur OR femoral
Anywhere: fracture*
Anywhere: random*
Limit from January 2014 to October 2020
Narrow search by Orthopaedic Proceedings

Total = 14

World Health Organization (WHO) International Clinical Trials Registry Platform Search Portal

apps.who.int/trialsearch

fem* AND distal AND fracture*

Total = 54

ClinicalTrials.gov

(femur OR femoral) AND distal | Fracture

Total = 76

WHAT'S NEW

Date	Event	Description
5 October 2022	New citation required but conclusions have not changed	Conclusion: our conclusion is largely similar to the previous version of the review, but recommends a larger, pragmatic randomised controlled trial evaluating RIMN versus locking plate.
5 October 2022	Amended	Review authors: we added two new review authors (HC, HS), and removed two review authors (MM Zbaeda, J McArthur). Methods: we altered the outcomes to critical and important outcomes. Searches and data extraction: we updated and re-ran our literature search for studies. We extracted data, assessed risk of bias and quality for all new studies, and included the new data in this review. Results: this review included new data from seven new studies. We decided to focus our findings on RIMN versus locking plate as we feel this is the most important clinical comparison. Conclusion: our conclusion is largely similar to the previous version of the review, but recommends a larger, pragmatic randomised controlled trial evaluating RIMN versus locking plate.

HISTORY

Protocol first published: Issue 6, 2013
Review first published: Issue 8, 2015

CONTRIBUTIONS OF AUTHORS

HC: co-joint first author; extracted study data, interpreted findings, drafted the review.

HS: co-joint first author; extracted study data, interpreted findings, drafted the review.

NP: reviewed and approved final review.

XG (guarantor and Co-ordinating Editor of the Cochrane Bone, Joint and Muscle Trauma Group): reviewed and approved the final review, and is the guarantor of the content.

DECLARATIONS OF INTEREST

HC (joint first author): none.

HS (joint first author): none.

NP (statistician): none.

XG (guarantor and Co-ordinating Editor of the Cochrane Bone, Joint and Muscle Trauma Group): author of study included in review, co-editor of Trauma & Orthopaedics group. XG was not involved in data extraction, risk assessment or GRADE assessment of studies of which he was an author.

SOURCES OF SUPPORT

Internal sources

- University of Warwick, UK

  Salary provided to one or more of the authors.

External sources

- No sources of support provided

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Types of interventions

We had initially anticipated that older designs of fixed-angle implants, such as condylar plate or screw implants (DCS), might be readily grouped with more modern fixed-angle plates, where the screw 'locks' to the plate. However, the included studies included comparisons between these interventions that prevented such a grouping. Therefore, we grouped extramedullary plating systems into non-fixed-angle plates, single component fixed-angle plates (e.g. DCS) and locking plates. We included more comparisons due to more surgical interventions being analysed from included studies.

Objectives

We had planned to divide participants into three distinct populations: those sustaining a fracture in a normal (native) knee, in the bone near an intact knee replacement or in the bone near a loose knee replacement. However, there were not enough participants for periprosthetic fractures to enable this.

Assessment of risk of bias in included studies

Contrary to our initial intentions, we did not separate our assessments of risk of detection bias for subjective and objective outcome measures as we considered that rating was unlikely to be affected by the type of outcome for these types of trials.

Primary and secondary outcomes

We decided to change our primary outcomes and secondary outcomes into critical outcomes and other important outcomes as per the Methodological Expectations of Cochrane Intervention Reviews. For adverse events, we decided to report the most clinically relevant effect estimate to avoid potential unit of analysis errors.

Review authors

Two authors left the review team (MM Zbaeda, J McArthur) and two authors (HC, HS) joined the team.

INDEX TERMS

Medical Subject Headings (MeSH)

Femur; *Fracture Fixation [adverse effects] [methods]; *Fractures, Bone; Pain [etiology]; Quality of Life

MeSH check words

Adult; Humans