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[Intervention Review]

Anaesthesia for hip fracture surgery in adults

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ABSTRACT

Background

The majority of people with hip fracture are treated surgically, requiring anaesthesia.

Objectives

The main focus of this review is the comparison of regional versus general anaesthesia for hip (proximal femoral) fracture repair in adults. We did not consider supplementary regional blocks in this review as they have been studied in another review.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library; 2014, Issue 3), MEDLINE (Ovid SP, 2003 to March 2014) and EMBASE (Ovid SP, 2003 to March 2014). We reran the search in February 2017. Potential new studies of interest were added to a list of "Studies awaiting Classification" and will be incorporated into the formal review findings during the review update.

Selection criteria

We included randomized trials comparing different methods of anaesthesia for hip fracture surgery in adults. The primary focus of this review was the comparison of regional anaesthesia versus general anaesthesia. The use of nerve blocks preoperatively or in conjunction with general anaesthesia is evaluated in another review. The main outcomes were mortality, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, deep vein thrombosis and return of patient to their own home.

Data collection and analysis

Two reviewers independently assessed trial quality and extracted data. We analysed data with fixed-effect ($I^2 < 25\%$) or random-effects models. We assessed the quality of the evidence according to the criteria developed by the GRADE working group.

Main results

In total, we included 31 studies (with 3231 participants) in our review. Of those 31 studies, 28 (2976 participants) provided data for the meta-analyses. For the 28 studies, 24 were used for the comparison of neuraxial block versus general anaesthesia. Based on 11 studies that included 2152 participants, we did not find a difference between the two anaesthetic techniques for mortality at one month: risk ratio (RR) 0.78, 95% confidence interval (CI) 0.57 to 1.06; $I^2 = 24\%$ (fixed-effect model). Based on six studies that included 761 participants, we did not find a difference in the risk of pneumonia: RR 0.77, 95% CI 0.45 to 1.31; $I^2 = 0\%$. Based on four studies that included 559 participants, we did not find a difference in the risk of myocardial infarction: RR 0.89, 95% CI 0.22 to 3.65; $I^2 = 0\%$. Based on six studies that included 729

participants, we did not find a difference in the risk of cerebrovascular accident: RR 1.48, 95% CI 0.46 to 4.83; $I^2 = 0\%$. Based on six studies that included 624 participants, we did not find a difference in the risk of acute confusional state: RR 0.85, 95% CI 0.51 to 1.40; $I^2 = 49\%$. Based on laboratory tests, the risk of deep vein thrombosis was decreased when no specific precautions or just early mobilization was used: RR 0.57, 95% CI 0.41 to 0.78; $I^2 = 0\%$; (number needed to treat for an additional beneficial outcome (NNTB) = 3, 95% CI 2 to 7, based on a basal risk of 76%) but not when low molecular weight heparin was administered: RR 0.98, 95% CI 0.52 to 1.84; I^2 for heterogeneity between the two subgroups = 58%. For neuraxial blocks compared to general anaesthesia, we rated the quality of evidence as very low for mortality (at 0 to 30 days), pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, decreased rate of deep venous thrombosis in the absence of potent thromboprophylaxis, and return of patient to their own home. The number of studies comparing other anaesthetic techniques was limited.

Authors' conclusions

We did not find a difference between the two techniques, except for deep venous thrombosis in the absence of potent thromboprophylaxis. The studies included a wide variety of clinical practices. The number of participants included in the review is insufficient to eliminate a difference between the two techniques in the majority of outcomes studied. Therefore, large randomized trials reflecting actual clinical practice are required before drawing final conclusions.

PLAIN LANGUAGE SUMMARY

Regional or general anaesthesia for hip fracture surgery in adults

Background: The majority of people with hip fracture are elderly and are treated surgically, which requires anaesthesia. The fracture usually results from a simple fall. These patients often have many other medical problems associated with ageing, which places them at high risk of mortality after anaesthesia. The most common types of anaesthesia are 'general' and 'regional anaesthesia'. General anaesthesia involves a loss of consciousness (induced sleep). Regional anaesthesia involves an injection of a solution containing local anaesthetic inside the spine (neuraxial block) or around the nerves outside the spine (peripheral nerve block) to prevent pain in the leg with the hip fracture. We reviewed the evidence about the effect of regional anaesthesia on patients undergoing surgery for hip fracture.

Study characteristics: The evidence is current to March 2014. In total, we included 31 studies (with 3231 participants) in our review. Of those 31 studies, 28 (2976 participants) provided data for the meta-analyses. The mean age of the participants varied from 75 to 86 years. Those studies were published between 1977 and 2013 and so covering a wide range of clinical practices and improvements in techniques over time. Two studies were funded by the anaesthetic drug manufacturer or by an agency with a commercial interest, one received charitable funding, and one was funded by a government agency. We reran the search in February 2017. Potential new studies of interest were added to a list of "Studies awaiting Classification" and will be incorporated into the formal review findings during the review update.

Key results : The trial reports of many of the studies indicated a sub-suboptimal level of methodological rigour and the number of participants included was often insufficient to allow us to draw a definitive conclusion on many of the outcomes studied. We did not find any difference in mortality at one month (11 trials with 2152 participants) between neuraxial blocks and general anaesthesia. We also did not find a difference for pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, congestive heart failure, acute kidney injury, pulmonary embolism, number of patients transfused with red blood cells, length of surgery and length of hospital stay between these two anaesthetic techniques in two to twelve studies. Likewise, when potent prophylactic drugs (such as low molecular weight heparin) were used against postoperative clot formation, we did not find a difference in the risk of deep venous thrombosis. Without prophylaxis with potent anticoagulant drugs the risk of deep venous thrombosis was less with neuraxial block.

Quality of the evidence: The level of evidence was very low for mortality, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, decrease in the incidence of deep venous thrombosis in the absence of potent prophylaxis, and return of patient to their own home. This means that any estimate of effect is very uncertain.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Neuraxial block compared to general anaesthesia for hip fracture repair

Neuraxial block compared to general anaesthesia for hip fracture repair

Patient or population: Patients with hip fracture repair

Settings: Surgery

Intervention: Neuraxial block

Comparison: General anaesthesia

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	General anaesthesia	Neuraxial block				
Mortality Follow-up: 0-1 month	Study population		RR 0.78 (0.57 to 1.06)	2152 (11 studies)	⊕⊕⊕⊕ very low 1,2,3,4,5,6,7,8	
	80 per 1000	62 per 1000 (46 to 85)				
	Low					
	35 per 1000	27 per 1000 (20 to 37)				
	High					
	95 per 1000	74 per 1000 (54 to 101)				
Pneumonia Follow-up: 0-7 days	Study population		RR 0.77 (0.45 to 1.31)	761 (6 studies)	⊕⊕⊕⊕ very low 1,2,3,4,6,7,9,10	
	64 per 1000	50 per 1000 (29 to 84)				
	Low					
	30 per 1000	23 per 1000 (13 to 39)				
	High					

	80 per 1000	62 per 1000 (36 to 105)			
Myocardial infarction Follow-up: 0-7 days	Study population		RR 0.89 (0.22 to 3.65)	559 (4 studies)	⊕○○○ very low 1,2,3,4,6,7,9,10
	10 per 1000	9 per 1000 (2 to 38)			
	Low				
	5 per 1000	4 per 1000 (1 to 18)			
	High				
	50 per 1000	44 per 1000 (11 to 183)			
Cerebrovascular accident Follow-up: 0-7 days	Study population		RR 1.48 (0.46 to 4.83)	729 (6 studies)	⊕○○○ very low 1,2,3,4,6,7,9,10
	8 per 1000	12 per 1000 (4 to 38)			
	Low				
	10 per 1000	15 per 1000 (5 to 48)			
	High				
	50 per 1000	74 per 1000 (23 to 241)			
Acute confusional state Follow-up: 0-7 days	Study population		RR 0.85 (0.51 to 1.40)	624 (6 studies)	⊕○○○ very low 1,3,4,6,7,9,10,11
	177 per 1000	150 per 1000 (90 to 247)			
	Low				
	50 per 1000	42 per 1000 (25 to 70)			



	High				
	250 per 1000	212 per 1000 (127 to 350)			
Deep vein thrombosis Follow-up: 0-10 days	Study population		RR 0.57 (0.41 to 0.78)	116 (2 studies)	⊕○○○ very low 1,2,4,7,9,10,12,13
	780 per 1000	444 per 1000 (320 to 608)			For this outcome, we retained only studies without adequate prophylaxis
	Low				
	200 per 1000	114 per 1000 (82 to 156)			
	High				
900 per 1000	513 per 1000 (369 to 702)				
Return of patient to their own home Follow-up: 1 year	Study population		RR 0.84 (0.61 to 1.16)	130 (1 study)	⊕○○○ very low 1,3,4,6,7,10,14
	578 per 1000	486 per 1000 (353 to 671)			
	Low				
	400 per 1000	336 per 1000 (244 to 464)			
	High				
800 per 1000	672 per 1000 (488 to 928)				

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

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

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

- 1 Allocation concealment and/or blinding of outcome assessors unclear/inadequate in 75% or more of the included studies.
- 2 I^2 smaller than 25%.
- 3 Direct comparison only: all outcomes were based on direct comparisons, were performed on the population of interest, and were not surrogate markers.
- 4 Optimal information size not achieved.
- 5 Correcting for the possibility of publication bias would change the conclusion.
- 6 RR greater than 0.5 and less than 2.0.
- 7 We did not identify any confounding factors that could change the effect.
- 8 We upgraded the quality on absence of effect because the effect seemed to be present only in older studies.
- 9 Either no evidence of a publication bias or correcting for the possibility of publication bias would not modify the conclusion.
- 10 No evidence of a dose response effect.
- 11 I^2 statistics close to 50%.
- 12 This is a surrogate marker for a clinical outcome: systematic venography instead of clinically relevant event.
- 13 RR 0.57, excluding studies where heparin was given as prophylaxis.
- 14 Not available due to low number of studies.

BACKGROUND

Description of the condition

The term 'proximal femoral fracture', or 'hip fracture', refers to a fracture of the femur in the area of bone immediately distal to the articular cartilage of the hip, to a level of about five centimetres below the lower border of the lesser trochanter. The majority of these fractures occur in the elderly population, and more than 30% of the patients are 85 years or older (Brauer 2009). In the United States, while the age-adjusted incidence of hip fracture increased from 1986 to 1995, a steady decline from 1995 to 2005 has been reported. In women, the incidence increased by 9.0% in 1995 compared to 1986, with a subsequent decline of 24.5% in 2005. In men, the increase in incidence from 1986 to 1995 was 16.4%, and the subsequent decrease to 2005 was 19.2% (Brauer 2009). Despite this improvement, hip fractures in the elderly are still quite common, and this improvement may not apply to developing countries. Between 1986 and 2005, in the United States, the annual mean number of hip fractures was 957.3 per 100,000 (95% confidence interval (CI), 921.7 to 992.9) for women and 414.4 per 100,000 (95% CI, 401.6 to 427.3) for men (Brauer 2009). The injury is usually the result of a simple fall.

