Cochrane
Library

Cochrane Database of Systematic Reviews

Surgical interventions for treating extracapsular hip fractures in adults: a network meta-analysis (Protocol)

Sreekanta A, Eardley WGP, Parker MJ, Felix LM, Wood H, Glanville JM, Cook J, Griffin XL

Sreekanta A, Eardley WGP, Parker MJ, Felix LM, Wood H, Glanville JM, Cook J, Griffin XL.

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

Cochrane Database of Systematic Reviews 2019, Issue 8. Art. No.: CD013405.

DOI: 10.1002/14651858.CD013405.

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	4
METHODS	4
ACKNOWLEDGEMENTS	12
REFERENCES	12
ADDITIONAL TABLES	16
APPENDICES	32
CONTRIBUTIONS OF AUTHORS	33
DECLARATIONS OF INTEREST	34
SOURCES OF SUPPORT	34

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

Ashwini Sreekanta¹, Will GP Eardley², Martyn J Parker³, Lambert M Felix¹, Hannah Wood⁴, Julie M Glanville⁴, Jonathan Cook¹, Xavier L Griffin¹

¹Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, UK.

²Department of Trauma and Orthopaedics, The James Cook University Hospital, Middlesbrough, UK. ³Department of Orthopaedics, Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough, UK. ⁴York Health Economics Consortium, York, UK

Contact address: Ashwini Sreekanta, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Kadoorie Centre, John Radcliffe Hospital, Headley Way, Oxford, OX3 9DU, UK. ashwini.sreekanta@ndorms.ox.ac.uk, ashcanbereached@gmail.com.

Editorial group: Cochrane Bone, Joint and Muscle Trauma Group.

Publication status and date: New, published in Issue 8, 2019.

Citation: Sreekanta A, Eardley WGP, Parker MJ, Felix LM, Wood H, Glanville JM, Cook J, Griffin XL. Surgical interventions for treating extracapsular hip fractures in adults: a network meta-analysis. *Cochrane Database of Systematic Reviews* 2019, Issue 8. Art. No.: CD013405. DOI: 10.1002/14651858.CD013405.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

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

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 seen 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 fractures 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 also 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 have 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).

Extracapsular hip fracture

Hip fractures either involve the region of the bone which is enveloped by the ligamentous hip joint capsule (intracapsular), or that outside the capsule (extracapsular). Extracapsular fractures traverse the femur within the area of bone bounded by the intertrochanteric line proximally, up to a distance of 5 cm from the distal part of the lesser trochanter. Several classification methods have been proposed to define different types of extracapsular fractures (AO Foundation 2018; Evans 1949; Jensen 1980). They are generally subdivided depending on their relationship to the greater and lesser trochanters (the two bony projections present at the upper end of the femur) and the complexity of the fracture configuration. It is increasingly clear that each of these classifications is limited in its generalisability since inter- and intra-observer agreement is poor. Table 1 provides a description of the most recent classification of trochanteric fractures (AO Foundation 2018). For this review we plan to use a pragmatic simplification of these classifications, as follows.

- Trochanteric fractures: those which lie mostly between the intertrochanteric line and a transverse line at the level of the lesser trochanter. These can be further divided into simple two-part stable fractures, and comminuted or reverse obliquity unstable fractures.
- Subtrochanteric fractures: those which mostly lie in the region bordered by the lesser trochanter and 5 cm distal to the lesser trochanter.

Approximately 40% of hip fractures are extracapsular, of which 90% are trochanteric and 10% are subtrochanteric (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 pre-morbid function while minimising the complication risk. This approach has been associated with reductions in mortality in many worldwide registries (Neufeld 2016; Sayers 2017).

Osteosynthesis

The most common surgical treatment for extracapsular fractures is osteosynthesis. A variety of internal fixation implants exist, including both extramedullary and intramedullary types. External fixation, where external bars traverse the fracture and are attached to the bones by threaded pins, has also been applied. A description and proposed grouping of interventions is given in Table 2. Although less common, arthroplasty is an option in the management of these fractures. A description and proposed grouping of arthroplasty interventions is provided in Table 3.

In general, the majority of fractures must be reduced prior to fixation. Typically, fragility fractures are reduced closed, under X-ray control using an image intensifier. However, if a fracture is irreducible using closed means, the fracture may be reduced open (exposed surgically to aid reduction). The reduced fracture is held by an implant passed across the fracture, or is bridged by an external fixator.

Extramedullary implants are those where a side plate is screwed to the lateral edge of the femur; they 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. There are also variable angles between the plate and the interfragmentary components of the system. In general there are those which approximate a right angle, such as condylar screws and blade plates, and those which approximate the native angle of the femoral neck (approximately 130 degrees), such as the sliding hip screw.

Intramedullary implants are those which run along the internal course of the femur. They are grouped into cephalocondylic nails which are advanced in an antegrade fashion into the femur, and condylocephalic nails which are advanced retrograde. Retrograde nails, such as Ender nails, are passed from distal to proximal and a single implant traverses both the femoral canal and the fracture. Cephalomedullary nails, such as the Gamma or Proximal Femoral Nail (PFN), are passed from the tip of the greater trochanter or piriformis fossa into the medullary canal and subsequently an interfragmentary component is passed separately from the lateral femur through the centre of the nail and across the fracture. Cephalomedullary implants are grouped into short nails (where the tip of the nail ends in the region of the mid femur) and long nails (where the tip ends in the region of the distal metaphysis).

