Surgical interventions for treating intracapsular hip fractures in adults: a network meta-analysis

Protocol information

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What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

Objectives

Search methods

Selection criteria

Data collection and analysis

Main results

Authors' conclusions

Plain language summary

[Summary title]

[Summary title]

[Summary text]

Background

This protocol has been written in accordance with guidance for authors on preparing a protocol for a systematic review with multiple interventions (Chaimani 2017; CMIMG 2014).

Description of the condition

Epidemiology

A hip fracture, or proximal femoral fracture, is a break in the upper region of the femur (thigh bone) between the subcapital region (the area just under the femoral head) and 5 cm below the lesser trochanter (a bony projection of the upper femur). The incidence of hip fractures rises with age; they are most common in the older adult population (Court-Brown 2017; Kanis 2001). Those in younger adults are usually associated with poor bone health (Karantana 2011; Rogmark 2018). A very small proportion of fractures in younger people are caused by high-energy trauma such as road traffic collisions, industrial injuries and sports injuries. The overwhelming majority of hip fractures are fragility fractures associated with osteoporosis; such fractures are caused by mechanical forces that would not ordinarily result in fracture. The World Health Organization has defined fragility fracture as those sustained from injuries equivalent to a fall from a standing height or less (Kanis 2001). In the UK, the mean age of a person with hip fracture is 83 years, and approximately two-thirds occur in women (NHFD 2017).

Hip fractures are a major healthcare problem at the individual and population level; they present a huge challenge and burden to patients, healthcare systems and society. The increased proportion of older adults in the world population means that the absolute number of hip fractures is rising rapidly across the globe. For example, in 2016 there were 65,645 new presentations of hip fracture to 177 trauma units in England, Wales and Northern Ireland (NHFD 2017). Based on population estimates for these regions for mid-2016, this equates to an incidence rate of 109 cases per 100,000 population (ONS 2016). By 2050, it is estimated that the annual worldwide incidence of hip fracture will be 6 million (Cooper 2011; Johnell 2004). Incident hip fracture rates are higher in industrialised countries than in developing countries. Northern Europe and the USA have the highest rates of hip fracture, whereas Latin America and Africa have the lowest (Dhanwal 2011). European studies show that there are more hip fractures in the north of the region than in the south, and there is a similar north-south gradient in the USA (Dhanwal 2011). Factors thought to be responsible for this variation are population demographics (with older populations in countries with higher incidence rates) and the influence of ethnicity, latitude, and environmental factors such as socioeconomic deprivation (Bardsley 2013; Cooper 2011; Dhanwal 2011; Kanis 2012).

Burden of disease

Hip fractures are associated with a high risk of death. For example, in England, Wales and Northern Ireland, the 30-day mortality rate in 2016 remained high at 6.7% despite a decline from 8.5% in 2011 and 7.1% in 2015 (NHFD 2017). The mortality rate one year after a hip fracture is approximately 30%; however, fewer than half of deaths are attributable to the fracture itself, which reflects the frailty of the patients and associated high prevalence of comorbidities and complications (Parker 1991; SIGN 2009). The impact of morbidity associated with hip fractures is similar to that of stroke, and entails a substantial loss of healthy life-years in older people (Griffin 2015). Hip fractures commonly result in reduced mobility and greater dependency, with many people failing to return to their pre-injury residence. In addition, the public health impact of hip fractures is significant: data from large prospective cohorts show the burden of disease due to hip fracture is 27 disability-adjusted life years (DALYs) per 1000 individuals, which equates to an average loss of 2.7% of the healthy life expectancy in the population at risk of fragility hip fracture (Papadimitriou 2017). The direct economic burden of hip fractures is also substantial. Hip fractures are among the most expensive conditions seen in hospitals; the aggregated cost for 316,000 inpatient episodes in the USA in 2011 was nearly USD 4.9 billion (Torio 2011). In England, Wales and Northern Ireland, hip fracture patients occupy 1.5 million hospital bed days each year, and cost the National Health Service and social care GBP 1 billion (NHFD 2017). Combined health and social care costs incurred during the first year following a hip fracture has been estimated at USD 43,669, which is greater than the cost for non-communicable diseases such as acute coronary syndrome (USD 32,345) and ischaemic stroke (USD 34,772) (Williamson 2017). In established market economies, hip fractures represent 1.4% of the total healthcare burden (Johnell 2004)

Intracapsular hip fracture

Hip fractures either involve the region of the femur which is enveloped by the ligamentous hip joint capsule (intracapsular), or that outside the capsule (extracapsular). Intracapsular fractures include subcapital (immediately below the femoral head), transcervical (across the mid-femoral neck), or basicervical (across the base of the femoral neck). These injuries are also commonly termed fractures of the 'neck of femur' (Lloyd-Jones 2015).

Intracapsular fractures can be further subdivided by fracture morphology using several different

classification systems, such as those by Garden (Garden 1961) or Pauwels (Pauwels 1935). The reliability of these various classifications is poor (Parker 1993; Parker 1998). A more appropriate grouping distinguishes only those fractures which are displaced (where the anatomy of the bone has been disrupted at the fracture site) and those which are undisplaced (Blundell 1998; Parker 1999). This system broadly corresponds with prognosis; the more displaced, the more likely the blood supply to the femoral head is compromised, which can lead to complications such as avascular necrosis and collapse of the femoral head. Furthermore, displaced fractures are less stable, so that treatments involving fixation have a higher risk of failure compared with undisplaced fractures. Approximately 60% of hip fractures are intracapsular; of these, approximately 70% to 90% are displaced (Keating 2010; NHFD 2017).

Description of the intervention

Internationally, many guidelines exist concerning the management of hip fracture (e.g. AAOS 2014; Mak 2010; NICE 2011; SIGN 2009). Each recommend that early surgical management, generally within 24 to 48 hours, is the mainstay of care for the majority of hip fractures. The overall goal of surgery in the older population is to facilitate early rehabilitation, which enables early mobilisation and the return to premorbid function while minimising the complication risk. This approach has been associated with reductions in mortality in many worldwide registries (Neufeld 2016; Sayers 2017).

For intracapsular fractures that are treated surgically, two types of operative strategy are commonly employed: joint preserving surgery (where the fracture is fixed with various types of internal fixation), or prosthetic replacement with any one of a number of arthroplasty options. A description and proposed grouping of interventions is given in Table 1.

Internal fixation

Once the decision is made to preserve the hip joint, the surgeon must elect whether to reduce or fix the fracture in situ. In general, displaced fractures must be reduced and undisplaced fractures are fixed in situ. Quality of the reduction is an important predictor of a successful outcome after fixation. Typically, fragility fractures are reduced closed, under X-ray control using an image intensifier. However, if a fracture is irreducible using closed means, it may be reduced open (exposed surgically to aid reduction). The reduced fracture is then held by an implant passed across the fracture under X-ray guidance. This may then be secondarily attached to a plate, which is attached to the outer aspect of the femur. These plates are designed to create an angular-stable implant that may confer biomechanical advantages to the bone-implant construct.