The majority of these fractures are treated surgically; thus hip fracture surgery represents one of the most common emergency orthopaedic procedures. Surgical treatment may be either fixation of the fracture or replacement of the femoral head with an arthroplasty. Internal fixation involves using screws or pins, either alone, or in combination with a side plate applied to the femur, or by the use of an intramedullary nail with a cross screw inserted into the femoral head. Arthroplasty involves excision of the fractured area of bone and replacement with a partial or total hip replacement, which may be cemented in place.

Description of the intervention

The term 'regional anaesthesia' may include neuraxial blocks or peripheral nerve blocks. Neuraxial blockade refers to placement of a solution containing local anaesthetics close to the spinal cord. Neuraxial blocks may be executed by spinal or epidural or combined spinal/epidural blockade. For a spinal block, the solution containing the local anaesthetics is placed in the cerebrospinal fluid. For an epidural block, the solution containing the local anaesthetic is placed in the epidural space, outside the dura matter (membrane surrounding the cord and the cerebrospinal fluid). Peripheral nerve blocks refer to placement of local anaesthetics around peripheral nerves or plexus outside the spine. Peripheral nerve blocks for this indication are usually performed by a posterior lumbar plexus block (psoas compartment block), with or without additional blocks (sacral plexus block, iliac crest infiltration). For posterior lumbar plexus blocks and for sacral plexus blocks, the local anaesthetics are placed around the roots of the nerves, immediately after their exit from the spine at the lumbar level (posterior lumbar plexus block) or at the sacral level (sacral plexus block). An iliac crest infiltration is the deposition of local anaesthetics under the skin above the iliac crest along its superior border. Neuraxial or peripheral nerve blocks may be performed by a single shot injection or by incremental doses, with or without a continuous infusion thereafter. When a patient is having an operation under regional anaesthesia alone, he/she remains conscious, but insensitive to pain. The muscle relaxation obtained is also usually sufficient to allow the surgeon to repair the fracture.

General anaesthesia refers to the use of a variety of intravenous and or inhalation drugs to render the patient unconscious, amnesic of the procedure and insensitive to pain. Neuromuscular blocking agents are often added for a hip fracture repair under general anaesthesia.

How the intervention might work

Whilst the hip fracture is usually the only injury, the patients frequently have many other medical problems associated with ageing. Indeed, an increase in all comorbidities (except paralysis) in patients with hip fracture was recorded from 1986 to 2005 (Brauer 2009). Advanced age and frequent multiple associated comorbidities put these patients at high risk of mortality after anaesthesia. The 10-year probability of survival of patients with comorbidities (American Society of Anesthesiologists) physical status (ASA) III or IV undergoing major surgery is lower than that of patients without significant comorbidities (ASA I or II) (Kennedy 2010). A recent Cochrane Overview, found that the 0 to 30-day mortality of patients undergoing high or moderate cardiac risk procedures is lower in patients having an operation under neuraxial blocks compared to those having an operation under general anaesthesia: risk ratio (RR) 0.71, 95% CI 0.53 to 0.94; moderate quality of evidence (Guay 2014). Major orthopaedic surgeries such as hip fracture repairs are considered moderate cardiac risk procedures (Fleisher 2007).

Why it is important to do this review

In a previous version of this review, we concluded that regional anaesthesia was associated with a borderline decreased mortality at one month: RR 0.69, 95% CI 0.50 to 0.95 (Parker 2004). This finding however, is not corroborated with a recent large retrospective study, where the authors concluded that the use of regional anaesthesia compared with general anaesthesia was not associated with lower 30-day mortality, but only with a modestly shorter length of hospital stay (Neuman 2014).

This review is an update of previous versions (Parker 2001; Parker 2004; Urwin 2000). We undertook this update to search for new studies and adjust the methodology to the latest Cochrane requirements.

OBJECTIVES

The main focus of this review is the comparison of regional versus general anaesthesia for hip (proximal femoral) fracture repair in adults. The scope of this review, originally published in 2000 (Urwin 2000), was expanded in the second update (Parker 2001) to also cover other methods of anaesthesia. We did not consider supplementary regional blocks in this review as they have been studied in another review (Parker 2002).

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomized controlled trials (RCTs). We excluded cluster and cross-over trials. We included all RCTs regardless of language of publication or publication status.

Types of participants

We considered studies that included participants ≥ 16 years old undergoing hip fracture surgery (an emergency surgery).

Types of interventions

We included studies that compared any combination of the following interventions.

1. Neuraxial blocks: epidural (single shots or continuous), spinal (single shots or continuous), or combined spinal/epidural (single shots or continuous), with or without intravenous sedation.
2. Peripheral nerve blocks: posterior lumbar (psoas) plexus blocks, with or without sacral plexus blocks, or any other peripheral nerve blocks, with or without sedation.
3. General anaesthesia based on inhalational agents (with or without opioids and/or neuromuscular blocking agents), or on total intravenous anaesthesia (ketamine-based technique or other). Any technique where an endotracheal tube or a laryngeal mask airway was used was considered as general anaesthesia.

Types of outcome measures

Primary outcomes

1. Mortality from any cause at 30 days, three months, six months, and one year (cumulative).
2. Pneumonia (author's definition).
3. Myocardial infarction (author's definition).

Secondary outcomes

1. Cerebrovascular accident (author's definition).
2. Acute confusional state (author's definition).
3. Deep vein thrombosis.
4. Return of patient to their own home.
5. Congestive cardiac failure (author's definition).
6. Acute kidney injury (author's definition).
7. Pulmonary embolism.
8. Unsatisfactory surgical results.
9. Number of patients transfused.

10. Length of hospital stay.
11. Length of surgery (in minutes).
12. Operative hypotension (author's definition).
13. Urine retention.
14. Incomplete or unsatisfactory analgesia.

Please see [Table 1](#) for the definitions and time points of these outcomes.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library; 2014, Issue 3, see [Appendix 1](#)), MEDLINE (Ovid SP, 2003 to March 2014, see [Appendix 2](#)) and EMBASE (Ovid SP, 2003 to March 2014, see [Appendix 3](#)). We also screened the reference lists of all studies retained. We reran the search in February 2017. We will deal with the two studies of interest when we update the review.'

We imposed no language restriction. We considered articles of all languages and translated them if necessary

Searching other resources

We looked at: <http://www.clinicaltrials.gov>, <http://isrctn.org>, <http://www.umin.ac.jp/ctr/index.htm>, <http://www.anzctr.org.au/>, <http://www.trialregister.nl/>, and <https://eudract.ema.europa.eu/> for trials in progress in 2014.

Data collection and analysis

Selection of studies

Two review authors (JG and SK) independently screened abstract/titles. We retrieved all potentially relevant studies. We excluded duplicate publications based on the sites and dates of data collection. We noted reasons for exclusion. We resolved disagreements by discussion; involvement of a third review author was never required. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram (see [Figure 1](#); [Moher 2009](#)), and 'Characteristics of excluded studies' table.'

Figure 1. Study flow diagram.

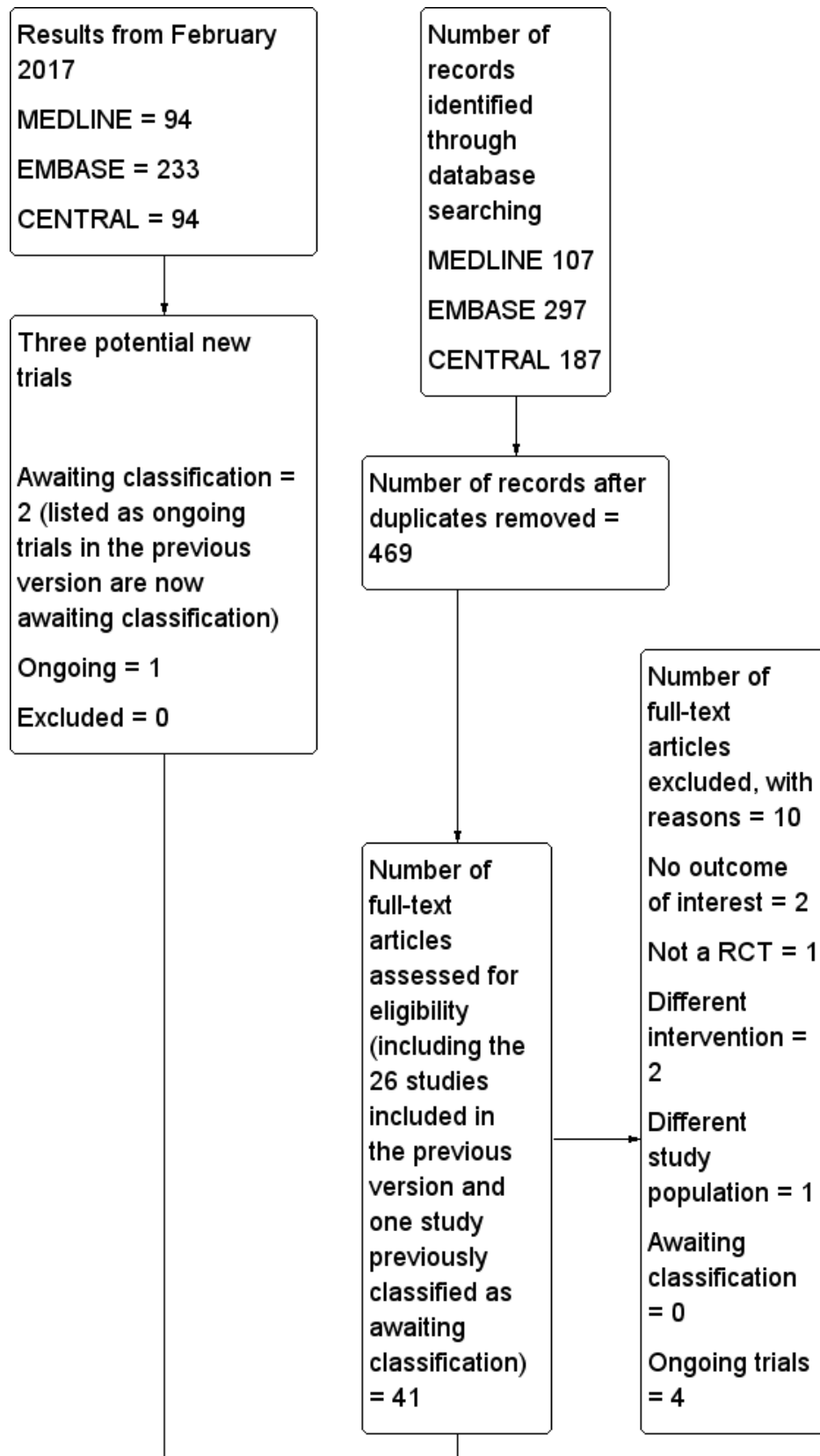
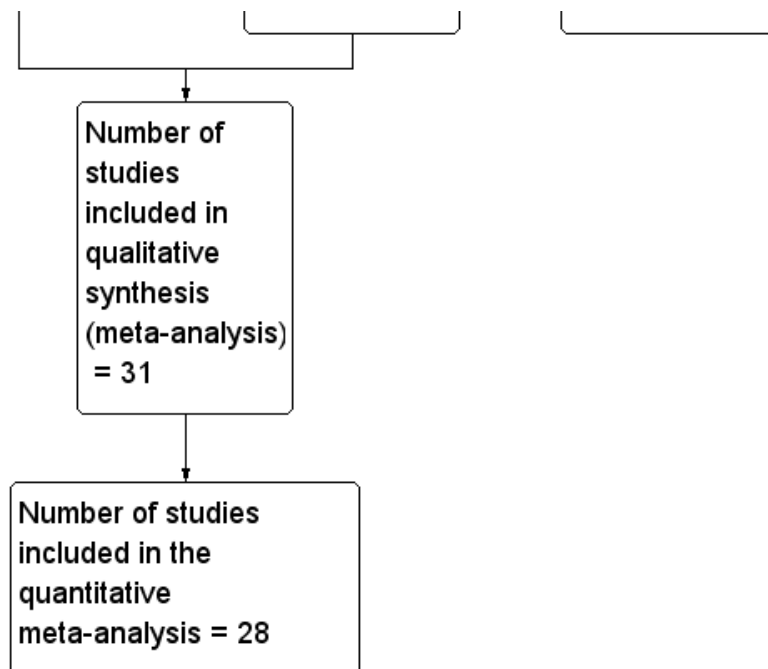