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

(THR) (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 ingrowth into the fenestrations can occur. The Thompson prosthesis has a smaller stem without fenestrations and is 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 which measures between 22 and 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 as grout between the prosthesis and the implant at 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, and are caused by 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 extracapsular fractures are treated surgically, some patients have non-operative or conservative treatment. In 2016, 0.6% of patients with an extracapsular fracture in England and Wales did not receive surgical management ([NHFD 2017](#)). Conservative or non-operative management can consist of traction and may be of two types: skeletal traction (where traction is applied to the injured limb either via a pin inserted into the proximal tibia or distal femur) or skin traction (where adhesive tape or bandages are applied to the injured leg). Traction is then maintained, for a period of two to four months, by using 4 kg to 9 kg of weight. This ensures that the injured leg is immobilised whilst the fracture heals. 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.

Why it is important to do this review

Currently, there are six independent Cochrane Reviews that have focused on specific interventions for extracapsular fracture ([Parker 2000](#); [Parker 2006](#); [Parker 2009](#); [Parker 2010](#); [Parker 2013](#); [Queally 2014](#)). The findings of the reviews varied and although the sliding hip screw (SHS) is widely used in practice, there is uncertainty about the beneficial effects of intramedullary implants or the most appropriate implant for the specific type of extracapsular fracture ([Mak 2010](#)). Moreover, the implant design of the intramedullary nail is evolving substantially and a body of evidence supporting their use in certain situations is building. It is difficult to determine the most effective treatment option for extracapsular 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 the different interventions in order of effectiveness, and assessment of their relative effectiveness.

A related Cochrane NMA, the protocol of which has been developed in parallel with this protocol, on surgical interventions for treating intracapsular hip fractures in adults is also underway ([Sreekanta 2019](#)).

OBJECTIVES

To assess the relative effects (benefits and harms) of all surgical treatments used in the management of extracapsular 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 extracapsular 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) extracapsular hip fracture (trochanteric or subtrochanteric) 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 a 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 the 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 extracapsular 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 fixation of an extracapsular 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 2](#) and [Table 3](#). 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. Subcategories, e.g. number of nails, will be similarly ordered within the category. For example:

- intramedullary nail;
- extramedullary implant;
- external fixation;
- arthroplasty.

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 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 and including four months' follow-up); or
 - late (greater than four months' follow-up).
- Health-related quality of life (HRQoL), measured using recognised scores such as the Short Form-36 (SF-36) ([Ware 1992](#)) or EuroQol-5D (EQ-5D) ([Dolan 1997](#); [EQ-5D](#)), defined as:
 - early (up to and including 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 stipulated 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) (the 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 the following conference abstracts (2016 to present)

- Fragility Fractures Network Congress
- British Orthopaedic Association Congress
- Orthopaedic World Congress (SICOT)
- Orthopaedic Trauma Association Annual Meeting
- Bone and Joint Journal Orthopaedic Proceedings
- American Academy of Orthopaedic Surgeons Annual Meeting

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 and funding for the 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 stability 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: 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 postoperative care (e.g. rehabilitation).

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 will 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 extracapsular hip fractures, these have been identified as age, gender, baseline comorbidity, cognitive status, fracture type, and fracture stability.

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 confidence interval (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 (MDs) 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. 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, but 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 up to and including 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 2011e](#)).

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 plausibility of 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/plot of all competing interventions (using the STATA command 'networkplot' ([StataCorp 2015](#))). 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; see [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 10 relevant studies are available. We will therefore consider the use of comparison-adjusted 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 risk ratios 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 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 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 χ^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 χ^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 χ^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 (τ^2) 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).

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 χ^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 (Dias 2010).

Investigation of heterogeneity and inconsistency

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 performing network meta-regression. For extracapsular hip fractures, the effect modifiers have been identified as:

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

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.

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 type (trochanteric versus subtrochanteric) in separate networks.

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 is rated 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-Núñez 2019).

ACKNOWLEDGEMENTS

We thank Joanne Elliott, Helen Handoll and Maria Clarke for editorial support. We thank Harman Chaudhry (external referee), Gordon Guyatt and Maria Petropoulou (methodological referees), and MingHui Yang (content expert, Trauma and Orthopaedics) for their helpful comments.

This project was funded and supported by the National Institute for Health Research (NIHR). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

REFERENCES

Additional references

AAOS 2014

American Academy of Orthopaedic Surgeons (AAOS). Management of hip fractures in the elderly. Evidence-based clinical practice guideline. www.aaos.org/research/guidelines/HipFxGuideline.pdf (accessed 22 March 2019).

AO Foundation 2018

AO Foundation. Femur. *Journal of Orthopaedic Trauma* 2018;**32** Suppl 1:S33–44. [PUBMED: 29256948]

Bardsley 2013

Smith P, Ariti C, Bardsley M. Nuffield Trust & Health Foundation: Focus on hip fracture. Trends in emergency admissions for fractured neck of femur, 2001 to 2011. www.nuffieldtrust.org.uk/research/focus-on-hip-fracture (accessed 9 January 2019).