Numerous implants have been developed over time for the internal fixation of fractures. Implants may be divided into those which are smooth (pins) and those which are threaded (screws). The diameter, thread depth and pitch and core of these screws each vary. In addition, the proportion of the screw which is threaded may vary, from the tip only to the entire length. The number of pins or screws inserted across the fracture can range from one to in excess of 10, depending on the size of the implant used. Screws or pins may also be connected to a side plate which is then fixed with screws to the side of the femur.

Implants which are attached to a side plate are grouped into static and dynamic designs. In static designs, the part of the implant that crosses the fracture is fixed in relation to the side plate; in dynamic designs, this can slide within the side plate, allowing collapse of the fracture along the axis of the femoral neck until the fracture is stable.

Arthroplasty

Arthroplasty entails replacing part or all of the hip joint with an endoprosthesis, an implant constructed of non-biological materials such as metal, ceramic, or polyethylene. Arthroplasties can be grouped into two main categories: hemiarthroplasty (where only the femoral head and neck are replaced) and total hip replacement (where both the femoral head and the acetabulum or socket are replaced).

Hemiarthroplasty

Hemiarthroplasty involves replacing the femoral head with a prosthesis whilst retaining the natural acetabulum and acetabular cartilage. The type of hemiarthroplasty can be broadly divided into two groups: unipolar and bipolar. In unipolar hemiarthroplasties the femoral head is a solid block of metal. Bipolar femoral heads include a single articulation which allows movement to occur, not only between the acetabulum and the prosthesis, but also at this joint within the prosthesis itself.

The best-known of the early hemiarthroplasty designs are the Moore prosthesis (1952) and the FR Thompson Hip Prosthesis (1954). These are both monoblock implants and were designed before the development of poly(methyl methacrylate) bone cement; they were therefore originally inserted as a 'press fit'. The Moore prosthesis has a femoral stem, which is fenestrated and also has a square stem with a shoulder to enable stabilisation within the femur, which resists rotation within the femoral canal. It is generally used without cement and, in the long term, bone in-growth into the fenestrations can occur. The Thompson prosthesis has a smaller stem without fenestrations and now often used in conjunction with cement. Numerous other designs of unipolar hemiarthroplasties exist, based on stems that have been used for total hip replacements.

In bipolar prostheses there is an articulation within the femoral head component itself. In this type of prosthesis there is a spherical inner metal head with a size between 22 to 36 millimetres in diameter. This fits into a

polyethylene shell, which in turn is enclosed by a metal cap. The objective of the second joint is to reduce acetabular wear by promoting movement at the interprosthetic articulation rather than with the native acetabulum. There are a number of different types of prostheses with different stem designs. Examples of bipolar prostheses are the Charnley-Hastings, Bateman, Giliberty and the Monk prostheses, but many other types with different stem designs exist.

Total hip replacement

Total hip replacement involves the replacement of the acetabulum in addition to the femoral head. The first successful total hip replacement was developed by John Charnley, using metal alloy femoral heads articulating with polyethylene acetabular components. Subsequently, the articulating materials have diversified and designs using metal alloys, ceramics and various polyethylenes in various combinations have all been used.

Component fixation

Irrespective of the nature of the articulating surfaces, the components must be fixed to the bone to ensure longevity of the arthroplasty. The two approaches used to achieve this fixation are cemented and uncemented designs.

Cemented systems

In this approach, poly(methyl methacrylate) bone cement may be inserted at the time of surgery. It sets hard and acts a grout between the prosthesis and the implant the time of surgery. Potential advantages of cement are a reduced risk of intra-operative fracture and later peri-prosthetic fracture, and that it does not rely on integration of the prosthesis with osteoporotic bone. Major side effects of cement are cardiac arrhythmias and cardio-respiratory collapse, which occasionally occur following its insertion. These complications may be fatal; the cause is either embolism from marrow contents forced into the circulation (Christie 1994), or a direct toxic effect of the cement.

Uncemented systems

Uncemented systems rely on osseous integration forming a direct mechanical linkage between the bone and the implant. A prosthesis may be coated with a substance such as hydroxyapatite which promotes bone growth into the prosthesis. Alternatively, the surface of the prosthesis may be macroscopically and microscopically roughened so that bone grows onto the surface of the implant.

The complications of arthroplasty are those that are general to surgical management of hip fracture, for example, pneumonia, venous thromboembolism, infection, acute coronary syndrome and cerebrovascular accident; and those that are specific to arthroplasty, including dislocation of the prosthesis, loosening of the components, acetabular wear and periprosthetic fracture.

Non-operative management

Although the majority of intracapsular fractures are treated surgically, some patients have non-operative or conservative treatment, which can involve traction, bed rest or restricted mobilisation (Handoll 2008). Non-operative treatment may be acceptable where modern surgical facilities are unavailable, where low income or different systems of care preclude the patient to surgery, or in medically unfit patients with an unacceptably high risk of perioperative death. Non-operative treatment has been found to result in secondary fracture displacement of up to 62%, increased medical complications, higher mortality rates and poor functional outcomes (Lowe 2010; Rozell 2016; van de Ree 2017).

Why it is important to do this review

Despite previous efforts to establish standardised hospital care pathways, the indications for certain treatment options in the management of intracapsular fractures varies among orthopaedic surgeons. The question of which surgical treatments are optimum has been debated for decades (Chua 1997; Dickson 1953; Garden 1961; Parker 2006), and depends on many factors including age and comorbidities of the patient and type of fracture.

Numerous randomised controlled trials have compared pairs of different treatments, including internal fixations, hemiarthroplasty and total hip replacement. Additionally, several systematic reviews and meta-analyses have made direct comparisons of many different pairs of interventions, for example: different types of hemiarthroplasty (e.g. cemented versus uncemented; unipolar versus bipolar (Hedbeck 2011; Li 2013; Liu 2014; Parker 2010); internal fixation versus hemiarthroplasty (Dai 2011; Parker 2006a); internal fixation versus total hip replacement (Parker 2006a); and total hip replacement versus hemiarthroplasty (Hopley 2010; Burgers 2012; Parker 2010). Generally the meta-analyses of these treatments are inconclusive due to heterogeneity between trials and a lack of high-quality data for some comparisons.

It is difficult to determine the most effective treatment option for intracapsular fractures from the results of conventional pair-wise meta-analyses of direct evidence for three reasons:

1. some pairs of treatments have not been directly compared in a randomised controlled trial;
2. sometimes the direct evidence does not provide sufficient data and we need to support it with indirect evidence;
3. there are frequently multiple overlapping comparisons that potentially give inconsistent estimates of effect.

A network meta-analysis (NMA) overcomes these problems by simultaneously synthesising direct and indirect evidence (comparisons of treatments that have not been tested in a randomised controlled trial). For each outcome, an NMA provides estimates of effect for all possible pairwise comparisons. This allows the ranking of different interventions in order of effectiveness, and an assessment of their relative effectiveness.