Figure 1. (Continued)



Data extraction and management

When the study was already included in the previous version, one review author (JG) rechecked all entries from the manuscripts. For the five new studies (Biboulet 2012; Cao 2008; Heidari 2011; Hoppenstein 2005; Messina 2013), two review authors independently extracted the data for our selected outcomes. We entered the number of participants with events and total number of patients included in each treatment group in an Excel sheet for mortality from any cause at 30 days, three months, six months, and one year (cumulative), pneumonia, myocardial infarction, congestive heart failure, cerebrovascular accidents, acute confusional state, acute kidney injury, deep venous thrombosis, pulmonary embolism, return of patient to their own home, unsatisfactory surgical results, number of patients transfused, operative hypotension and urine retention. For continuous data (length of surgery and of hospital stay) we entered mean, standard deviation and total number of participants in each group, or P values and number of participants in each group when the former were not available.

We resolved all disagreements by discussion, involvement of a third review author was never required. One review author (JG) also entered in Comprehensive Meta-Analysis software the information required for heterogeneity exploration (<http://www.meta-analysis.com>): year when the study was published, mean age of participants, percentage of participants undergoing arthroplasty, cut-off point for operative hypotension definition, preinduction administration of fluids, regional anaesthetic technique in the treatment group (type of block [spinal versus epidural versus peripheral nerve block], single shot versus continuous technique, uni- versus bilateral spinal), inhalational agent used in the control group, mean ASA physical status, delay before the surgery, thromboprophylaxis, and use of neuromuscular blocking agent in the control group.

Assessment of risk of bias in included studies

Two review authors (JG and SK) independently assessed the quality of the studies with the Cochrane 'Risk of bias' tool (Higgins 2011). We assessed the risk of bias based on the information presented in the reports, with no assumptions: low risk, high risk or unclear risk of bias. When there was not enough information in the report to make an assessment, we judged the item as high risk for blinding (blinding of participants and personnel and blinding of outcome assessment) and as unclear for all other items. We resolved any disagreements by discussion; involvement of a third review author was never required.

Measures of treatment effect

Data are expressed as risk ratios (RRs) (dichotomous), mean difference (MDs) (continuous data) or standardized mean difference (SMDs) and their 95% CI.

Unit of analysis issues

We included only parallel RCTs. When the study contained more than two groups, in order to avoid including duplicate data, we either selected only the groups relevant to the review, or fused two subgroups, or split the control group in half. The choice between the two latter options was made according to the solution that best fitted our criteria for heterogeneity exploration.

Dealing with missing data

We only analysed the available data; we made no imputation.

Assessment of heterogeneity

We measured statistical heterogeneity using the I² statistic.

Assessment of reporting biases

We judged a study to have used selective reporting when data were collected as stated in the methods section, but not reported in the results section. We mentioned data that were provided as per the protocol (not on an intention-to-treat basis) as other risk of bias.

Data synthesis

We analysed data with Comprehensive Meta-analysis software (<http://www.meta-analysis.com>). In addition, we used Review Manager 5 with fixed-effect ($I^2 < 25\%$; Higgins 2003) or random-effects models (RevMan 2014). We expressed data as RRs (dichotomous), MDs (continuous data) or SMDs and their 95% CI. When we found an effect, we calculated the number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH) from the odds ratio (<http://www.nntonline.net/visualrx/>). When we did not find any effect, we calculated the optimal information size according to Pogue 1997 from <http://stat.ubc.ca/~rollin/stats/ssize/b2.html> and power with Power and Precision V3.2 for our major outcomes (<http://power-analysis.com/>).

Subgroup analysis and investigation of heterogeneity

We explored any moderate amount of heterogeneity ($I^2 > 25\%$; Higgins 2003) by visual inspection of the forest plots, with studies placed in order according to a specific moderator, subgroupings (categorical moderators) or meta-regressions (continuous moderators). We considered the following factors in the heterogeneity exploration: year when the study was published; fixation versus joint replacement; single shot versus incremental dose for neuraxial block; uni- versus bilateral spinal; inhalational agents or not (type); neuromuscular blocking agents or not; ASA physical status; mean age of participants; administration of an intravenous bolus fluid before the neuraxial block; and thromboprophylaxis. We used the Egger's regression intercept to assess the possibility of a small-study effect (Rucker 2011).

Sensitivity analysis

A sensitivity analysis could be performed when the results of one single study appeared as an outlier on the forest plot or on the basis of the 'Risk of bias' assessment.

Grading the body of evidence

We judged the quality of the body of evidence using GRADEProGDT (<http://ims.cochrane.org/revman/gradepr>) (Guyatt 2011a), and presented in a 'Summary of findings' table each major outcome: mortality at one month, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, deep venous thrombosis, and return of patient to their own home. For risk of bias, we judged the quality of evidence as low risk of bias when most information came from studies at low risk of bias, we downgraded by one level when most information came from studies at low or unclear risk of bias and downgraded by two levels when the proportion of information from studies at high risk of bias was sufficient to affect the interpretation of results.

For inconsistency, we downgraded the quality of evidence by one when the I^2 statistic was 50% or higher without satisfactory explanation and by two levels when the I^2 statistic was 75% or higher without an explanation. We did not downgrade the quality of evidence for indirectness as all outcomes were based on direct

comparisons, were performed on the population at interest and were not surrogate markers (Guyatt 2011b), except for deep venous thrombosis. In the included studies, the latter was evaluated by systematic venographies performed within 10 days after surgery. This was considered as a surrogate marker for clinically relevant events.

For imprecision (Guyatt 2011c), we downgraded the quality of evidence by one when: the CI around the effect size was large or overlapped an absence of effect, and failed to exclude an important benefit or harm; and the number of participants was lower than the optimal information size. We downgraded the quality by two levels when the CI was very wide and included both appreciable benefit and harm.

For publication bias, we downgraded the quality of evidence by one when correcting for the possibility of publication as assessed by the Duval and Tweedie's fill and trim analysis changed the conclusion. We upgraded the quality of evidence by one when the effect size was large (< 0.5 or > 2.0) and by two when the effect size was very large ($RR < 0.2$ or > 5) (Guyatt 2011d). We applied the same rules for OR when the basal risk was lower than 20%. For SMD, we used 0.8 as the cut-off point for a large effect (Pace 2011). We also upgraded the quality by one when evidence of a dose related response was found.

We upgraded the quality by one when the possible effect of confounding factors would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. When the quality of the body of evidence is high quality, further research is very unlikely to change our confidence in the estimate of effect. When the quality is moderate, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. When the quality is low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. When the quality is very low, any estimate of effect is very uncertain (Guyatt 2008).

RESULTS

Description of studies

Results of the search

The flow diagram of the study selection is included in Figure 1 (Moher 2009). From the previous version, we reassessed 26 included studies and one study awaiting classification. We also assessed 14 new studies from the electronic search or from the reference lists of studies. We excluded ten studies for the following reasons: no outcome of interest for this review (Darling 1994; Messaoudi 2009), quasi-randomized trial (Adams 1990), different intervention (Ungemach 1987; Yao 1997), different study population (Lattermann 2005), and ongoing trials (ISRCTN36381516; NCT00590707; NCT02190903; NCT02213380). We reran the search in February 2017. The search terms were slightly modified from those of the previous searches. The modified strategy used for 2014 and onwards can be found in Appendix 4. Three hundred and eighty-two new citations were found: 55 in CENTRAL, 233 in Embase and 94 in Medline.

Included studies

In total, we included 31 studies (with 3231 participants) in our review. Of those 31 studies, 28 (2976 participants) provided data for the meta-analyses. The reasons for not including three studies in the meta-analysis were: the time point at which mortality was measured was unclear (Tasker 1983); the time point did not correspond to the time points chosen for this review (mortality data provided at two weeks only; Ungemach 1993); and results provided for our study population were mental tests (Wajima 1995). Therefore, we included 28 studies with 2976 participants published between 1977 and 2013 for the quantitative meta-analysis.

Two studies were funded by the drug manufacturer or by an agency with a commercial interest (Davis 1987; Valentin 1986), one received charitable funding (Davis 1981), and one was funded by a government agency (Berggren 1987). The source of funding was unspecified for the other studies. The mean age of the participants varied from 74.8 to 86 years. Their mean ASA physical status varied from 2.0 to 3.3. The mean delay before the surgery varied from 24 to 240 hours. The percentage of participants undergoing arthroplasty varied from 0% to 100%. The thromboprophylaxis used was: early mobilization (Davis 1981); socks (Valentin 1986); dextran (Berggren 1987); antivitamine K drugs (Couderc 1977); unfractionated heparin (Heidari 2011; Racle 1986); or low molecular heparin (Brichant 1995). The neuraxial blocks used were: spinal (Biboulet 2012; Biffoli 1998; Bigler 1985; Bredahl 1991; Casati 2003; Davis 1981; Davis 1987; de Visme 2000; Eyrolle 1998; Hoppenstein 2005; Ibanez 1993; Juelsgaard 1998; Kamitani 2003; Maurette 1988; McKenzie 1984; McLaren 1978; Messina 2013; Racle 1986; Svarting 1986; Valentin 1986; White 1980); epidural (Berggren 1987; Cao 2008; Couderc 1977; Wajima 1995); or any of these two techniques (Brichant 1995; Heidari 2011). Inhalational agents used for general anaesthesia were: nitrous oxide alone (Bigler 1985; Bredahl 1991; Davis 1981; Davis 1987; McLaren 1978; Spreadbury 1980; Svarting 1986); methoxyflurane (Couderc 1977); halothane (Berggren 1987; Heidari 2011; McKenzie 1984; White 1980); enflurane (Juelsgaard 1998; Maurette 1988; Racle 1986); enflurane or nitrous oxide (Valentin 1986); isoflurane (Biffoli 1998; Hoppenstein 2005); or sevoflurane (Casati 2003; Kamitani 2003; Messina 2013; Wajima 1995).