Brignardello-Petersen 2018a

Brignardello-Petersen R, Bonner A, Alexander PE, Siemieniuk RA, Furukawa TA, Rochwerg B, et al. GRADE Working Group. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *Journal of Clinical Epidemiology* 2018;**93**:36–44.

Brignardello-Petersen 2018b

Brignardello-Petersen R, Mustafa RA, Siemieniuk RAC, Murad MH, Agoritsas T, et al. GRADE approach to rate the certainty from a network meta-analysis: addressing

incoherence. *Journal of Clinical Epidemiology* 2018;**108**: 77–85.

Caldwell 2005

Caldwell DM, Ades AE, Higgins JPT. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;**331**(7521):897–900.

Chaimani 2012

Chaimani A, Salanti G. Using network meta-analysis to evaluate the existence of small-study effects in a network of interventions. *Research Synthesis Methods* 2012;**3**(2): 161–76. [PUBMED: 26062088]

Chaimani 2013

Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G. Graphical Tools for Network Meta-Analysis in STATA. *PLOS ONE* 2013;**8**(10):e76654.

Chaimani 2015

Chaimani A, Salanti G. Visualizing assumptions and results in network meta-analysis: the network graphs package. *Stata Journal* 2015;**15**(4):905–50.

Chaimani 2017

Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Additional considerations are required when preparing a protocol for a systematic review with multiple interventions. *Journal of Clinical Epidemiology* 2017;**83**:65–74.

Chaimani 2018

Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Chapter 11: Undertaking network meta-analyses. Draft version (16 September 2018) for inclusion in: Higgins JPT, Thomas J, Chandler J, Cumpston MS, Li T, Page MJ, Welch V (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. London: Cochrane.

Christie 1994

Christie J, Burnett R, Potts HR, Pell AC. Echocardiography of transatrial embolism during cemented and uncemented hemiarthroplasty of the hip. *Journal of Bone and Joint Surgery - British Volume* 1994;**76**(3):409–12.

Cipriani 2013

Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. *Annals of Internal Medicine* 2013;**159**(2):130–7.

CMIMG 2014

Comparing Multiple Interventions Methods Group. Protocol template for a Cochrane intervention review that compares multiple interventions. methods.cochrane.org/cmi/comparing-multiple-interventions-cochrane-reviews (accessed 31 October 2018).

Cochrane 2018

Cochrane. Glossary. community.cochrane.org/glossary (accessed 2 November 2018).

Cooper 2011

Cooper C, Cole ZA, Holroyd CR, Earl SC, Harvey NC, Dennison EM, et al. Secular trends in the incidence of hip and other osteoporotic fractures. *Osteoporosis International* 2011;**22**(5):1277–88.

Court-Brown 2017

Court-Brown CM, Clement ND, Duckworth AD, Biant LC, McQueen MM. The changing epidemiology of fall-related fractures in adults. *Injury* 2017;**48**(4):819–24.

Covidence [Computer program]

Veritas Health Innovation. Covidence systematic review software. Melbourne, Australia: Veritas Health Innovation, 2013. Available at www.covidence.org.

Deeks 2019

Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10: Analysing data and undertaking meta-analyses. Draft version (29 January 2019) for inclusion in: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page M, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. London: Cochrane.

Dhanwal 2011

Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: worldwide geographic variation. *Indian Journal of Orthopaedics* 2011;**45**(1):15–22.

Dias 2010

Dias S, Welton N J, Caldwell D M, Ades A E. Checking consistency in mixed treatment comparison meta-analysis. *Statistics in Medicine* 2010;**29**(7-8):932–44.

Dolan 1997

Dolan P. Modeling valuations for EuroQol health states. *Medical Care* 1997;**35**(11):1095–108.

Donegan 2013

Donegan S, Williamson P, D'Alessandro U, Tudur Smith C. Assessing key assumptions of network meta-analysis: a review of methods. *Research Synthesis Methods* 2013;**4**(4): 291–323. [PUBMED: 26053945]

EQ-5D

EQ-5D. <https://euroqol.org/> (accessed 14 August 2019).

Evans 1949

Evans EM. The treatment of trochanteric fractures of the femur. *Journal of Bone and Joint Surgery - British Volume* 1949;**31**(2):190–203. [PUBMED: 18150534]

Griffin 2015

Griffin XL, Parsons N, Achten J, Fernandez M, Costa ML. Recovery of health-related quality of life in a United Kingdom hip fracture population: The Warwick Hip Trauma Evaluation - a prospective cohort study. *Bone and Joint Journal* 2015;**97**(3):372–82.

Guyatt 2008

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**(7650):924–6.

Haywood 2014

Haywood KL, Griffin XL, Achten J, Costa ML. Developing a core outcome set for hip fracture trials. *Bone and Joint Journal* 2014;**96-B**(8):1016–23.

Higgins 2011a

Higgins JPT, Altman DG. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook.