We have added: This review can be considered a sister protocol to a Cochrane protocol for an NMA of surgical interventions for treating extracapsular hip fractures in adults (Sreekanta 2019).

Objectives

To assess the relative effects (benefits and harms) of all surgical treatments used in the management of intracapsular hip fractures in adults, using a network meta-analysis of randomised trials, and to generate a hierarchy of interventions according to their outcomes.

Methods

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and quasi-RCTs assessing surgical interventions for the management of patients with intracapsular hip fracture. Quasi-RCTs are defined as trials in which the methods of allocating people to a trial are not random, but are intended to produce similar groups when used to allocate participants (Cochrane 2018). Studies published as conference abstracts will be eligible for inclusion in the review, provided sufficient data relating to the methods and outcomes of interest are reported. Unpublished data will also be considered for inclusion.

Types of participants

Population

The fundamental assumption underpinning a network meta-analysis is that of transitivity (Caldwell 2005; Cipriani 2013). This implies that the distribution of potential treatment effect modifiers is balanced across the available direct comparisons. Therefore, we assume that any patient who meets the inclusion criteria below is, in principle, equally able to have been randomised to any of the eligible interventions examined in this review, i.e. they are 'jointly randomisable' (Salanti 2012).

In order to be able to report the generality of evidence available for these patients we plan to take a wide and pragmatic approach to defining the eligibility criteria. We will report details of the population in the 'Characteristics of included studies' table (See Data extraction and management).

As a benchmark, representative of the general hip fracture population, we would expect trial populations to have a mean age of between 80 and 85 years, and include 70% women, 30% with chronic cognitive impairment, and 50% with an American Society of Anesthesiologists (ASA) score greater than two (NHFD 2017; NICE 2011).

To be included in this network meta-analysis, studies must report:

- all adults with a fragility (low energy trauma) intracapsular hip fracture (displaced or undisplaced) undergoing surgery.

Studies will be excluded if they focus solely on the treatment of:

- patients younger than 16 years;
- patients with fractures caused by specific pathologies other than osteoporosis;
- patients with high-energy fractures.

Mixed populations

Studies with mixed populations (fragility and other mechanisms, ages or pathologies, or both) will also be eligible for inclusion. Where data are reported separately we will extract those subgroup data. Where a study has a mixed population, but subgroups are not reported, the proportion of participants who have standard fragility fracture is likely to vastly outnumber the proportion of those with high-energy or local pathological fractures; therefore the results will be generalisable to fragility-fracture population. We will consider sensitivity analyses, where possible, to test this assumption (see Sensitivity analysis).

Healthcare setting

The expected healthcare setting will be hospitals where operative acute care is undertaken.

Types of interventions

Trials comparing at least two of the competing interventions in the synthesis set will be eligible for inclusion. All the eligible interventions are assumed to be legitimate treatment alternatives for patients with intracapsular fractures and therefore ‘jointly randomisable’. Randomised groups are expected to be similar with respect to cointerventions.

We plan to include the following interventions:

- any implant used for internal fixation of an intracapsular hip fracture;
- all hip endoprostheses — unipolar hemiarthroplasty, bipolar hemiarthroplasty, or total hip replacement (small and large head) — applied with or without cement;
- non-operative treatment, including treatment with or without traction.

Details of the interventions will be recorded in the 'Characteristics of included studies' table.

Grouping interventions

We plan to ask our clinical authors to group our interventions into homogenous therapeutic classes by a consensus approach, and to determine which are in worldwide use. We plan to then create a more detailed table of the interventions displaying this information. We will do this in collaboration with the clinical authors and the International Fragility Fracture Network. A preliminary exercise resulted in the proposed implant groupings given in Table 1. We will also specify the direction of the comparisons by numbering the intervention groups and specifying that the intervention will be designated as the group with the lower number., ~~s~~Subcategories, e.g. number of pins or screws will be similarly ordered within the category. For example:

- smooth pins: single or multiple;
- screw treatment: single or multiple;
- fixed angle plates: static or dynamic.

Once interventions have been grouped, these will form the main nodes of the network. The nodes of the network may be split to explore differences within intervention nodes in a secondary analysis. The decision on grouping or splitting the nodes of the network will be guided by the data as well as by considering the underlying assumptions, such as whether merging insufficiently similar interventions might violate transitivity.

In addition to the aforementioned interventions, there may be unspecified interventions that may be considered for post hoc inclusion in the network. The decision as to whether to include these will be also be considered in the contexts of the transitivity assumption and whether they provide information to the network via a closed loop of treatment effects.

Interventions of direct and indirect interest

We will confirm with our clinical collaborators and the International Fragility Fracture Network those interventions that are currently in use anywhere in the world. We will include studies that evaluate one or more of these interventions. If we identify interventions that we are not aware of, we will consider them as eligible and we will include them in the network after assessing their comparability with the prespecified set of competing interventions. We will report the findings for these interventions in the results and the conclusions of the review.

To supplement the analysis and increase the available indirect information in the network, we will also consider studies that evaluate any other surgical interventions that are not currently in worldwide use as eligible for inclusion.

Types of outcome measures

We have prioritised early outcomes over late recovery, in accordance with the core outcome set for hip fracture (Haywood 2014). We have selected four months as the definition of 'early', since the majority of early recovery has been achieved at this time point (Griffin 2015).

We will extract the following outcomes.

- Mortality, defined as:
  - early (up to or before four months' follow-up); or
  - late (greater than four months' follow-up).
- Health-related quality of life (HRQoL), using recognised scores such as Short Form (SF)-36 (Ware 1992)~~SF-36~~ or EuroQol (EQ)-5D) (Dolan 1997; Rabin 2003)~~EQ-5D~~, defined as:
  - early (up to or before four months' follow-up); or
  - late (greater than four months' follow-up).
- Unplanned return to theatre: secondary procedure required for a complication resulting directly or indirectly from the index operation/primary procedure.

These outcomes were also chosen by considering all relevant outcomes of benefit and harm and also taking into account input from our stakeholder workshop (Sreekanta 2018). Depending on the length of follow-up reported, we plan to categorise the end points for each outcome as described above.

Search methods for identification of studies

We will search for all published, unpublished and ongoing relevant RCTs, without restrictions on language or date. Animal studies will be removed where possible using the strategy.

We will develop general search strategies for the large bibliographic databases to find records to feed into a number of Cochrane Reviews on hip fracture surgery. We will use three approaches to identify eligible studies. The approaches are described conceptually as:

1. hip fractures AND RCT filter;
2. hip replacement AND fractures AND RCT filter;

3. internal fixtures AND hip fractures AND RCT filter;
4. 1 OR 2 OR 3.

In MEDLINE, we will use the sensitivity-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2018). In Embase, we will use the Cochrane Embase filter (https://www.cochranelibrary.com/central/central-creation) to focus on RCTs.

Electronic searches

We will search the following electronic databases from their inception.

- Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE ALL (Ovid)
- Embase (Ovid)
- Science Citation Index (Web of Science)
- Cochrane Database of Systematic Reviews (CDSR) (Cochrane Library)
- Database of Abstracts of Reviews of Effects (DARE) (CRD website)
- Health Technology Assessment (HTA) database (CRD website)
- Epistemonikos (https://www.epistemonikos.org/)
- ClinicalTrials.gov (https://clinicaltrials.gov/)
- WHO ICTRP (www.who.int./ictrp/en/)

As CENTRAL is kept fully up-to-date with all records from the BJMT Group's Specialised Register we do not plan to search the latter separately.

The search strategies for the above databases will be modelled on the search strategy designed for MEDLINE (Appendix 1), Adaptation includes consideration of database interface differences as well as adaptation to different indexing languages. The final search strategies for each of the databases searched will be documented in the review.

Searching other resources

Unpublished research, conference reports or research reported in the grey literature will be sought by searching a range of resources, including the following.

- Handsearching of the following conference abstracts (2016 to present):
  - Fragility Fractures Network Congress
  - British Orthopaedic Association Congress
  - Orthopaedic WorldCongress (SICOT)
  - Orthopaedic Trauma Association Annual Meeting
  - Bone and Joint Journal Orthopaedic Proceedings
  - American Academy of Orthopaedic Surgeons Annual Meeting
- Proquest Dissertations and Theses
- National Technical Information Service (NTIS, for technical reports)

To identify further studies, we will screen the reference lists of eligible studies and systematic reviews published within the last five years that have been retrieved by the searches. We will screen the reference lists of the Cochrane Reviews that are relevant, irrespective of the date they were published.

Data collection and analysis

Selection of studies

Two review authors will screen titles and abstracts of all the retrieved bibliographic records in web-based systematic reviewing platform, Rayyan (Ouzzani 2016). We will retrieve the full texts of all potentially eligible records that pass the title and abstract screening, and two review authors will independently examine them for eligibility (see Criteria for considering studies for this review). Full-text screening will be carried out in another web-based platform, Covidence. Disagreements will be resolved by discussion or adjudication by another author. Where necessary, we will correspond with trial investigators where clarification is required to inform study selection. Duplicates will be excluded and multiple reports of the same study collated so that each study, rather than each report, is the unit of interest in the review. A PRISMA flow diagram (Moher 2009) will outline the study selection process, numbers of records at each stage of selection, and reasons for exclusions for full-text articles. We will also record details in a 'Characteristics of excluded studies' table.

Data extraction and management

Data will be extracted independently by two review authors using a piloted, structured form to ensure consistency of information and appraisal of each study. The form will be piloted independently on at least one study before implementation. The data will be extracted in agreement with recommendations in the DECiMAL (Data Extraction for Complex Meta-Analysis) guide developed by Pedder and colleagues, which optimises data extraction for NMAs (Pedder 2016). The two review authors will ascertain that the data are entered correctly into the final data set. We plan to extract details on the following characteristics, where reported.

Study methodology

Sponsorship/funding for trial and any notable conflicts of interest of trial authors; study design; trial phase; number of centres and location(s); size and type of setting (e.g. in-hospital, out-of-hospital, mixed or community); study period and length of follow-up; stated study objectives; study inclusion and exclusion criteria; randomisation method; masking; study disposition (number randomised, number by protocol, number available for analysis).

Population

Baseline characteristics of the participants; these include age, gender, comorbidities, functional status such as previous mobility, fracture type and displacement and cognitive status. See also 'Data on potential effect modifiers', below.

Interventions

We plan to extract data concerning the exact nature of the interventions tested. These data may include detailed intervention descriptions; for example, for internal fixation: screw and pin treatments (number and type) and plate treatment (type and dynamic versus static); for arthroplasty: type (e.g. total or hemiarthroplasty; monoblock and modular; hydroxyapatite coated or grit-blasted stem design); fixation strategy (cement or not); articulation (e.g. hemi: monopolar, bipolar; total: single, dual and triple; large and small head).

We will also extract, where available, any information on cointerventions; for example, preoperative care (e.g. prophylaxis: antibiotics, venous thromboembolism, delirium); anaesthetic management; and post-operative care (e.g. rehabilitation, etc.).

Outcome data

Where possible we will extract data by arm rather than the summary effect sizes. Outcome worksheets will be in 'one study per row format' and specify the number of arms for each study and number of participants in each arm; numbers randomised and analysed for each outcome at each time point; number of events in each arm (for rate, binary or categorical data); and means and standard deviations, effect measures, point estimates and confidence limits (for continuous variables). Where available, outcomes will be split into early and late, as previously described.

Data on potential effect modifiers

Where reported, we will extract data on the clinical and methodological variables that can act as effect modifiers across treatment comparisons. For intracapsular hip fractures, these have been identified as age, gender, baseline comorbidity, fracture displacement and cognitive status.

Assessment of risk of bias in included studies

We will assess risk of bias in the included studies, using the tool described for standard systematic reviews in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). The assessment will be performed by two independent review authors and any discrepancies will be resolved through discussion or by consulting a third author. Where details of methods are unclear or not reported, study authors will be contacted for more information.

We will evaluate risk of bias for each study, in the following domains: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting) and other bias. Each potential source of bias will be graded as high, low or unclear, and a quote will be provided from the study report together with a justification for our judgement in the 'Risk of bias' table. We will summarise our 'Risk of bias' judgements across different studies for each of the domains listed.

Assessment of risk of bias is specific to a particular result for a particular outcome (and time point) in the study. However, some domains will apply generally to the whole study (such as random sequence generation and allocation concealment); some will apply mainly to the outcome being measured or measurement method being used (such as blinding of participants and personnel, and blinding of outcome assessment); and some will apply to the specific result (such as selective reporting bias).

In the domains specific to particular outcomes, considerations of risk of bias for different types of outcomes will be given and assessments made separately, for example for participant-reported outcomes (e.g. HRQoL), observer-reported outcomes not involving judgement (e.g. all-cause mortality), and outcomes that reflect decisions made by the intervention provider (e.g. unplanned return to theatre).

As trials frequently contribute multiple results, mainly through contributing to multiple outcomes, several 'Risk of bias' assessments may be needed for each study. These assessments are likely to align with the outcomes included in a 'Summary of findings' table.

Measures of treatment effect

Summary measures

At each data point, we will extract either:

- number of observations, mean or mean change from the baseline and standard deviations (SDs), or the information from which SDs could be derived, such as standard error or CI for continuous outcomes per arm;

- number of observations and number of events per arm, or odds ratio with a measure of uncertainty such as a standard error, 95% CI, or an exact P value for dichotomous data;
- number of observations, counts and total number of participants per arm, or rate ratio with a measure of uncertainty such as a standard error, 95% CI, or an exact P value for count outcomes.

If a trial presents outcomes at more than one time point, we will extract data for all relevant time points; however, we will analyse early and late outcomes separately.