Table 2 contains the anaesthetic agents used to produce general anaesthesia or sedation. Twenty-four studies were involved in the comparison neuraxial block versus general anaesthesia (Berggren 1987; Biboulet 2012; Biffoli 1998; Bigler 1985; Bredahl 1991; Brichant 1995; Cao 2008; Casati 2003; Couderc 1977; Davis 1981; Davis 1987; Heidari 2011; Hoppenstein 2005; Ibanez 1993; Juelsgaard 1998; Kamitani 2003; Maurette 1988; McKenzie 1984; McLaren 1978; Messina 2013; Racle 1986; Svarting 1986; Valentin 1986; Wajima 1995). Three studies were involved in the comparison neuraxial block versus peripheral nerve block (Cao 2008; de Visme 2000; Eyrolle 1998). One study compared a neuraxial block added to general anaesthesia versus general anaesthesia alone (White 1980). The same study was also used for a comparison between peripheral nerve block added to general anaesthesia compared to general anaesthesia alone (White 1980), and one study compared intravenous ketamine to classic general anaesthesia (Spreadbury 1980).

(See [Characteristics of included studies](#))

Excluded studies

We excluded 10 studies (see [Characteristics of excluded studies](#) for the reasons for their exclusion).

Awaiting classification

There are two studies awaiting classifications (Neuman 2016; Parker 2015). For further details see [Characteristics of studies awaiting classification](#).

Ongoing studies

We found four ongoing trials (ISRCTN36381516; NCT00590707; NCT02190903; NCT02213380; see [Characteristics of ongoing studies](#)) in the 2014 search. When the search was reran in February 2017, two of the ongoing trials were now published and are classified as awaiting classification (ISRCTN36381516; NCT02190903). A new ongoing trial (NCT02507505) was found.

Risk of bias in included studies

The risk of bias of included studies can be found in [Figure 2](#) and [Figure 3](#).

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

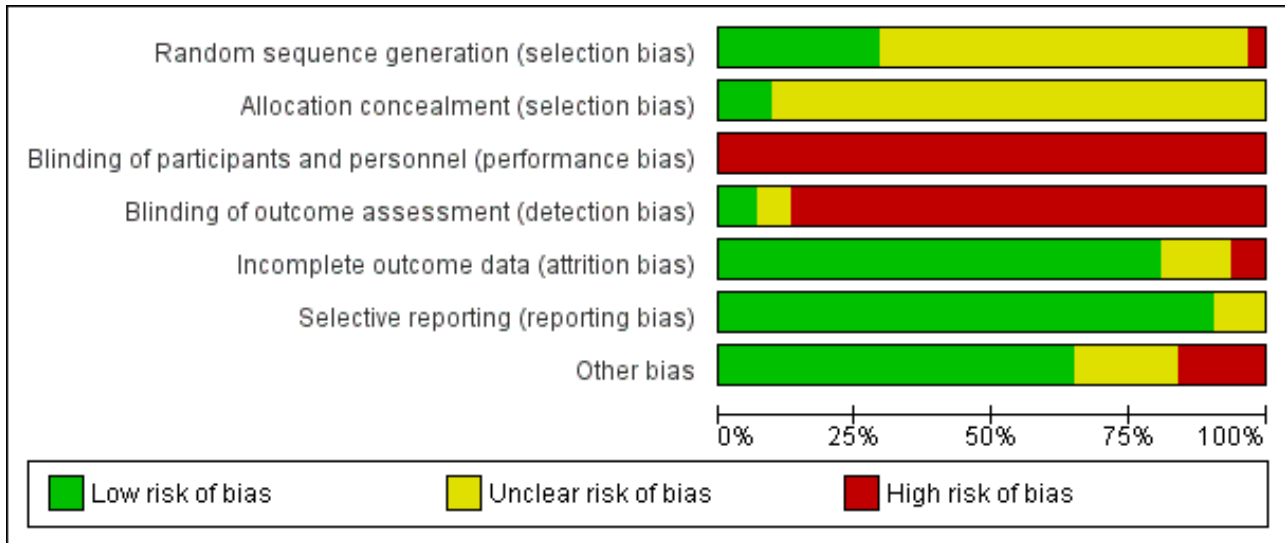


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Berggren 1987	?	?	-	?	?	?	+
Biboulet 2012	?	?	-	-	+	+	-
Biffoli 1998	?	?	-	-	+	+	+
Bigler 1985	?	?	-	?	+	+	+
Bredahl 1991	?	?	-	-	+	+	+
Brichant 1995	?	?	-	+	-	+	+
Brown 1994	+	?	-	-	+	+	+
Cao 2008	?	?	-	-	+	+	+
Casati 2003	+	+	-	-	+	+	+
Couderc 1977	+	?	-	-	+	+	+
Davis 1981	?	?	-	-	-	+	+
Davis 1987	+	?	-	-	+	+	+
de Visme 2000	?	+	-	-	+	+	?
Eyrolle 1998	?	?	-	-	+	+	+
Heidari 2011	+	?	-	-	?	+	-
Hoppenstein 2005	+	+	-	-	+	+	+
Ibanez 1993	?	?	-	-	+	?	?
Juelsgaard 1998	?	?	-	+	+	+	+
Kamitani 2003	?	?	-	-	+	+	+
Maurette 1988	+	?	-	-	+	+	+

Figure 3. (Continued)

Maurette 1988	+	?	-	-	+	+	+
McKenzie 1984	?	?	-	-	+	+	-
McLaren 1978	?	?	-	-	+	+	?
Messina 2013	+	?	-	-	+	+	+
Racle 1986	+	?	-	-	+	+	+
Spreadbury 1980	?	?	-	-	+	+	-
Svarting 1986	?	?	-	-	+	+	+
Tasker 1983	?	?	-	-	?	?	?
Ungemach 1993	?	?	-	-	+	+	+
Valentin 1986	?	?	-	-	?	+	-
Wajima 1995	-	?	-	-	+	+	?
White 1980	?	?	-	-	+	+	?

Allocation

We judged allocation concealment to be at low risk of bias for three studies (Casati 2003; de Visme 2000; Hoppenstein 2005), and unclear for all other included studies (Figure 3).

Blinding

For a comparison between neuraxial and general anaesthesia, blinding of participants is not possible, and blinding of personnel taking care of the patient is probably an unrealistic expectation, at least for the personnel taking care of the patient during the first few hours after the surgery. We judged blinding of the outcome assessor to be at unclear risk of bias in Berggren 1987 and Bigler 1985 and at low risk of bias in Brichant 1995 and Juelsgaard 1998 (see Figure 2; Figure 3).

Incomplete outcome data

We classified six studies as unclear or at high risk of bias for this item (Berggren 1987; Brichant 1995; Davis 1981; Heidari 2011; Tasker 1983; Valentin 1986; see Figure 2; Figure 3).

Selective reporting

We classified three studies as unclear for selective reporting (Berggren 1987; Ibanez 1993; Tasker 1983; see Figure 2; Figure 3).

Other potential sources of bias

We classified 11 studies as unclear or at high risk for other risks of bias (Biboulet 2012; de Visme 2000; Heidari 2011; Ibanez 1993; McKenzie 1984; McLaren 1978; Spreadbury 1980; Tasker 1983; Valentin 1986; Wajima 1995; White 1980; Figure 2; Figure 3).

Effects of interventions

See: [Summary of findings for the main comparison Neuraxial block compared to general anaesthesia for hip fracture repair](#)

Neuraxial block versus general anaesthesia

The definition and time points for all outcomes retained, can be found in Table 1.

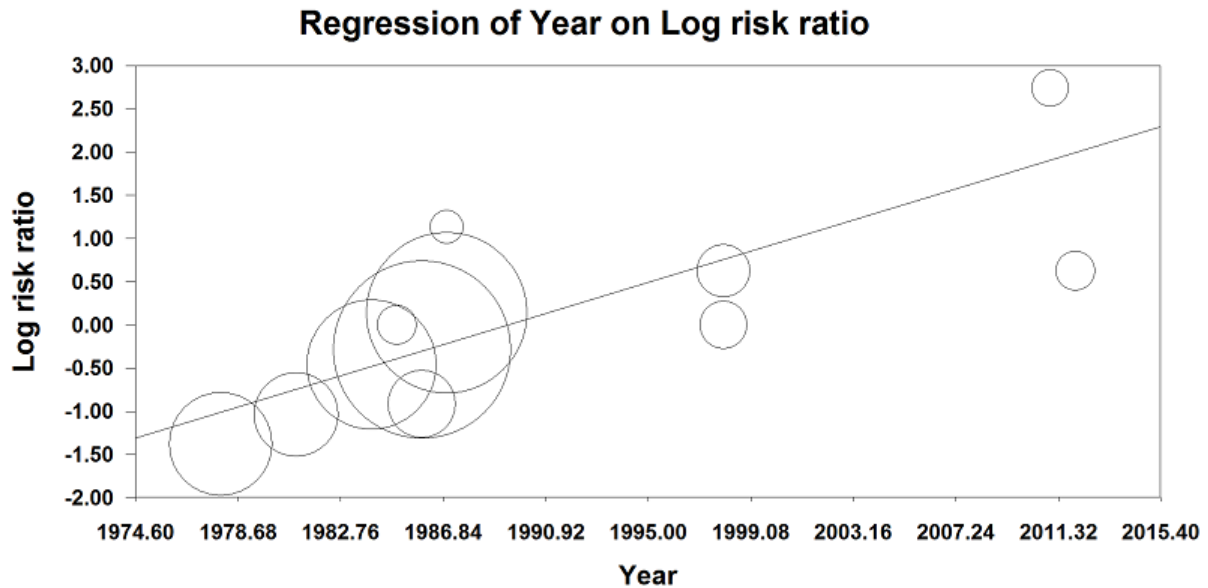
Primary outcomes

1. Mortality

Mortality at one month

Based on 11 studies that included 2152 participants, we did not find a difference between the two techniques for mortality at one month: risk ratio (RR) 0.78, 95% confidence interval (CI) 0.57 to 1.06; $I^2 = 24%$ (fixed-effect model) (Berggren 1987; Biboulet 2012; Bigler 1985; Davis 1981; Davis 1987; Heidari 2011; Juelsgaard 1998; McKenzie 1984; McLaren 1978; Racle 1986; Valentin 1986; Analysis 1.1). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed that two studies might be missing to the left for an adjusted point of estimate: RR 0.70, 95% CI 0.51 to 0.97. Accepting that a publication bias occurred, and considering a basal rate of mortality of 8%, the number needed to treat for an additional beneficial outcome (NNTB) would be 42, 95% CI 26 to 339. A meta-regression with the year where the study was published showed that effect size favouring neuraxial blockade compared to general anaesthesia might be higher in older studies (Figure 4). The number of participants included here allows to eliminate a difference of 25% in the risk of mortality at one month with a power of 0.57 (α 0.05; β 0.2; one-sided test). A number of 4024 (2012 per group) would be required for a power of 0.8 (α 0.05; β 0.2; one-sided test) if a large study would be done.