Higgins 2011b

Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16.3.4: Approximate analyses of cluster-randomized trials for meta-analysis: effective sample sizes. 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. The Cochrane Collaboration.

Higgins 2011c

Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16.5: Studies with more than two intervention groups. 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.

Higgins 2011d

Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16.6: Indirect comparisons and multiple treatments meta-analysis. 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. The Cochrane Collaboration.
- Higgins 2011e**
Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16: Special topics in statistics. 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.
- Higgins 2012**
Higgins JP, Jackson D, Barrett JK, Lu G, Ades AE, White IR. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Research Synthesis Methods* 2012;**3**(2):98–110. [PUBMED: 26062084]
- Jackson 2014**
Jackson D, Barrett JK, Rice S, White IR, Higgins JP. A design-by-treatment interaction model for network meta-analysis with random inconsistency effects. *Statistics In Medicine* 2014;**33**(21):3639–54. [PUBMED: 24777711]
- Jensen 1980**
Jensen JS. Classification of trochanteric fractures. *Acta Orthopaedica Scandinavica* 1980;**51**(5):803–10. [PUBMED: 7468173]
- Johnell 2004**
Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. *Osteoporosis International* 2004;**15**(11):897–902.
- Kanis 2001**
Kanis JA, Oden A, Johnell O, Jonsson B, de Laet C, Dawson A. The burden of osteoporotic fractures: a method for setting intervention thresholds. *Osteoporosis International* 2001;**12**(5):417–27.
- Kanis 2012**
Kanis JA, Oden A, McCloskey EV, Johansson H, Wahl DA, Cooper C. A systematic review of hip fracture incidence and probability of fracture worldwide. *Osteoporosis International* 2012;**23**(9):2239–56.
- Karantana 2011**
Karantana A, Boulton C, Bouliotis G, Shu KS, Scammell BE, Moran CG. Epidemiology and outcome of fracture of the hip in women aged 65 years and under: a cohort study. *Journal of Bone Joint Surgery - British volume* 2011;**93**(5): 658–64.
- Konig 2013**
Konig J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and characterizing mixed treatment comparisons. *Statistics in Medicine* 2013;**32**(30): 5414–29.
- Lefebvre 2018**
Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I, et al. Chapter 4: Searching for and selecting studies. Draft version (13 September 2018) for inclusion in Higgins JPT, Thomas J, Chandler J, Cumpston MS, Li T, Page MJ, Welch V (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. London: Cochrane.
- Mak 2010**
Mak JC, Cameron ID, March LM. Evidence-based guidelines for the management of hip fractures in older persons: an update. *Medical Journal of Australia* 2010;**192**(1):37–41. [PUBMED: 20047547]
- Mavridis 2015**
Mavridis D, Giannatsi M, Cipriani A, Salanti G. A primer on network meta-analysis with emphasis on mental health. *Evidence-Based Mental Health* 2015;**18**(2):40–6.
- Moher 2009**
Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009;**6**(7): e1000097.
- Neufeld 2016**
Neufeld ME, O'Hara NN, Zhan M, Zhai Y, Broekhuijsen HM, Lefavre KA, et al. Timing of hip fracture surgery and 30-day outcomes. *Orthopedics* 2016;**39**(6):361–8.
- NHFD 2017**
NHFD. The National Hip Fracture Database (NHFD) annual report 2017. www.nhfd.co.uk (accessed 30 October 2018).
- NICE 2011**
National Clinical Guideline Centre (UK). The management of hip fracture in adults. NICE clinical guidelines, no. 124. London: Royal College of Physicians (UK); 2011. www.nice.org.uk/guidance/cg124/evidence/full-guideline-pdf-183081997 (accessed 30 October 2018).
- ONS 2016**
Office for National Statistics. Mid-2016 population estimates for the UK, England and Wales, Scotland and Northern Ireland. <https://bit.ly/28IITPF> (accessed 30 October 2018).
- Ouzzani 2016**
Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews* 2016;**5**(1):210.
- Papadimitriou 2017**
Papadimitriou N, Tsilidis KK, Orfanos P, Benetou V, Ntzani EE, Soerjomataram I, et al. Burden of hip fracture using disability-adjusted life-years: a pooled analysis of prospective cohorts in the CHANCES consortium. *Lancet Public Health* 2017;**2**(5):e239–e46.
- Parker 1991**
Parker MJ, Anand JK. What is the true mortality of hip fractures?. *Public Health* 1991;**105**(6):443–6.
- Parker 2000**
Parker MJ, Handoll HH, Bhonsle S, Gillespie WJ. Condylcephalic nails versus extramedullary implants for extracapsular hip fractures. *Cochrane Database Systematic Reviews* 2000;**2**:CD000338. [PUBMED: 10796346]

Parker 2006

Parker MJ, Handoll HH. Replacement arthroplasty versus internal fixation for extracapsular hip fractures in adults. *Cochrane Database Systematic Reviews* 2006;**2**:CD000086. [PubMed: 16625528]

Parker 2009

Parker M J, Handoll HH. Osteotomy, compression and other modifications of surgical techniques for internal fixation of extracapsular hip fractures. *Cochrane Database of Systematic Reviews* 2009, Issue 2. DOI: 10.1002/14651858.CD000522.pub2