Relative treatment effects

We will report mean differences (MD) with 95% CIs for continuous outcomes measured using the same scale. Where different measures are used to assess the same outcome, data will be pooled using standardised mean difference (SMD) (Hedges's adjusted g). We will enter data presented as a scale with a consistent direction of effect across studies.

For dichotomous outcomes, we will report the risk ratio (RR) and 95% CI. Results from NMA will be presented as summary relative effect sizes — MD, SMD or risk ratio (RR) — for each possible pair of treatments.

Relative treatment ranking

We will obtain a treatment hierarchy using the surface under the cumulative ranking curve (SUCRA), which is used to evaluate superiority of different treatments (Konig 2013; Mavridis 2015; Rucker 2015; Salanti 2008b; Salanti 2011; Salanti 2012). Generally, a larger SUCRA means a more effective intervention. SUCRA can be expressed as a percentage, interpreted as the percentage of efficacy/safety of a treatment that would be ranked first without uncertainty. ~~We will use the rank-heat plot to visually present the treatment hierarchy across the multiple outcomes of this review (Veroniki 2016).~~ Computations for SUCRA values will be implemented in STATA using the command 'sucra' (Chaimani 2013; Rucker 2015; Salanti 2011).

Unit of analysis issues

Cluster-randomised trials

We anticipate that the participant will be the unit of analysis. We do not expect to encounter any within-person randomised trials or cluster-randomised trials. If we do identify any, we will treat them in accordance with the advice given in Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b).

Reports of outcomes at different time points

We anticipate outcomes to be reported at various time points. We consider those reported before four months to be 'early' and those around one year to be 'late'. Depending on the availability of the data and geometry of the network we will consider alternative methods of grouping these time points (see Sensitivity analysis).

Studies with multiple treatment groups

We will include multi-armed trials and will account for the correlation between the effect sizes in the network meta-analysis. We will follow guidance provided in the *Cochrane Handbook for Systematic Reviews of Interventions* on dealing with multiple groups from one study (Higgins 2011c) and NMA (Higgins 2011d).

We will assume that studies of different comparisons are similar in all ways apart from the interventions being compared.

Dealing with missing data

We will contact corresponding authors of included studies to obtain any unreported and missing data. Our primary interest is the effect of assignment to intervention, so we will seek results for the intention-to-treat (as randomised) population. If data are missing due to participant dropout, we will use reported results for participants that completed the study. A sensitivity analysis for unreported and missing data will be performed, and any issues will be recorded using the approaches adapted from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of clinical and methodological heterogeneity within treatment comparisons

We will assess clinical and methodological diversity in terms of participants, interventions, outcomes and study characteristics for the included studies to determine whether a meta-analysis is appropriate. We will conduct this assessment by generating the descriptive statistics for trial and study population characteristics across all eligible trials that compare each pair of interventions, and observing these data from the data extraction tables.

Assessment of transitivity across treatment comparisons

We will assess the assumption of transitivity by comparing the distribution of the potential effect modifiers across the different pairwise comparisons to ensure that they are, on average, balanced. We will assess control groups for their similarity across treatment comparisons.

Geometry of the network

Different eligibility criteria for interventions will result in different collections of evidence in the synthesis, and because of the inter-relationships across direct and indirect evidence, this can lead to different effect estimates and relative rankings. A qualitative description of network geometry will be provided and accompanied by a

network diagram of all competing interventions. The diagram will give a comprehensive definition of the nodes in the network and present any intended grouping or splitting of interventions as part of secondary analyses. The network diagram will graphically depict the available evidence and give an indication of the volume of evidence behind each comparison. The network diagram also gives a visual representation of the possible comparisons where any two modalities can be compared, as long as both are connected to the network. We will evaluate the quantitative metrics by assessing features of network geometry: the size of the nodes will reflect the amount of evidence accumulated for each treatment (total number of participants), the breadth of each edge will be proportional to the inverse of the variance of the summary effect of each direct treatment comparison, and the colour of each edge will represent risk of bias (low risk, unclear risk, or high risk; Assessment of risk of bias in included studies) (Salanti 2008a). To understand which are the most influential comparisons in the network, and how direct and indirect evidence influences the final summary data, we will use a contribution matrix that describes the percentage contribution of each direct meta-analysis to the entire body of evidence (Chaimani 2015).

Presentation of results

We plan to present the following in our review, based on Salanti 2011:

- a network diagram as described in 'Geometry of the network', above;
- direct pairwise results, i.e. the observed data, which we plan to report in a triangle table as an appendix;
- relative effects and measure of between-study heterogeneity;
- relative effects for all pairwise comparisons, based on NMA;
- methods for ranking treatments, as described in Measures of treatment effect.

Assessment of reporting biases

Standard systematic reviews consider the impact of possible reporting biases and small-study effects (e.g. funnel plots and Egger's test). These approaches have been extended for NMAs and will be explored when more than ten relevant studies are available. We will therefore consider the use of comparison-adjusted ~~and contour-enhanced funnel~~ plots using the *netfunnel* command in Stata to investigate any relationship between effect estimates and study size or precision (Chaimani 2012; Chaimani 2013). For the comparison-adjusted funnel plot, we will order interventions from the oldest to newest treatments in the entire evidence base. As this ordering may be difficult, we will use date of publication as a proxy for old to new. We anticipate that published small trials may tend to be biased in the direction of new treatments. We may also run network meta-regression models to detect associations between study size and effect size (Chaimani 2012).

Data synthesis

Methods for direct treatment comparisons

Initially, for every treatment comparison with at least two studies we will perform standard pairwise meta-analyses using a random-effects model in STATA (StataCorp 2015; White 2015). If there are any problems evident with convergence we will re-analyse the data using a fixed-effect model (White 2015). Please see 'Assessment of statistical heterogeneity', below.

Methods for indirect and mixed comparisons

For each pairwise comparison, we will synthesise data to obtain summary SMDs for continuous outcomes or RRs for dichotomous outcomes. If the collected studies appear to be sufficiently similar with respect to the distribution of effect modifiers, we will conduct a random-effects NMA to synthesise all evidence for each outcome and obtain a comprehensive ranking of all treatments. We intend to perform our NMA model with contrast-level data by running the consistency and inconsistency (design by treatment interaction) models, using multivariate meta-analysis approaches within the frequentist framework (White 2015). We will use the network suite of STATA commands (StataCorp 2015).

Assessment of statistical heterogeneity

Assumptions when estimating the heterogeneity

The network model will allow for heterogeneity between studies within trial design by incorporating a study specific random effect. In standard pairwise meta-analyses we will estimate different heterogeneity variances for each pairwise comparison. In NMA we will assume a common estimate for the heterogeneity variance across the different comparisons.

Measures and tests for heterogeneity

Pairwise comparisons

We will assess statistical heterogeneity within each pairwise comparison by visual inspection of the forest plots to detect at any large differences of intervention effects across included studies. If the studies are estimating the same intervention effect, there should be overlap between the CIs for each effect estimate on the forest plot; however if overlap is poor, or there are outliers, then statistical heterogeneity may be likely.