Figure 4. Meta-regression of mortality at 0-1 month versus the year when the study was published. The effect size decreases with time: P value = 0.002. This meta regression plot was not produced in RevMan. The figure was generated automatically by the software, and cannot be amended. The software has expressed the years as decimals.



For mortality at one month, we downgraded the level of evidence by two for risk of bias based on the fact that we judged 75% or more of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. We did not downgrade an absence of effect for inconsistency because the I^2 statistic was lower than 25%. We included direct comparisons only, and this outcome was not a surrogate marker. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. We downgraded the level by one for publication bias because correcting for this possibility would make the effect present instead of absent (RR after correction 0.70, 95% CI 0.51 to 0.97 versus RR 0.78, 95% CI 0.57 to 1.06 without correction). We did not change the level for amplitude of effect size (RR 0.78 and therefore > 0.5). We did not identify any confounding factors justifying upgrading. We upgraded the level for a dose response effect because we concluded to an absence of effect, and the meta-regression showed that an effect was present only in older studies. We rated the quality of evidence as very low.

Mortality at three months

Based on five studies that included 953 participants (Berggren 1987; Couderc 1977; McKenzie 1984; Racle 1986; Valentin 1986), we did not find a difference in mortality at 3 months: RR 0.77, 95% CI 0.55 to 1.08; $I^2 = 0\%$ (Analysis 1.2). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed that one study might be missing to the left for an adjusted point of estimate: RR 0.78, 95% CI 0.56, 1.09. Considering a basal mortality rate of 13.8%, 2204 participants (1102 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large study would be done.

Mortality at six months

Based on two studies that included 726 participants (McKenzie 1984; Valentin 1986), we did not find a difference in mortality at six months: RR 1.00, 95% CI 0.73 to 1.37; $I^2 = 0\%$ (Analysis 1.3). Considering a basal mortality rate of 17.5%, 1678 participants (839 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large study would be done.

Mortality at one year

Based on two studies that included 726 participants (McKenzie 1984; Valentin 1986), we did not find a difference in mortality at one year after the surgery: RR 1.06, 95% CI 0.81 to 1.39; $I^2 = 0\%$ (Analysis 1.4). Considering a basal mortality rate of 21.8%, 1310 participants (655 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large study would be done.

2. Pneumonia

Based on six studies that included 761 participants (Berggren 1987; Bigler 1985; Davis 1981; Heidari 2011; McLaren 1978; Racle 1986), we did not find a difference in the risk of pneumonia: RR 0.77, 95% CI 0.45 to 1.31; $I^2 = 0\%$ (Analysis 1.5). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed that three studies might be missing to the right for an adjusted point of estimate: RR 1.15, 95% CI 0.71 to 1.86. Considering a pneumonia rate of 6.4%, 5106 participants (2553 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large study would be done. Likewise, the number of participants included here would give a power of 0.29 ($\alpha 0.05$; $\beta 0.2$; one-sided test).

For pneumonia, we downgraded the level of evidence by two for risk of bias based on the fact that we judged 75% or more of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. We did not

downgrade for inconsistency because the I^2 statistic was lower than 25%. We included direct comparisons only, and this outcome was not a surrogate marker. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. We did not downgrade the level for publication bias because correcting for this possibility would not change the conclusion (RR after correction 1.15, 95% CI 0.71 to 1.86 versus RR 0.77, 95% CI 0.45 to 1.31 without correction). We did not change the level for amplitude of effect size (RR 0.77 and therefore > 0.5). We did not identify any confounding factors or dose response effect justifying upgrading. We rated the quality of evidence as very low.

3. Myocardial infarction

Based on four studies that included 559 participants (Biboulet 2012; Couderc 1977; Heidari 2011; Juelsgaard 1998), we did not find a difference in the risk of myocardial infarction: RR 0.89, 95% CI 0.22 to 3.65; $I^2 = 0\%$ (Analysis 1.6). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed no evidence of a publication bias. Considering a basal myocardial infarction rate of 1%, 34318 participants (17159 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large study would be done. Likewise, the number of participants included here would give a power of 0.09 ($\alpha 0.05$; one-sided test).

For myocardial infarction, we downgraded the level of evidence by two for risk of bias based on the fact that we judged 75% or more of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. We did not downgrade for inconsistency because the I^2 statistic was lower than 25%. We included direct comparisons only, and this outcome was not a surrogate marker. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. We found no evidence of a publication bias. We found no evidence of a large effect size, confounding factors justifying upgrading, or dose response effect. We rated the quality of evidence as very low.

Secondary outcomes

1. Cerebrovascular accident (stroke)

Based on six studies that included 729 participants (Berggren 1987; Biboulet 2012; Bigler 1985; Davis 1981; Heidari 2011; Racle 1986), we did not find a difference in the risk of cerebrovascular accident: RR 1.48, 95% CI 0.46 to 4.83; $I^2 = 0\%$ (Analysis 1.7). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed no evidence of a publication bias. Considering a basal cerebrovascular accident rate of 2%, 17,008 participants (8504 per group) would be required to eliminate a difference of 25% ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large RCT would be done. Likewise, the power obtained with the number of participants included here is 0.13 ($\alpha 0.05$; $\beta 0.2$; one-sided test).

For cerebrovascular accident, we downgraded the level of evidence by two for risk of bias based on the fact that we judged more than 75% of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. We did not downgrade for inconsistency because the I^2 statistic was lower than 25%. We included direct comparisons only, and this outcome was not a surrogate marker. We downgraded the level by one for imprecision based on the fact that the optimal information size was

not achieved. We found no evidence of a publication bias. We found no evidence of a large effect size, confounding factors justifying upgrading, or dose response effect. We rated the quality of evidence as very low.

2. Acute confusional state

Based on six studies that included 624 participants (Berggren 1987; Bigler 1985; Casati 2003; Heidari 2011; Kamitani 2003; Racle 1986), we did not find a difference in the risk of acute confusional state (see Table 1 for exact definition): RR 0.85, 95% CI 0.51 to 1.40; $I^2 = 49\%$ (Analysis 1.8). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed no evidence of a publication bias. Excluding the Heidari 2011 study, the RR would be 1.08, 95% CI 0.75, 1.55; $I^2 = 0\%$. We classified Heidari 2011 at low risk of bias for two items only (randomization and selective reporting). The study enrolled 400 participants and randomized them to either general anaesthesia, maintained with nitrous oxide and halothane, or to a neuraxial block (spinal or epidural (5.7% continuous)). Intravenous morphine was given at participants' request for postoperative analgesia in both groups. Results are provided as a per-protocol basis with 10 participants excluded from the neuraxial group and three excluded from the general anaesthesia group. Cognitive dysfunctions were noted before discharge from recovery room, and at 24 and 48 hours after the end of the surgery based on time, person, and place disorientation (unclear who assessed the participants and whether or not outcome assessors were blinded for this specific item). In the general anaesthesia group the number of participants who were classified as disorientated were 22 at the recovery room, six on first postoperative day, and three on the second postoperative day. For the neuraxial group, the number of participants classified as disorientated were seven, six, and one for the same periods. Halothane, an inhalational agent slowly eliminated from the body, is no longer in use in the vast majority of developed countries, and the choice of inhalational agent may influence mental function after general anaesthesia, particularly in the elderly (Rortgen 2010). Furthermore, the choice of morphine as the primary mode of analgesia after a major hip surgery may also contribute to postoperative cognitive dysfunction (Hebl 2005). These two factors may have contributed to a higher effect size of regional anaesthesia compared with general anaesthesia in the study of Heidari 2011, especially considering that the main difference was found in the postanesthesia care unit. Considering a basal rate of 17.7%, 1652 participants (826 per group) would be required to eliminate a 25% difference ($\alpha 0.05$; $\beta 0.2$; one-sided test) if a large RCT would be done. Likewise, the power obtained with the number of participants included here is 0.46 ($\alpha 0.05$; $\beta 0.2$; one-sided test).

For acute confusional state, we downgraded the level of evidence by two for risk of bias based on the fact that we judged more than 75% of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. We downgraded the level by one for inconsistency because the I^2 statistic was 49%. We included direct comparisons only, and this outcome was not a surrogate marker. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. We found no evidence of a publication bias. We found no evidence of a large effect size, confounding factors justifying upgrading, or dose response effect. We rated the quality of evidence as very low.

3. Deep vein thrombosis

The diagnosis of deep venous thrombosis was done by injection of 125-iodine fibrinogen (Davis 1981), or venography (Brichant 1995; McKenzie 1984), or as diagnosed by the consultant specialist (Heidari 2011). Two studies including 116 participants did not use any potent thromboprophylaxis (Davis 1981; McKenzie 1984). The risk of deep vein thrombosis decreased when no specific precautions except just use of early mobilization was used (RR 0.57, 95% CI 0.41 to 0.78; $I^2 = 0\%$; NNTB = 3, 95% CI 2 to 7; based on a basal risk of 76%), but not when low molecular weight heparin was administered (RR 0.98, 95% CI 0.52 to 1.84; $I^2 = 58\%$ for heterogeneity between the two subgroups) (Analysis 1.9). On the same basal risk the optimal information size for a large trial would be 152 participants (76 per group) for a 25% decrease (α 0.05; β 0.2; one-sided test).

For deep venous thrombosis in the absence of potent thromboprophylactic agents, we downgraded the level of evidence by two for risk of bias based on the fact that we judged more than 75% of the included studies as unclear or inadequate for allocation concealment and/or blinding of outcome assessors. There was no evidence of inconsistency. We downgraded the level by one based on indirectness due to the fact that systematic venographies and injection of marked fibrinogen are surrogate markers for clinically relevant events. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. We found no evidence of a publication bias. We found no evidence of a large effect size, confounding factors justifying upgrading, or dose response effect. We rated the quality of evidence as very low.

4. Return of patient to their own home

Data were available for one study only: RR 0.84, 95% CI 0.61 to 1.16 (McKenzie 1984; Table 3). Considering a basal rate of 5.3% (Brauer 2009), 7898 (3949 per group) would be required to eliminate a 25% difference (α 0.05; β 0.2; one-sided test) if a large RCT would be done. Likewise, the power obtained with the number of participants included here is 0.1 (α 0.05; one-sided test).