Parker 2010

Parker MJ, Handoll HH. Gamma and other cephalocondylic intramedullary nails versus extramedullary implants for extracapsular hip fractures in adults. *Cochrane Database of Systematic Reviews* 2010, Issue 9. DOI: 10.1002/14651858.CD000093.pub5

Parker 2013

Parker MJ, Das A. Extramedullary fixation implants and external fixators for extracapsular hip fractures in adults. *Cochrane Database of Systematic Reviews* 2013, Issue 2. DOI: 10.1002/14651858.CD000339.pub3

Pedder 2016

Pedder Hugo, Sarri Grammati, Keeney Edna, Nunes Vanessa, Dias Sofia. Data extraction for complex meta-analysis (DECiMAL) guide. *Systematic Reviews* 2016;**5**:212.

Puhan 2014

Puhan MA, Schunemann HJ, Murad MH, Li T, Brignardello-Petersen R, Singh JA, et al. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. *BMJ* 2014; **349**:g5630. [PubMed: 25252733]

Queally 2014

Queally JM, Harris E, Handoll HH, Parker MJ. Intramedullary nails for extracapsular hip fractures in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 9. DOI: 10.1002/14651858.CD004961.pub4

Review Manager 2014 [Computer program]

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

Rhodes 2015

Rhodes KM, Turner RM, Higgins JP. Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. *Journal of Clinical Epidemiology* 2015;**68**(1):52–60.

Rogmark 2018

Rogmark C, Kristensen MT, Viberg B, Ronnquist SS, Overgaard S, Palm H. Hip fractures in the non-elderly-Who, why and whither?. *Injury* 2018;**49**(8):1445–50.

Rucker 2015

Rucker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Medical Research Methodology* 2015;**15**:58.

Salanti 2008a

Salanti G, Kavvoura FK, Ioannidis JP. Exploring the geometry of treatment networks. *Annals of Internal Medicine* 2008;**148**(7):544–53.

Salanti 2008b

Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Statistical Methods in Medical Research* 2008;**17**(3):279–301.

Salanti 2011

Salanti G, Ades AE, Ioannidis JPA. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *Journal of Clinical Epidemiology* 2011;**64**(2):163–71.

Salanti 2012

Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Research Synthesis Methods* 2012;**3**(2):80–97.

Sayers 2017

Sayers A, Whitehouse MR, Berstock JR, Harding KA, Kelly MB, Chesser TJ. The association between the day of the week of milestones in the care pathway of patients with hip fracture and 30-day mortality: findings from a prospective national registry - The National Hip Fracture Database of England and Wales. *BMC Medicine* 2017;**15**:62.

SIGN 2009

Scottish Intercollegiate Guidelines Network (SIGN). Management of hip fracture in older people. A national clinical guideline. <https://www.sign.ac.uk/assets/sign111.pdf> (accessed 30 October 2018).

Sreekanta 2018

Sreekanta A, Felix L, Grant R, Handoll H, Elliott J, Cook JA, Griffin XL. Optimising stakeholder engagement for informing direction and scope of a programme of Cochrane Reviews on hip fracture management. In: Abstracts of the 25th Cochrane Colloquium, Edinburgh, UK. Cochrane Database of Systematic Reviews 2018;(9 Suppl 1):204 <https://doi.org/10.1002/14651858.CD201801>.

Sreekanta 2019

Sreekanta A, Eardley WGP, Wood H, Glanville JM, Yang M, Cook J, et al. Surgical interventions for treating intracapsular hip fractures in adults: a network meta-analysis. *Cochrane Database of Systematic Reviews* 2019, issue In Press.

StataCorp 2015

StataCorp, 2017. Stata Statistical Software: Release 2015. College Station, TX: StataCorp LLC.

Torio 2011

Torio CM, Andrews RM. National inpatient hospital costs: The most expensive conditions by Payer, 2011. Healthcare Cost and Utilization Project Statistical Brief # 160. www.hcup-us.ahrq.gov/reports/statbriefs/sb160.pdf (accessed 9 January 2019).

Turner 2012

Turner RM, Davey J, Clarke MJ, Thompson SG, Higgins JP. Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of Systematic Reviews. *International Journal of Epidemiology* 2012;**41**(3):818–27. [PUBMED: 22461129]

Ware 1992

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 1992;**30**(6):473–83.

White 2012

White IR, Barrett JK, Jackson D, Higgins JPT. Consistency and inconsistency in network meta-analysis: model estimation using multivariate meta-regression. *Research Synthesis Methods* 2012;**3**(2):111–25.

White 2015

White IR. Network meta-analysis. *Stata Journal* 2015; Vol. 15, issue 4.

Williamson 2017

Williamson S, Landeiro F, McConnell T, Fulford-Smith L, Javaid MK, Judge A, et al. Costs of fragility hip fractures globally: a systematic review and meta-regression analysis. *Osteoporosis International* 2017;**28**(10):2791–800.

Yepes-Núñez 2019

Yepes-Núñez JJ, Li S, Guyatt G, Jack, SM, Brozek, JL, Beyene J, et al. Development of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Summary of Findings (SoF) table for network meta-analysis. *Journal of Clinical Epidemiology* 2019 [Epub ahead of print]:<https://doi.org/10.1016/j.jclinepi.2019.04.018>.