Review Manager 5 software automatically generates statistics that test for heterogeneity when performing meta-analysis (Review Manager 2014). These are: the Chi^2 statistic, which is the test for heterogeneity; and the I^2

statistic, which is the test used to quantify heterogeneity and which calculates the proportion of variation due to heterogeneity rather than due to chance. Heterogeneity is indicated by a Chi^2 statistic greater than the degrees of freedom (df) and a small P value (e.g. P value less than 0.05). We will interpret a Chi^2 test P value of 0.10 or less as indicative of statistical heterogeneity.

The I^2 value ranges from 0% to 100%, with higher values indicating greater heterogeneity. As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, an I^2 value of 0% to 40% may be interpreted as 'might not be important'; 30% to 60% as 'may represent moderate heterogeneity'; 50% to 90% as 'may represent substantial heterogeneity'; and 75% to 100% as 'considerable heterogeneity'(Deeks 2019).

Entire network

The assessment of statistical heterogeneity in the entire network will be based on the magnitude of the heterogeneity variance parameter (τ2) estimated from the NMA models (Jackson 2014). For dichotomous outcomes the magnitude of the heterogeneity variance will be compared with the empirical distribution, as derived by Turner (Turner 2012). For continuous outcomes where an SMD is produced, the same approach will be carried out using the empirical distribution produced by Rhodes (Rhodes 2015). ~~We will also estimate a total I^2 value for heterogeneity in the network, as described elsewhere~~ .

~~We will assess heterogeneity in the results of the random-effects model by using the method described by Dias 2012 which compares the size of the treatment effect to the extent of between-trials variation. This method tries to answer the question of what is the reasonable CI of the log odds ratio of an outcome for the prediction of the confidence interval of the log odds ratio of the same outcome of a future trial of infinite size.~~

Assessment of statistical inconsistency

We will evaluate the statistical inconsistency — which is the statistical disagreement between direct estimates (from direct comparisons of treatment) and indirect estimates (derived from the network comparisons) — by both local and global approaches, as follows (Chaimani 2017; Donegan 2013).

Global approaches for evaluating inconsistency

To check the assumption of consistency in the entire network we will use the 'design-by-treatment interaction' model (Higgins 2012; White 2012). This method accounts for different sources of inconsistency that can occur when studies with different designs (two-armed trials versus three-armed trials) give different results, as well as disagreement between direct and indirect evidence. Using this approach, we will infer about the presence of inconsistency from any source in the entire network based on a Chi^2 test. The design-by-treatment model will be performed in STATA using the 'mvmeta' command (StataCorp 2015). The results of this overall approach will also be presented graphically in a forest plot using the network forest command in STATA (StataCorp 2015).

Local approaches for evaluating inconsistency

To evaluate the presence of inconsistency locally, we will consider using approaches such as the 'loop-specific' approach. This method evaluates the consistency assumption in each closed loop of the network separately as the difference between direct and indirect estimates for a specific comparison in the loop (inconsistency factor). Then, the magnitude of the inconsistency factors and their 95% CIs can be used to infer about the presence of inconsistency in each loop. We will assume a common heterogeneity estimate within each loop. We will present the results of this approach graphically in a forest plot using the 'ifplot' command in STATA (StataCorp 2015). Moreover, the inconsistency between direct and indirect comparisons will be evaluated using a statistical approach referred to as 'node splitting', conducted with the 'sidesplit' command in STATA, when a closed triangle or quadratic loop connecting no less than three arms exists~~. In this method, two or more different treatments replace what was previously included as one treatment~~ (Dias 2010).

Investigation of heterogeneity and inconsistency

~~Inconsistency and heterogeneity are interlinked; to distinguish between these two sources of variability, we will employ the I^2 statistic for inconsistency, which measures the percentage of variability that cannot be attributed to random error or heterogeneity (within-comparison variability) (Jackson 2014).Jackson 2014~~

If we find important heterogeneity or inconsistency (or both) across treatment comparisons, we will explore the possible sources. We will investigate the distribution of clinical and methodological variables that can act as effect modifiers across treatment comparisons, and should sufficient studies be available, we will consider performan~~a~~ing ~~ce~~ network meta-regression. ~~or subgroup analyses.~~ For intracapsular hip fractures, the effect modifiers have been identified as:

- age;
- gender;
- baseline comorbidity index;
- baseline functional status;
- cognitive status;
- fracture type.

Sensitivity analysis

If sufficient studies are available, we will assess the effect of excluding:

- studies with high risk of bias;
- studies with either substantial amounts of missing data or where study authors have imputed data from the analyses (to ensure that imputations do not bias our NMA results);
- different approaches to grouping fracture subgroups;
- different approaches to pooling 'early' and 'late' outcome data;
- studies reporting interventions which are no longer in clinical use.

~~We also consider outliers detected by the comparison-adjusted funnel plots; for this we would implement the NMAoutlier package in software R (https://cran.r-project.org/web/packages/NMAoutlier/NMAoutlier.pdf)~~.

Subgroup analysis

Consistent with the grouping described in Description of the condition, if sufficient data are available, we will consider subgrouping the data by fracture displacement in separate networks. This reflects the importance of fracture displacement as a prognostic variable.

Credibility of the evidence and 'Summary of findings' table

Credibility of the evidence

We will use the GRADE approach to assess the certainty of the evidence for each outcome of interest in each paired comparison for which there is direct evidence (i.e. where two interventions have been compared in randomised trials). The GRADE system classifies evidence as high, moderate, low, or very low certainty. The starting point for certainty in estimates for randomised trials is high, but for direct comparisons may be rated down based on limitations concerning risk of bias, imprecision, inconsistency, and indirectness and publication bias (Guyatt 2008). We will present our GRADE assessment in a 'Summary of findings' table.

We will also use the GRADE approach to assess the certainty in indirect and network (mixed) effect estimates (Brignardello-Petersen 2018a; Puhan 2014). Using the 'node splitting' method, we will calculate indirect effect estimates from the available 'loops' of evidence, including loops with a single common comparator (first order) or more than one intervening treatment (higher order) connecting the two interventions of the comparison of interest. To assess the certainty in evidence for each indirect comparison we will focus on the dominant first-order loop (i.e. the first-order loop that contributes most to the indirect estimate). The certainty-of-evidence rating for indirect comparisons will be the lower of the ratings of certainty for the two direct estimates contributing to the dominant first-order loop. For instance, if one of the direct comparisons is rated as low-certainty and the other as moderate-certainty evidence, we will rate the certainty of indirect evidence as low.

For ratings of certainty for indirect comparisons, we may additionally downgrade the certainty for intransitivity (Brignardello-Petersen 2018a; Puhan 2014). The transitivity assumption implies similarity of the bodies of evidence (for instance, the trials assessing A versus C and B versus C informing a comparison of A versus B) informing indirect comparisons in terms of population, intervention, outcomes, settings and trial methodology (Salanti 2008b).