For this outcome, we downgraded the level by two for risk of bias based on the fact that we judged the sole study included as unclear or inadequate for allocation concealment and blinding of outcome assessors. Inconsistency could not be evaluated. The included study was a direct comparison. We downgraded the level by one for imprecision based on the fact that the optimal information size was not achieved. Publication bias could not be evaluated. We found no evidence of a large effect size, confounding factors justifying upgrading, or dose response effect. We rated the quality of evidence as very low.

5. Congestive cardiac failure

Based on six studies that included 729 participants (Berggren 1987; Biboulet 2012; Bigler 1985; Davis 1981; Racle 1986), we did not find a difference in the risk of congestive heart failure: RR 0.78, 95% CI 0.31 to 1.96; $I^2 = 0\%$ (Analysis 1.10). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed no evidence of a publication bias. Considering a basal congestive heart failure of 6%, 5466 participants (2733 per group) would be required to eliminate a difference of 25% (α 0.05; β 0.2; one-sided test) if a large RCT

would be done. Likewise, the power obtained with the number of participants included here is 0.23 (α 0.05; β 0.2; one-sided test).

6. Acute kidney injury

Data were available only for two small studies that included 202 participants: RR 1.02, 95% CI 0.18 to 5.83; $I^2 = 0\%$ (Davis 1981; Racle 1986; Analysis 1.11).

7. Pulmonary embolism

Based on five studies that included 642 participants (Berggren 1987; Bigler 1985; Brichant 1995; Heidari 2011; Racle 1986), we did not find a difference in the risk of pulmonary embolism: RR 3.35, 95% CI 0.82 to 13.57; $I^2 = 0\%$ when data were analysed as risk ratio. However, if the Peto odds ratio method was used (Analysis 1.12), the difference became statistically significant in favour of general anaesthesia: Peto odds ratio 7.51, 95% CI 1.51 to 37.38; $I^2 = 0\%$. Egger's regression intercept did not show a small-study effect. Duvall and Tweedie's trim and fill analysis did not show any evidence of a publication bias. The classical fail-safe number was three. Because there was no event on the side of general anaesthesia a NNTH could not be calculated. Based on a rate of 1.9% in the treatment group, the NNTB would be 61, 95% CI 55 to 157, when general anaesthesia is used.

8. Unsatisfactory surgical results

There were no data for this outcome for this comparison.

9. Number of patients transfused

Based on two studies that included 172 participants (Bigler 1985; Davis 1981), we did not find a difference in the number of transfused (red blood cells) participants for femur fixation: RR 0.93, 95% CI 0.76 to 1.15; $I^2 = 0\%$. Based on one study that included 30 participants (Svarting 1986), we could not demonstrate a difference in the number of transfused patients for arthroplasty: RR 0.20, 95% CI 0.03 to 1.51. Heterogeneity between the two subgroups = 55% (Analysis 1.13).

10. Length of hospital stay

Based on four studies that included 1143 participants (Davis 1987; Heidari 2011; McKenzie 1984; Racle 1986), we did not find a difference in length of hospital stay: mean difference (MD) - 0.20, 95% CI - 1.05 to 0.65; $I^2 = 0\%$ (Analysis 1.14). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed that one study might be missing to the left for an adjusted point of estimate of - 0.21, 95% CI - 1.05 to 0.63.

11. Length of surgery (in minutes)

Based on 12 studies that included 973 participants (Berggren 1987; Biffoli 1998; Bigler 1985; Bredahl 1991; Heidari 2011; Hoppenstein 2005; Kamitani 2003; Maurette 1988; McKenzie 1984; Messina 2013; Racle 1986; Svarting 1986), a neuraxial block would not reduce the surgical time: MD - 2.73, 95% CI - 8.50 to 3.04; $I^2 = 62\%$ (Analysis 1.15). Egger's regression intercept showed no significant evidence of a small-study effect. Duvall and Tweedie's trim and fill analysis showed that two studies might be missing to the right, for an adjusted point of estimate: -0.85, 95% CI -6.70 to 5.00.

12. Operative hypotension

The definition for operative hypotension varied from the number of participants who had a decrease of systolic arterial blood pressure of 20% (Casati 2003; Davis 1987; Racle 1986), mean arterial blood pressure of 20% (Maurette 1988), mean arterial blood pressure of 25% (Messina 2013), systolic arterial blood pressure of 30% (Berggren 1987; Svarting 1986), arterial blood pressure of 30% (Biffoli 1998), systolic arterial blood pressure of 33% (Juelsgaard 1998), arterial blood pressure \geq 40 mm HG (Couderc 1977), systolic arterial blood pressure of 50% (McLaren 1978), or undefined (Brown 1994). The risk of operative hypotension was lower with a neuraxial block when low dose unilateral (RR 0.57, 95% CI 0.37 to 0.89; $I^2 = 0\%$) (Casati 2003; Messina 2013), or incremental spinals were performed (RR 0.20, 95% CI 0.05 to 0.78) (Juelsgaard 1998); but not with bilateral sensory/motor blockade single shot spinal anaesthesia (RR 1.31, 95% CI 0.87 to 1.95; $I^2 = 36\%$) (Biffoli 1998; Brown 1994; Davis 1987; Juelsgaard 1998; Maurette 1988; McLaren 1978; Racle 1986; Svarting 1986), or epidural anaesthesia (RR 1.01, 95% CI 0.50 to 2.07; $I^2 = 73\%$) (Berggren 1987; Couderc 1977; Analysis 1.16). A bolus of fluid was administered before the neuraxial block for six studies (Biffoli 1998; Couderc 1977; Davis 1987; Juelsgaard 1998; Racle 1986; Svarting 1986).

13. Urine retention

Based on one small study we did not find a difference in the risk of urine retention: RR 0.86, 95% CI 0.30 to 2.51 (Berggren 1987; Table 3).

Neuraxial block added to general anaesthesia compared to general anaesthesia alone

We found only one small study for this comparison (White 1980; Table 3). The study contains three groups including one where a psoas compartment block was added to general anaesthesia. This group was not retained because it was considered outside the scope of the present review: RR 0.80, 95% CI 0.20 to 3.20 for pneumonia, RR 1.00, 95% CI 0.16 to 6.09 for acute confusional state, and RR 0.17, 95% CI 0.01 to 3.94 for deep vein thrombosis. The MD for length of surgery was 0.00, 95% CI -17.96 to 17.96 minutes.

Neuraxial block versus peripheral nerve block

Three studies that included 139 participants compared a neuraxial block (spinal or epidural) to peripheral nerve blocks (Cao 2008; de Visme 2000; Eyrolle 1998). For the peripheral nerve blocks, two studies used posterior lumbar (psoas compartment) block alone (Cao 2008; Eyrolle 1998), and one study added sacral plexus block and iliac crest infiltration to the lumbar plexus block (de Visme 2000). Neuraxial blocks reduce the risk of a failed block: RR 0.24, 95% CI 0.12 to 0.49; $I^2 = 0\%$ (Analysis 2.1). However, when the block combination was used (psoas compartment block plus sacral plexus block plus iliac crest infiltration), three out of the four participants (where the block was judged as incomplete), required only one bolus of 250 mcg of alfentanil at skin incision as supplemental analgesia (de Visme 2000).

We did not find a difference for the risk of acute confusional state: RR 0.89, 95% CI 0.35 to 2.28 (de Visme 2000; Table 3). Operative hypotension was more common with neuraxial blocks: RR 6.00, 95% CI 2.02 to 17.83 (Eyrolle 1998; Table 3) with a NNTH = 2 (95% CI 5 to 2) (basal rate of 12% in the peripheral nerve block group). This was also true for urine retention: RR 14.00, 95% CI 1.90 to 103.00;

$I^2 = 0\%$ (basal rate of 0% in the peripheral nerve block groups) (Cao 2008; Eyrolle 1998; Analysis 2.2). We found no difference in the surgical time based on one study: MD 17.00, 95% CI - 0.76 to 34.76 minutes (de Visme 2000; Table 3).

Intravenous ketamine versus general anaesthesia

We found only one study for this comparison (Spreadbury 1980; Table 3). We could not demonstrate a difference in the risk for unsatisfactory surgical results defined as unstable fixation or prosthesis dislocation by ketamine alone without neuromuscular blocking agents: RR 2.33, 95% CI 0.67 to 8.18; in mortality during hospital stay: RR 1.00, 95% CI 0.46 to 2.17; or the chances of the participant returning home: RR 0.95, 95% CI 0.66 to 1.38. Length of hospital stay for the survivors was longer in the ketamine group: MD 12.00, 95% CI 5.63 to 18.37 days.

DISCUSSION

Neuraxial block versus general anaesthesia

Many of the studies within this review involved small numbers of participants and reported only a few outcome measures. From the actual available RCTs, for adults undergoing hip fracture surgery, regional anaesthesia decreases the risk of deep venous thrombosis only in the absence of potent thromboprophylaxis (very low quality of evidence; Summary of findings for the main comparison). A unilateral or incremental spinal anaesthesia decreases the incidence of operative hypotension. The optimal information size for an alpha error of 0.05 and a beta error of 0.2 (one-sided test) to eliminate a difference of 25% was not achieved for: mortality at one month, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, and return of patient to their own home. Data were available from only one study for return of patient to their own home. The trial reports of many studies indicated a suboptimal level of methodological rigour, in particular regarding the exact method used for randomization, concealment of allocation, assessor blinding and intention-to-treat analysis (Figure 2; Figure 3). Therefore, an absence of difference cannot be stated with certainty for the vast majority of the outcomes included in the present review.

The type of anaesthetic techniques used in many of the studies may not reflect current clinical practice, and this may have prevented us in finding clinically relevant differences between general anaesthesia and regional anaesthesia. For instance, for acute confusional state, one study used diazepam as the induction agent in the general anaesthesia group and as a sedative in the regional anaesthesia group (Bigler 1985). Residual blood concentrations of benzodiazepines have not been shown to correlate with postoperative cognitive dysfunction (Rasmussen 1999). However, some authors reported a clear association between the risk of hip fractures and recently introduced benzodiazepines in the drug regimen of the elderly (Wang 2001), suggesting that newly introduced benzodiazepines will affect the elderly in some way. Therefore it is difficult to be certain that benzodiazepine administration in both groups did not mask an actual difference between general anaesthesia and regional anaesthesia. Likewise, halothane, an inhalational agent slowly eliminated from the body, that is no longer in use in the vast majority of developed countries, was administered in two of the studies and this may have increased the difference between the two anaesthetic techniques, this time favouring regional anaesthesia (Berggren 1987; Heidari 2011). The

choice of an inhalational agent may influence mental functions after general anaesthesia, particularly in the elderly (Rortgen 2010).