* Indicates the major publication for the study

ADDITIONAL TABLES

Table 1. Trochanteric region fractures: type and surgical management (Revised AO/OTA classification, Jan 2018)

Type	Features	Stability	Description
Simple, pertrochanteric fractures (A1)	<ul style="list-style-type: none"> Isolated pertrochanteric fracture Two-part fracture Lateral wall intact 	Stable	The fracture line can begin anywhere on the greater trochanter and end either above or below the lesser trochanter. The medial cortex is interrupted in only one place
Multifragmentary pertrochanteric fractures (A2)	<ul style="list-style-type: none"> With one or more intermediate fragments Lateral wall may be incompetent 	Unstable	The fracture line can start laterally anywhere on the greater trochanter and runs towards the medial cortex which is typically broken in two places. This can result in the detachment of a third fragment which may include the lesser trochanter
Intertrochanteric fractures (A3)	<ul style="list-style-type: none"> Simple oblique fracture Simple transverse fracture Wedge or multifragmentary fracture 	Unstable	The fracture line passes between the two trochanters, above the lesser trochanter medially and below the crest of the vastus lateralis laterally

AO/OTA: Arbeitsgemeinschaft für Osteosynthesefragen (German for “Association for the Study of Internal Fixation”)/Orthopaedic Trauma Association

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures

Implant category	Grouping variable	Implant subcategory (entry point/static or dynamic)	Examples ^a	Description	In worldwide use (yes/no)
Extracapsular fractures					

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

External fixation					
External fixator	n/a	n/a	<ul style="list-style-type: none"> • Hoffman (Stryker) • Large External Fixator (Depuy Synthes) • Lower Extremity Fixator (Orthofix) 	Threaded pins are passed into the bone proximal and distal to the fracture. These pins are attached to external bars which may be arranged in numerous configurations to bridge the fracture	
Internal fixation					
Intramedullary nails	n/a	Cephalomedullary nails	<ul style="list-style-type: none"> • Y-nail (Küntscher 1967) • Zickel nail (Zicker 1976) • Gamma nail (first generation, Howmedica) • Gamma nail (second generation, Stryker) • Gamma3 nail (Stryker) <ul style="list-style-type: none"> ◦ Gamma3 Trochanteric Nail ◦ Gamma3 Long Nail ◦ Gamma3 RC Lag Screw ◦ Gamma3 Distal Targeting System • Gamma3 sliding lag screw (Stryker) • Gamma3 non-sliding lag screw (Stryker) • Proximal femoral nail (PFN) • Proximal femoral nail antirotation 	<p>A nail is inserted antegrade into the intramedullary canal of the femur. Once the nail is in place a pin, nail or screw is passed from the lateral cortex of the femur across the fracture and through the nail into the femoral head. The pin or screw can be fixed to the nail in various ways to allow or prevent sliding as well as provide rotational stability about the axis of the femoral neck</p> <p>Küntscher Y nail: an early intramedullary nail based on the principles of stable fixation and closed nailing</p> <p>Zickel nail: similar to the Küntscher Y-nail. The Küntscher Y-nail was considered to be more dif-</p>	