If both direct and indirect evidence are available and yield similar results, the NMA mixed-estimate certainty rating will come from the higher certainty of the two that contribute substantially to the pooled estimate. If the direct and indirect estimates show important differences (incoherence) — addressed by the difference in point estimates, the extent of overlap of CIs, and a statistical test of incoherence — we will consider further downgrading the certainty assessment of the mixed NMA effect (Brignardello-Petersen 2018b).

The full table presenting direct, indirect and network estimates, and the associated GRADE judgements of certainty, will be presented in an appendix.

'Summary of findings' tables

Typically, a 'Summary of findings' table presents the GRADE ratings, along with the intervention effects for the most important outcomes of the systematic review. In NMA, the comparison of multiple interventions is the main feature of the network and is likely to drive the structure of the tables. We will follow the guidance for producing 'Summary of findings' tables for NMAs as outlined in Chapter 11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Chaimani 2018). If the network of interventions is small (up to five competing interventions), we may produce a separate table for each main outcome. In the presence of many competing interventions (more than five), we may select and report a reduced number of pairwise comparisons. Depending on our work to group interventions and create a decision set (interventions of direct interest to our main conclusions, for example those in worldwide use) we will provide a clear rationale for the choice of the comparisons, which we will report in the 'Summary of findings' tables (Chaimani 2018). We plan to present in the tables: relative effect estimates for the highest certainty of the evidence; baseline risk information for the population in included studies; certainty of the evidence for the NMA; estimates with judgements for downgrading the body of the evidence; ranking treatment and its uncertainty; and text with definitions of NMA aspects (e.g. ranking, absolute effects) (Yepes-Nuñez 2019).

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Contributions of authors

AS (systematic reviewer): drafted the protocol, reviewed and approved the final protocol.
WE (content expert, Trauma and Orthopaedics): reviewed and approved the final protocol.
HW (senior information specialist): designed the search strategies, reviewed and approved the final protocol.
JMG (senior information specialist): designed the search strategies, drafted the protocol, reviewed and approved the final protocol.
JC (statistician): reviewed and approved the final protocol.

MY (content expert, Trauma and Orthopaedics): reviewed and approved the final protocol.
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Contributions of the editorial base

Helen Handoll (Co-ordinating Editor): edited the protocol; advised on methodology and protocol content; and approved the final version for publication.
Joanne Elliott (Managing Editor): coordinated the editorial process; advised on content; and edited the protocol.
Maria Clarke (Information Specialist): checked the search methods section.

Declarations of interest

AS: none.
WE: has an advisory role on infection control with Orthofix and Bone Support, but this is unrelated to this review. He has no known conflicts of interest~~none.~~
HW: none.
JMG: none.

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Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

1 Categorisation of interventions for intracapsular hip fractures

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Intracapsular fractures					
Internal fixation					

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Smooth pins	n/a	Single or multiple pins	• Hansson pins • Hessel pins	Smooth pin: any pin, hook pin or nail treatment, regardless of the number implanted. Smooth pins are unthreaded and may offer greater stiffness than their threaded counterparts. Hansson pin (Elos Medtech, 1982): a hook pin designed like a Rydell nail, with the same spring pin but with removed flanges. Earlier the pin was hammered in place, but in 1985 the instrument became more sophisticated and it was instead gently inserted with the use of a three-part system. The pin implant was offered in lengths from 70 to 140 mm, in increasing steps of 5 mm, with a diameter of 6.5mm. It was manufactured in stainless steel for the European market and in titanium for the Japanese market. Since 2006, Anodizing Type II, which is an oxide formula, has been used in Japan to prevent osseointegration of the pin. The surfaces had to be extremely smooth and fine, partly so that the pin implant should not grow solid into the bone, and partly because it had to be easy to assemble the pin implant. Hessel pin: a thin, smooth pin without threads, which is inserted by hammering.	
	n/a	Single or multiple nails	• Smith-Petersen nail • Rydell four-flanged nail • Nystrom nails	Smith-Petersen nail: a three-flanged steel nail introduced in 1925 for insertion across the fracture site in hip fractures. Rydell four-flanged nail: a spring-loaded nail which had four flanges and was hammered in over a guide pin. The pin had a curved end which extruded through a hole in the nail and anchored the pin in the bone in order to prevent slippage. Nystrom nail: a sharp-tipped smooth nail which was hammered across the fracture and thought to have better penetrating ability.	

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Screw treatment	n/a	Single or multiple screws	• Garden screws • Richards screws • Tronzon (VLF) screws • Uppsala/Olmed screws • Von Bahr screws • AO screws • Gouffon screws • Mecron screws • Ulleval screws • Scand screws	Any screw providing fixation; the number of screws, size of screws, thread length, diameter and configuration may all vary. Hip screws are typically cancellous screws that have coarser threads and may have an unthreaded portion allowing it to act as a lag screw. However, both fully and partially threaded variants are available.	

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Fixed angle plates	n/a	Static	• Holt nail plate • Jewett nail plate • McLaughlin nail plate • Thornton nail plate	Static device consisting of a nail, pin or screw which is passed across the fracture into the femoral head and connected to a plate on the lateral femur. These implants have no capacity for 'sliding' between the plate and pin or screw components and hence are termed 'static implants'. Holt nail plate: a four-flanged nail connected to a plate at the time of surgery Jewett nail: the nail is fixed to the plate at manufacture. Thornton and McLaughlin nail plates: the nail is connected to the plate at the time of surgery with a locking bolt.	
		Dynamic	• Dynamic hip screw • Precimed Hip Screw System • AMBI/Classic Hip Screw System (Smith & Nephew Richards) • HDS/DCS Dynamic Hip & Condylar Screw System • Syntec-Taichung DHS/DCS Plate System • Targon Femoral Neck hip Screw	Dynamic device consisting of a nail, pin or screw which is passed across the fracture into the femoral head and connected to a plate on the lateral femur. These implants allow 'sliding' between the plate and pin or screw components and hence are termed dynamic implants. Weight bearing or translation during surgery causes the femoral head to become impacted on the femoral neck producing compression of the fracture. Precimed Hip Screw System: compression fixation system used for the treatment of femoral neck and distal femoral fractures. It consists of compression plates, lag screws, compression screws, bone screws and angled blade plates. The system functions to provide immediate stability and temporary fixation during the natural healing process following fractures of the femoral neck or distal femur. AMBI/Classic Hip Screw System: compression fixation system consisting of hip screw plates and nails. AMBI plates have a barrel design which is keyless but can be converted to keyed with the insertion of a small keying clip; Classic plates have a keyed barrel design only. AMBI/Classic Lag Screws: 18 lengths: 55 mm to 140 mm; nonself-tapping for cancellous bone. Targon Femoral Neck screws (B. Braun Group): distal and proximal screws are linked with a locking plate.	