The definitions of outcomes and the exact time points at which the participants were evaluated varied widely or were unclear (Table 1). For example, we took as "acute confusional state" all various authors' definitions without any discrimination. Although statistical heterogeneity disappeared ($I^2 = 0\%$) when Heidari 2011 was withdrawn from the analysis (Analysis 1.8), one can see from Table 3, that the definition of "acute confusional state" varied widely, and included various level of a possible transient decrease in mental function (minus 2 points out of 30 on the Mini Mental Status for Casati 2003 or a Mini Mental Status score lower than 5/30 for de Visme 2000), actual confusion (Berggren 1987; Bigler 1985; Heidari 2011), delirium with or without agitation (Kamitani 2003; Racle 1986), or was unspecified (White 1980). A transient decline in the ability to perform a mathematical test may not be as relevant as mental deterioration preventing the person from participating in their rehabilitation (confusion/delirium/agitation). Finally, the exact time point where the outcome was taken also varies widely (up to four weeks: White 1980). Although, there may not be any clinically relevant difference between general anaesthesia and regional anaesthesia after seven days, when any type of mental evaluation is accepted (Guay 2011), a transient decline in mental function sufficient to affect adequate communication between the patient and personnel taking care of her/him, may affect rehabilitation, or even put her/him at risk of further injury (Wang 2001). Further studies performed with short acting drugs may need to differentiate between the various levels of transient decline in mental function (enough to prevent adequate participation in own care and rehabilitation programme or not) and from delirium, with or without agitation (requiring restraining procedures or potent psychotropic drugs).

Studies included were published between 1977 and 2013 and clinical practice has changed during this period. The vast majority of centres will now preferentially use shorter acting drugs in the hope of decreasing the length of time during which patients may be under the residual influence of the anaesthetic agents. This may influence the person's ability to actively participate in their rehabilitation, and possibly their overall outcome. Therefore, we decided to explore the year when the study was published as a factor of heterogeneity and, indeed, we found a correlation between the effect size for mortality and the year when the study was published (Figure 4). This suggests that a lower mortality rate associated with regional anaesthesia compared with general anaesthesia might have been more pronounced in the oldest trials, before the widespread use of short acting anaesthetic drugs. Many of the included trials are relatively old and may not represent contemporary practice, nor account for the advances in safety in the field of anaesthesia. From 1986 to 2005, the one-year mortality rate after a hip fracture decreased by 8.8% for women and 20.0% for men (Brauer 2009). This overall decrease in mortality associated with hip fractures probably reflects advances in the global care of this population. Among other factors, a reduction of the delay before surgery, improved surgical devices and movement toward replacement arthroplasty, combined with a push for earlier weight bearing exercise are all possible factors that may have contributed to this higher rate of survival. If the overall rate of mortality is lower, then the number of participants that will be needed to be included to eliminate a difference between regional and general anaesthesia will be higher.

Neuraxial block decreases the incidence of deep venous thrombosis compared to general anaesthesia only when potent antithrombotic agents such as low molecular weight heparin are not used (Analysis 1.9). It is important to note however that none of the three studies included in the present review used clinical symptoms of deep venous thrombosis as an outcome (Brichant 1995; Davis 1981; McKenzie 1984).

In the present review, regional anaesthesia was associated with a higher risk of pulmonary embolism (its statistical significance depended on the technique of analysis used). It is important to note that an absence of event in the general anaesthesia group, such as found here, is quite exceptional. Particularly considering the fact that the thromboprophylaxis used in these studies was below actual standards for at least four of them: dextran (Berggren 1987), unfractionated heparin (Heidari 2011; Racle 1986), or unspecified (Bigler 1985). The rate of pulmonary embolism found here with regional anaesthesia (1.9%) is consistent with the rate found after lower limb arthroplasty with modern potent thromboprophylaxis: incidence 1.1%, 95% CI 0.3 to 1.9% (Samama 2007). A meta-analysis performed on the efficacy of various regimen of thromboprophylaxis after hip arthroplasty found that compared with the risk obtained after a placebo (1.51%), only warfarin (0.16%), pneumatic compression (0.26%), and low molecular weight heparin (0.36%) were associated with a significantly lower risk of symptomatic pulmonary embolism (Freedman 2000). Therefore, this finding cannot be considered a clear demonstrated effect of an intervention because the 0% rate of pulmonary embolism found with general anaesthesia and suboptimal prophylaxis is not consistent with the medical literature. We have to attribute this exceptionally low rate to an absence of systematic screening, unclear outcome definitions and/or inadequate period of follow-up.

Length of hospital stay can be considered as an indirect marker for cost. We did not find a difference in the mean length of hospital stay for hip fracture between these two anaesthetic techniques (Analysis 1.14). The length of hospital stay of patients operated for hip fracture has decreased from a median of 12 days (interquartile range (IQR), 8.0 to 16.0) between 1986 and 1988 to five days (IQR, 4.0 to 12.0) between 2003 and 2005 (Brauer 2009). This reduced length of hospital stay may however be falsely reassuring because it is associated with a decreased percentage of patients returning home after a hip fracture. In the Brauer 2009 study, 34.3% (95% CI 34.0% to 34.6%) of patients were going home with self care after a hip fracture between 1986 and 1988, while only 5.3% (95% CI 5.2% to 5.4%) were doing so between 2003 and 2005. Between 2003 and 2005, 52.8% of patients with hip fracture (95% CI 52.5% to 53.2%) were discharged to a skilled nursing facility. From limited data, we did not find a difference between the two techniques in the percentage of patients returning home after a fracture hip repair (Analysis 1.13).

In the past, operative hypotension associated with neuraxial blocks has been considered a major drawback to the use of neuraxial blocks in the aged population. One can see however, that this problem can be overcome with the use of a small dose unilateral spinal or incremental dose spinal anaesthesia (Analysis 1.16). Epidurals will not affect the incidence of operative hypotension compared to general anaesthesia (Analysis 1.16).

Neuraxial block added to general anaesthesia compared to general anaesthesia alone

The sole study to address this question involved only 20 participants in each group (White 1980). There was no statistically significant difference between techniques for any of the outcome measures reported. Because of the small numbers of participants involved, no conclusions about the lack of difference between the two techniques can be made.

Neuraxial block versus peripheral nerve block

The three included trials involved only 139 participants in total (Cao 2008; de Visme 2000; Eyrolle 1998). The limited results available suggest that the neuraxial anaesthesia is associated with a lower risk of incomplete or unsatisfactory analgesia (RR 0.24, 95% CI 0.12 to 0.47), and this would be particularly true if a posterior lumbar plexus block is used alone, without the addition of a sacral plexus block plus an iliac crest infiltration. Altogether, the information available would suggest that peripheral nerve blocks could be used as the sole anaesthetic technique, but only when both neuraxial block and general anaesthesia pose special risks.

Intravenous ketamine versus general anaesthesia

The sole trial comparing ketamine with general anaesthesia involved only 60 participants (Spreadbury 1980). The numbers of participants were too small to show if the increase in 'unsatisfactory surgical results' in the ketamine group was a significant factor of ketamine use.

Summary of main results

For adults undergoing hip fracture surgery, regional anaesthesia is associated with a decreased incidence of deep venous thrombosis only in the absence of potent thromboprophylaxis. Due to the inclusion of old trials that may not reflect actual clinical practice, an absence of clear definitions for many outcomes, and the small number of participants included for the vast majority of outcomes, we cannot make a clear statement on the presence/absence of difference in outcomes between regional and general anaesthesia for hip fracture repair for any other outcome.

Overall completeness and applicability of evidence

A substantial part of the evidence is derived from old small studies with suboptimal methodology. Rare adverse events related to the anaesthetic techniques cannot be evaluated from these small studies. These studies however, suggest that results obtained with general anaesthesia or neuraxial blocks would be relatively similar.

Quality of the evidence

Details of reasons for upgrading of downgrading the quality of evidence are given in the section effects of interventions (Results).

For neuraxial blocks compared to general anaesthesia, we rated the quality of evidence as very low for mortality at 0 to 30 days, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, decreased rate of deep venous thrombosis in the absence of potent thromboprophylaxis, and return of patient to their own home.

Potential biases in the review process

We included all available RCTs. Those studies were published between 1977 and 2013, thus covering a wide range of clinical practices.

Agreements and disagreements with other studies or reviews

The absence of difference in the mortality rate between neuraxial blockade and general anaesthesia is in agreement with a recent retrospective study (Neuman 2014).

AUTHORS' CONCLUSIONS

Implications for practice

We did not find a difference between the two anaesthetic techniques, except for deep venous thrombosis in the absence of potent thromboprophylaxis and reduced operative hypotension (if a unilateral or incremental spinal anaesthesia is used). The studies included a wide variety of clinical practices. The number of participants included in the review is insufficient to eliminate a difference between the two anaesthetic techniques for the majority of outcomes studied. These outcomes were often insufficiently defined and the exact time point at which they were measured was often unclear. Therefore, large randomized trials reflecting actual clinical practice are required before drawing final conclusions.

Limited evidence suggests that ketamine anaesthesia without neuromuscular blocking agents may increase the incidence of poor surgical results.

Implications for research

Research in this population is often limited by the fact that many of these patients may have declined mental function, impeding their ability to give informed consent.

New large high quality trials are required to re-evaluate the effect of the anaesthetic technique on the mortality rate of patients undergoing surgery for hip fracture repair.

Because aspirin has now become a choice for thromboprophylaxis for hip fracture surgery in some countries (Falck-Ytter 2012), and bears no contraindication with neuraxial blocks (Horlocker 2010), trials evaluating the effect of a neuraxial block in patients receiving aspirin as their thromboprophylaxis could be relevant.