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

			<p>(PFNA) (DePuy Synthes)</p> <ul style="list-style-type: none"> ○ PFNA nail long ○ PFNA nail standard ● PFNA II ● ACE <p>Trochanteric nail System (ATN) (DePuy)</p> <ul style="list-style-type: none"> ● Russel-Taylor Recon nail <ul style="list-style-type: none"> ● Intramedullary hip screw clinically proven (IMHS CP) (Smith & Nephew) <ul style="list-style-type: none"> ● Targon proximal femoral nail (Aesculap) ● Zimmer® Natural Nail® System (Zimmer) ● Holland Nail™ System 	<p>difficult to insert that the Zickel nail. The major complication of the Kuntscher Y-nail was distal migration of the intramedullary nail, although this may be prevented by the insertion of a bolt through the upper end of the nail. Zickel developed his device to address the difficulties with the former</p> <p>Gamma nail (first generation, 1980s) or Standard Gamma Nail (SGN): a prototype intramedullary nailing system which became the most widely used for trochanteric fractures worldwide. Complications such as cut-out, implant breakage, femoral shaft fractures, and reduction loss were reported with its use</p> <p>Long Gamma Nail (LGN) (1992): used for subtrochanteric hip fractures, femoral shaft fractures and combined trochanter-diaphyseal fractures of the femur</p> <p>Trochanteric Gamma Nail (TGN) (1997): a modified SGN, re-</p>	
--	--	--	---	---	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>placed the SGN Gamma3 Nail-ing System: third generation of in-tramedullary short and long Gamma fixation nails. Four locking grooves al-low for quarter-turn advancement of 0.8 mm to allow for pre-cise lap screw posi-tioning</p> <p>PFN (Synthes, Solothurn, Switzer-land) and ATN (dePuy, Warsaw, IN, USA): developed to address the mechan-ical complica-tions of the standard gamma nail. These intramedullary im-plants provide slid-ing head-neck screws. How-ever complications still occurred, such as lateral migration of head-neck screw, cut-out from head-neck fragment and cut-through of the anti-rotation screw into the joint</p> <p>PFNA (Synthes, Solothurn, Switzer-land) was designed by the AO/ASIF group for improving the rotational stabil-ity. It used a sin-gle head-neck fixa-tion device called a 'helical blade'</p> <p>ACE Trochanteric</p>	
--	--	--	--	---	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>nail System (ATN) (DePuy): intended to treat stable and unstable proximal fractures of the femur including pertrochanteric fractures, intertrochanteric fractures, high subtrochanteric fractures and combinations of these fractures. Trochanteric Long Nail System: additionally indicated to treat pertrochanteric fractures associated with shaft fractures, pathologic fractures in osteoporotic bone of the trochanteric and diaphyseal areas, long subtrochanteric fractures, ipsilateral femoral fractures, proximal or distal nonunions and malunions and revision procedures</p> <p>Russel-Taylor Recon nail: a second-generation locking femoral nail</p> <p>Intramedullary hip screw (IMHS): a short intramedullary nail with interlocking screws that can be used to treat subtrochanteric and intertrochanteric fe-</p>	
--	--	--	--	--	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>mur fractures. This nail, which has the biomechanical advantage of being an intramedullary appliance but can be placed percutaneously, is inserted under fluoroscopic control with the patient on a fracture table. Reaming is not usually necessary</p> <p>Intramedullary hip screw clinically proven (IMHS™ CP): intramedullary hip screw device that provides a barrel through which a lag screw can slide. Introduced in 1991 with its design, the IMHS system provided a more minimally invasive technique than the traditional Compression Hip Screw. By featuring a Centering Sleeve to enhance Lag Screw sliding and medializing the implant to reduce the moment arm, this design improved implant biomechanics for the treatment of hip fractures</p> <p>Targon® PFT nailing system: targeting device is suitable for all CCD angles and permits shorter</p>	
--	--	--	--	---	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>and less invasive incisions thanks to an optimised geometry</p> <p>Zimmer</p> <p>Natural Nail System: intramedullary nails, screws, instruments and other associated implants</p> <p>Holland</p> <p>Nail™ System includes a short, universal nail in diameters of 9, 11, and 13 mm x 24 cm length and long, anatomic (L & R) nails in diameters of 9 mm and 12 mm in various lengths. A 7 mm cannulated, partially threaded screw is used for proximal reconstructive interlocking. A unique pilot thread screw is used for proximal and distal interlocking. Distal screw options offer shaft fracture compression while controlling rotation by a distal slot, or the option of static interlocking</p>	
	n/a	Condyllocephalic nails	<ul style="list-style-type: none"> • Ender nail (Pankoich and Tarabishy) • Harris nail 	<p>Condyllocephalic nails are intramedullary nails which are inserted retrograde through the femoral canal across the fracture and into the femoral head</p> <p>Ender nails are pre-bent flexible rods.</p>	

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				Three to five of these of appropriate length are inserted into the femoral canal. The femoral canal is thus 'stacked' with nails, whilst their tips should radiate out to produce a secure fixation within the femoral head Harris nail is a larger nail used as a single nail.	
Fixed angle plates	Sliding	Static	<ul style="list-style-type: none"> • Holt nail plate • Jewett nail plate • McLaughlin nail plate • Thornton nail plate • LCP (Locking Compression Plate) • Dynamic Helical Hip System (DHHS) 	<p>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</p> <p>Holt nail plate: a four-flanged nail connected to a plate at the time of surgery</p> <p>Jewett nail: the nail is fixed to the plate at manufacture.</p> <p>Thornton and McLaughlin nail plates: the nail is connected to the plate at the time of surgery with a locking bolt</p> <p>RAB plate: similar</p>	

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				to a Jewett fixed nail plate but has an additional oblique strut to connect the nail and the side plate	
		Dynamic	<ul style="list-style-type: none"> • Dynamic hip screw • Precimed Hip Screw System • AMBI/Classic Hip Screw System (Smith & Nephew Richards) • HDS/DCS Dynamic Hip & Condylar Screw System • Pugh nail • Medoff plate • Resistance Augmented or Rigidity Augmentation Baixauli (RAB) plate • Gotfried percutaneous compression plate (PCCP) • Dynamic condylar screw (DCS) • X-BOLT Hip System (XHS™) 	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, leading to 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	