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Arthroplasty					

Total hip arthroplasty	Articulation	Femoral head and acetabular bearing surface materials	• Metal-on-polyethylene (MoP) • Ceramic-on-polyethylene (CoP) • Ceramic-on-ceramic (CoC) • Metal-on-metal (MoM) • Polyethylene material ◦ highly cross linked (HCL) ◦ not HCL	Bearing surfaces may be grouped into hard (ceramic and metal) and soft (polyethylene variants). Arthroplasties exist with many of the possible combinations of these bearing surfaces.	
		Femoral head size	• large head ≥ 36 mm • standard small head < 36 mm	Over the development of hip arthroplasty different sizes of femoral head have been used, from 22 mm to very large diameters approximating that of the native femoral head. The size of the head represents a compromise between stability and linear and volumetric wear at the articulation. The optimum size varies by indication and bearing materials. 36 mm is considered as a cut-off between standard and large sizes.	
		Acetabular cup mobility	• Single • Dual	A standard total hip arthroplasty has a single articulating surface between the femoral head and acetabulum bearing surface. Alternative designs incorporate a further articulation within the structure of the femoral head.	
	Fixation technique	Cemented	• Exeter Hip System • CPT Hip System	Both components are cemented with poly(methyl methacrylate) bone cement that is inserted at the time of surgery. It sets hard and acts as grout between the prosthesis and the bone.	
		Modern uncemented	• Corail Hip System • Avenir Hip System • Taperloc Hip System	Neither component is cemented but rely on osseous integration forming a direct mechanical linkage between the bone and the implant. The femoral prosthesis may be coated with a substance such as hydroxyapatite which promotes bone growth into the prosthesis. Alternatively, the surface of the prosthesis may be macroscopically and microscopically roughened so that bone grows onto the surface of the implant. The acetabular component may be prepared similarly and may or may not be augmented with screws fixed into the pelvis.	
		Hybrid	Combinations	The femoral stem is cemented and the acetabular cup is uncemented.	
		Reverse hybrid	Combinations	The acetabular cup is cemented and the femoral stem is uncemented	

Implant	Grouping variable	Implant subcategory	Examples[a]	Description	In worldwide use (yes/no)
Hemiarthroplasty	Articulation	Unipolar	• Thompson • Austin-Moore • Exeter Trauma Stem • Exeter Unitrax	A single articulation between the femoral head and the native acetabulum. The femoral component can be a single 'monoblock' of alloy or be modular, assembled from component parts during surgery.	
		Bipolar	• CPT modular biploar • Exeter modular biploar • Bateman • Monk	The object of the second joint is to reduce acetabular wear. This type of prosthesis has a spherical inner metal head with a size between 22 and 36 mm in diameter. This fits into a polyethylene shell, which in turn is enclosed by a metal cap. There are a number of different types of prostheses with different stem designs.	
	Fixation technique	First generation uncemented	• Thompson • Austin Moore	These prostheses were designed before the development of poly(methyl methacrylate) bone cement and were therefore originally inserted as a 'press fit'. Long-term stability through osseus integration was not part of the design concept.	
		Cemented	• Thompson • Exeter Trauma Stem • Exeter Hip System • CPT Hip System	The femoral stem is cemented with poly(methyl methacrylate) bone cement that is inserted at the time of surgery. It sets hard and acts as grout between the prosthesis and the bone.	
		Modern uncemented	• Corail • Furlong • Avenir	The femoral stem relies on osseous integration forming a direct mechanical linkage between the bone and the implant. A prosthesis may be coated with a substance such as hydroxyapatite which promotes bone growth into the prosthesis. Alternatively, the surface of the prosthesis may be macroscopically and microscopically roughened so that bone grows onto the surface of the implant.	

Footnotes

[a] This list is not exhaustive. In the review, we will add any implant tested in included trials not already listed here.

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Other published versions of this review

Classification pending references

Data and analyses

Figures

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Internal sources

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Feedback

Appendices

1 MEDLINE search strategy

Ovid interface

1 exp Femoral Fractures/
2 ((hip or hips or cervical) adj5 (fracture$ or break$ or broke$)).ti,ab,kf.
3 ((femoral$ or femur$ or acetabul$) adj5 (fracture$ or break$ or broke$)).ti,ab,kf.
4 ((intracapsular or intra-capsular or subcapital or sub-capital or transcervical or trans-cervical or basicervical or basi-cervical) adj5 (fracture$ or break$ or broke$)).ti,ab,kf.
5 ((extracapsular or extra-capsular or trochant$ or subtrochant$ or pertrochant$ or intertrochant$) adj5 (fracture$ or break$ or broke$)).ti,ab,kf.
6 (((head or neck or proximal) adj5 (fracture$ or break$ or broke$)) and (femoral$ or femur$)).ti,ab,kf.
7 or/1-6
8 randomized controlled trial.pt.
9 controlled clinical trial.pt.
10 randomized.ab.
11 placebo.ab.
12 clinical trials as topic.sh.
13 randomly.ab.
14 trial.ti.
15 8 or 9 or 10 or 11 or 12 or 13 or 14
16 7 and 15
17 Arthroplasty, Replacement, Hip/ or Hip Prosthesis/
18 Arthroplasty, Replacement/ or Hemiarthroplasty/ or Joint Prosthesis/
19 (arthroplast$ or hemiarthroplast$).ti,ab,kf.
20 ((hip or hips) adj5 (replac$ or prosthes$ or implant$)).ti,ab,kf.
21 ((joint$1 adj5 (replac$ or prosthes$ or implant$)) and (hip or hips or femur$ or femoral$ or acetabul$)).ti,ab,kf.
22 or/17-21
23 fractures, bone/ or exp fracture dislocation/ or fractures, closed/ or fractures, comminuted/ or fractures, compression/ or fractures, malunited/ or fractures, multiple/ or fractures, open/ or fractures, spontaneous/ or exp fractures, stress/ or fractures, ununited/ or intra-articular fractures/ or osteoporotic fractures/ or periprosthetic fractures/ (92406)
24 fracture$.ti,ab,kf.
25 23 or 24
26 22 and 25 and 15
27 (pin or pins or nail or nails or screw or screws or plate or plates).ti,ab,kf.
28 internal fixators/ or bone nails/ or bone plates/ or exp bone screws/
29 (static adj (device$1 or implant$1)).ti,ab,kf.
30 (dynamic adj (device$1 or implant$1)).ti,ab,kf.
31 or/27-30
32 ((hip or hips or femur$ or femoral$ or acetabul$) and (fracture$ or break$ or broke$)).ti,ab,kf.
33 (hip or hips or femur$ or femoral$ or acetabul$).ti,ab,kf. and (fractures, bone/ or exp fracture dislocation/ or fractures, closed/ or fractures, comminuted/ or fractures, compression/ or fractures, malunited/ or fractures, multiple/ or fractures, open/ or fractures, spontaneous/ or exp fractures, stress/ or fractures, ununited/ or intra-articular fractures/ or osteoporotic fractures/ or periprosthetic fractures/)
34 or/32-33
35 31 and 34 and 15
36 16 or 26 or 35
37 exp animals/ not humans/

38 36 not 37