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>stability and temporary fixation during the natural healing process following fractures of the femoral neck or distal femur</p> <p>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</p> <p>Pugh nail: similar to SHS except instead of a lag screw being passed up the femoral neck, a nail with a trifin or three-flanged terminus is inserted by a punching mechanism. This is then connected to the side plate in the same manner as for a SHS</p> <p>Med-off plate: a modification of SHS, where a lag screw is passed up the femoral neck</p>	
--	--	--	--	--	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>and attached to a plate on the side of the femur. The difference is that the plate has an inner and outer sleeve, which can slide between each other. This creates an additional capacity for sliding to occur at the level of the lesser trochanter as well as at the lag screw. An additional variant of the Medoff plate is the capability of compressing the fracture distally using the two interlocking plates and a compression screw. In addition, sliding at the lag screw can be prevented with a locking screw to create a 'one way' sliding Medoff instead of a 'two way' sliding Medoff. At a later date the locking device on the lag screw can be removed to 'dynamise' the fracture</p> <p>Gotfried PCCP has a side plate that is inserted via a small incision level to the lesser trochanter by use of a connecting jig. Using the latter, two sliding proximal screws are passed up the femoral neck and</p>	
--	--	--	--	--	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>the plate is fixed to the femur shaft with three screws</p> <p>DCS is an implant assembly that consists of a lag screw, angled barrel plate fixed to the bone (usually distal femur) by 4.5 cortical screws. DCS and DHS work on the same principle of the sliding nail that allows impaction of the fracture. This is due to insertion of wide diameter into the</p> <p>condyle (or femoral head). A side plate, which has a barrel at a fixed angle, is slid over the screw and fixed to the femoral shaft. DCS has all other components the same as DHS; only the side plate is different. The plate barrel angle is 95 degrees and the plate is shaped to accommodate the lateral aspect of lateral condyle. DCS was mainly developed for fractures of distal femoral condyles. It is also used in fixation of subtrochanteric fractures of femur. Sometimes, it can be used in revision surgeries of selected</p>	
--	--	--	--	---	--

Table 2. Categorisation of internal and external fixation interventions for extracapsular hip fractures (Continued)

				<p>intertrochanteric fractures</p> <p>X-BOLT®: an expanding bolt akin to a Chinese lantern with a central drive shaft. The opposing threads compress the expandable section from both ends to expand the wings perpendicularly to the shaft, without spinning, pushing or pulling the femoral head</p>	
External fixation					
	n/a	Petrochanteric external fixator		<p>Petrochanteric external fixator: held outside the thigh by two pairs of pins. One pair is passed up the femoral neck under X-ray control. The other pair is placed in the femur. The fixator is left in place until the fracture has healed, which usually takes about three months. It is then removed under local anaesthesia, generally as an outpatient procedure</p>	

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

Table 3. Categorisation of arthroplasty interventions for extracapsular hip fractures

Implant	Grouping variable	Implant subcategory	Examples ^a	Description	In worldwide use (yes/no)
Extracapsular fractures					
Arthroplasty					
Total hip arthroplasty	Articulation	Femoral head and acetabular bearing surface materials	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Single • Dual 	A standard total hip arthroplasty has a single articulating surface	

Table 3. Categorisation of arthroplasty interventions for extracapsular hip fractures (Continued)

				between the femoral head and acetabulum bearing surface. Alternative designs incorporate a two further articulation within the structure of the femoral head	
	Fixation technique	Cemented	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	

Table 3. Categorisation of arthroplasty interventions for extracapsular hip fractures (Continued)

				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	
Hemiarthroplasty	Articulation	Unipolar	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • CPT modular bipolar • Exeter modular bipolar • 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	<ul style="list-style-type: none"> • Thompson • Austin Moore 	These prostheses were designed before the develop-	

Table 3. Categorisation of arthroplasty interventions for extracapsular hip fractures (Continued)

				ment of poly (methyl methacrylate) bone cement and were therefore originally inserted as a 'press fit'. Long-term stability through osseous integration was not part of the design concept	
		Cemented	<ul style="list-style-type: none"> • Thompson Stem • Exeter Trauma Hip System • 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	<ul style="list-style-type: none"> • 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	

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

APPENDICES

Appendix I. 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 prosthesis$ or implant$)).ti,ab,kf.
21 ((joint$1 adj5 (replac$ or prosthesis$ 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
```

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.

MP (content expert, Orthopaedics): drafted the protocol, reviewed and approved the final protocol.

LF (systematic reviewer): drafted the protocol, 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.

XG (content expert, Trauma and Orthopaedics): drafted the protocol, reviewed and approved the final protocol, and is the guarantor of the content.

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: has no known conflicts of interest.

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

MP: has received expenses and honorarium from a number of commercial companies and organisations for giving lectures on different aspects of hip fracture treatment. In addition he has received royalties from BBraun Ltd. related to the design and development of an implant used for the internal fixation of intracapsular hip fractures.

LF: has no known conflicts of interest.

HW: has no known conflicts of interest.

JMG: has no known conflicts of interest.

JC: has no known conflicts of interest.

XG is funded by a National Institute for Health Research Clinician Scientist Grant. Further funding from industry and charitable grants are and have been made available to his institution. All decisions relating to the design, conduct, analysis, write-up and publication of research are independent of these funders. He has ongoing expert consultancy with several companies; none involve the development of any implant for use in hip fracture care. He will remain independent of study selection decisions, 'Risk of bias' assessment and any data extraction of any of the studies on which he is an author, co-applicant or has had an advisory role.

SOURCES OF SUPPORT

Internal sources

- National Institute for Health Research Oxford Biomedical Research Centre, UK, UK.

External sources

- This project was supported by the National Institute for Health Research via Cochrane Infrastructure funding to the Cochrane Bone, Joint and Muscle Trauma Group, UK.

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.