Finally, future studies should include a measure of the quality of life.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Berggren 1987

Methods	RCT. The study was approved by the Ethics Committee of the University of Umeå. Informed consent
Participants	<p>Orthopaedic hospital in Umea, Sweden 57 patients with a femoral neck fracture Mean age 77/78 years (range 65-92 years) Male: 19% Number lost to follow-up: 4 (7%)</p> <p>Length of follow-up: 12 months</p> <p>Only fully lucid participants were included in the study</p> <p>For fixation, either hookpins or von Bahr screws were used. In two patients with fractures close to the trochanteric area, fixation was achieved with a sliding screw and a plate</p> <p>Forty-two of the patients (74%) were operated on within 36 hr of sustaining their fractures, the remaining patients were operated on within 72 hr</p>
Interventions	<p>Both groups premedicated with pethidine 25-50 mg</p> <p>Treatment group: Neuraxial block (epidural anaesthesia) with 2% prilocaine in the epidural space, mean volume used 12.5 mL. The catheter was removed in the postanesthesia care unit (n = 28)</p> <p>Control group: General anaesthesia with thiopentone 3-4 mg/kg, atropine 0.25-0.5 mg IV, succinylcholine ventilated with nitrous oxide and oxygen and halothane and succinylcholine infusion (n = 29)</p>
Outcomes	<p>Mortality at 30 days and 3 months</p> <p>Acute confusional state within 7 days (modified Organic Brain Syndrome Scale) (performed by 2 investigators with a 90% interrater reliability)</p> <p>Cerebrovascular accident</p> <p>Pneumonia (requiring treatment)</p>

Berggren 1987 (Continued)

Congestive heart failure (requiring treatment)
 Pulmonary embolism (requiring treatment)

 Operative hypotension (> 30% not responsive to treatment)

 Length of surgery

 Urine retention

Notes This study was designed to evaluate the difference in postoperative acute confusional state after the surgery. No a priori definition or specification time of evaluation was given for all other types of complications. Thromboprophylaxis with dextran plus mobilization on first postoperative day when possible. No mention on the type of drugs used for postoperative analgesia

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized", no detail
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessors were blinded for the postoperative acute confusional state but presence/absence of blinding not mentioned for all other outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Four participants lost to follow-up 4 died by 1 year, 1 in the epidural group on 1st postoperative day, the other 3 (group not given) by 5 months. Patients were interviewed at 6 and 12 months regarding living conditions and walking ability - data not presented
Selective reporting (reporting bias)	Unclear risk	Some results (see above) not provided
Other bias	Low risk	The two groups were comparable with regard to age, sex, pre-existing diseases, and preoperative medications (Table 1), except for drugs with anticholinergic effects, which were used significantly more frequently in the epidural group. We identified no other serious risk of bias

Biboulet 2012

Methods	RCT Ethics committee approval and written informed consent from all patients obtained
Participants	Forty-five patients older than 75 years, with ASA physical status III or IV, and with severe cardiac comorbidities, presenting for hip fracture and undergoing hip nailing or partial hip replacement The exclusion criteria were contraindication to spinal anaesthesia, allergy to any of the anaesthetic drugs used, and total hip replacement

Anaesthesia for hip fracture surgery in adults (Review)

Biboulet 2012 (Continued)

Mean delay before the surgery > 72 hours

75% nails

25% hemiarthroplasty

Interventions

Treatment group: Continuous spinal anaesthesia performed with a 19G Sprotte needle and a 23G multiple holes catheter inserted 3 cm cephalad (n = 15). The operated side was placed up at L3-L4 or L4-L5 with 2.5 mg boluses of plain bupivacaine to achieve T10 sensory level or 10 mg. Hyperbaric bupivacaine and 20° Trendelenburg position could be used to achieve T10 thereafter. The catheter was withdrawn in the postanesthesia care unit

Control groups:

1. Target control infusion of propofol infusion was started with an initial target plasma concentration set at 1.5 mcg/mL and adjusted for a BIS value of 50 plus remifentanyl (n = 15 randomized; 14 analysed)

2. Sevoflurane for a BIS value of 50 plus remifentanyl (n = 15 randomized; 14 analysed)

On arrival in the operating room, a femoral nerve block was performed in all patients with 30 mL of ropivacaine 0.5%. Before induction, 500 mL of crystalloid was administered for 30 minutes. During surgery, blood loss was compensated by crystalloid and/or 6% hydroxyethyl starch. Blood transfusion was carried out whenever the haemoglobin level dropped to less than 10 g/dL. Paracetamol and morphine for postoperative analgesia

Outcomes

Mortality at 1 month

Cerebrovascular accident

Myocardial infarction (EKG preoperatively and daily for 3 days after the surgery)

Cardiac heart failure

Notes

The two treatment groups were fused and compared to the treatment group

Follow-up of 1 month

Presence/absence of thromboprophylaxis not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly divided into 3 groups", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up. One patient withdrawn from each of the control groups

Biboulet 2012 (Continued)

Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	High risk	Groups well balanced. Not in intention-to-treat

Biffoli 1998

Methods	Randomized trial: method not stated Informed consent obtained from the patient or a relative
Participants	District hospital in Italy 60 patients ASA 1 or 2, with a femoral neck fracture aged 70 years and above Mean age 83 years (range not stated) Male: 13% Number lost to follow-up: probably none Patients with psychiatric disease or those taking psychoactive drugs or with visual, auditory or language disturbances were excluded from the study. No patients received meperidine or anticholinergic drugs
Interventions	<p>Treatment group: Spinal anaesthesia (L3-4 or L4-5) with a mean dose of 12.7 mg hyperbaric bupivacaine 1%. Supplemental oxygen 40% during the surgery. Ephedrine or atropine for HR < 50 b.p.m. or decrease of 30% or more of the arterial blood pressure (n = 30)</p> <p>Control group: General anaesthesia with propofol 1 mg/kg, atracurium besilate 0.5 mg/kg, nitrous oxide, isoflurane, atracurium infusion of 0.5 mg/kg/hr and fentanyl 1 mcg/kg as required (n = 30)</p> <p>Eight mL/kg of IV fluids before the induction for all patients. postoperative analgesia with IV ketorolac</p>
Outcomes	Length of surgery Operative hypotension (number of patients > 30%)
Notes	In Italian Patient group split into 2 groups depending on preoperative mental state: 38 who were not confused and 22 who were six points or less were considered orientated and seven or more disorientated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up

Anaesthesia for hip fracture surgery in adults (Review)

Biffoli 1998 (Continued)

All outcomes

Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Bigler 1985

Methods	Randomized trial: method not stated. Informed consent was obtained from all patients and the protocol was approved by the ethical committee of Copenhagen hospitals
Participants	<p>Place and country of study not stated</p> <p>40 patients with a proximal femoral fracture operated within 48 hours</p> <p>Mean age 79 years.</p> <p>Male: 17.5%</p> <p>Loss to follow-up: not known</p> <p>Patients in whom there were contraindications to spinal analgesia, with subtrochanteric fractures, severe dementia, cancer and with psychiatric or disseminated neurological disease were not studied</p> <p>Lateral approach to the hip fixation</p>
Interventions	<p>Treatment group: Spinal anaesthesia with 3 mL of 0.75% bupivacaine at L3-4 in the lateral decubitus position on the fractured side (n = 20)</p> <p>Control group: General anaesthesia using atropine, fentanyl, pancuronium, nitrous oxide/oxygen, diazepam and suxamethonium (n = 20)</p> <p>All were premedicated with intramuscular pethidine 75 mg and normal saline 10 mL/kg was given intravenously before anaesthesia. if systolic arterial blood pressure fall exceeded 30% of the preoperative value, intravenous and intramuscular ephedrine 12.5 and 37.5 mg respectively were given</p>
Outcomes	<p>Length of surgery</p> <p>Number of patients transfused</p> <p>Mortality at 1 month</p> <p>Acute confusional state within 7 days</p> <p>Pneumonia</p> <p>Cerebrovascular accident</p> <p>Congestive cardiac failure</p> <p>Pulmonary embolism</p>
Notes	Length of follow-up: 3 months. This study was designed to evaluate the difference in postoperative acute confusional state after the surgery. No a priori definition or specification time of evaluation was given for all other types of complications. Attempt to early mobilization only as thromboprophylaxis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were randomly allocated to spinal analgesia or general anaesthesia." No details

Bigler 1985 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor blinded to the anaesthetic technique used for mental tests Unspecified for the other outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropout or failed block reported
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	The two groups were comparable in relation to age, sex, ASA physical status, preoperative haemoglobin and blood pressure. Preoperative mental scores were slightly (not statistically significantly) lower in the spinal group

Bredahl 1991

Methods	Randomized trial: method not stated Approved by the Ethics Committee and informed consent obtained from each patient
Participants	Orthopaedic hospital Aalborg, Denmark 30 ASA I or II physical status women with a proximal femoral fracture Mean age 79 years (range 60-90) Male: 0% Loss to follow-up: not stated, but 2 excluded due to incomplete data Operated within 24 hours
Interventions	Treatment group: Ephedrine 25 mg IM plus IV ephedrine for pre-spinal hypotension (2 patients). Spinal anaesthesia at L2-3 or L3-4 with 2.5-3 mL of 0.5% plain bupivacaine in lateral decubitus. Oxygen supplement during the surgical intervention, sedation with IV diazepam (n = 15) Control group: General anaesthesia using thiopentone, pethidine, pancuronium, nitrous oxide/oxygen, IPPV, and suxamethonium (n = 15 randomized; 13 analysed) Premedication with pethidine 0.5 mg/kg for all patients. IM Nicomorphine for postoperative analgesia
Outcomes	Length of surgery
Notes	Study designed to examine the difference in body temperature between the two anaesthetic technique Length of follow-up: 3 days Presence/absence of thromboprophylaxis not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
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Bredahl 1991 (Continued)

Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two patients excluded from the general anaesthesia group for incomplete data
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Brichant 1995

Methods	RCT Approved by the Ethics Committee and informed consent obtained from each patient
Participants	Orthopaedic hospital in Brussels, Belgium 106 patients with proximal femoral fracture Age: not stated Male: percentage not stated Number lost to follow-up: not stated Operated between 10 and 72 hours after admission Length of follow-up: 10 days
Interventions	Treatment group: Neuraxial block (spinal or epidural) anaesthesia with bupivacaine (n = 54 randomized; 46 analysed) Control group: General anaesthesia administered according to 'local practice' (n = 52 randomized; 42 analysed)
Outcomes	Deep vein thrombosis (venography) Pulmonary embolism (confirmed with angiography or lung ventilation/perfusion scan)
Notes	Conference abstract only All patients had subcutaneous nadroparin for DVT prophylaxis for 10 days and contralateral stocking
Risk of bias	
Bias	Authors' judgement Support for judgement

Brichant 1995 (Continued)

Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent panel of experts unaware of the treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% excluded from analysis
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups said to be well balanced

Brown 1994

Methods	RCT Approved by the local Ethics Committee and signed written informed consent from each participant
Participants	Orthopaedic hospital in Hong Kong 20 ASA 2 or 3 patients with a proximal femoral fracture Mean age 77 years (range 66-91) Male: 50% Number lost to follow-up: not stated
Interventions	Premedication with pethidine or temazepam Treatment group: Spinal (subarachnoid) anaesthesia with 0.2 mg/kg hyperbaric bupivacaine (n = 10) Control group: General anaesthesia using thiopentone or propofol, isoflurane or enflurane atracurium and nitrous oxide/oxygen (n= 10)
Outcomes	Operative hypotension (requiring administration of vasopressor)
Notes	Length of follow-up: 2 days (up to 44 hours)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized trial: use of random numbers table
Allocation concealment (selection bias)	Unclear risk	Not mentioned

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Brown 1994 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed neuraxial block mentioned
Other bias	Low risk	Groups well balanced

Cao 2008

Methods	RCT Approved by the Ethics Committee and written informed consents obtained
Participants	60 ASA 2 or 3 participants, aged between 65 and 97 years old, weighting 45 to 75kg scheduled for unilateral intertrochanteric femoral fracture repair
Interventions	Treatment group : Posterior lumbar plexus block with 20 mL of bupivacaine 1.0% and 30 mL of ropivacaine 0.5% injected when a contraction of the quadriceps was obtained at 0.3 mA (disappearing at 0.2 mA) with the side to be blocked uppermost (n = 30) Control group : Lumbar epidural with ropivacaine 0.75% for a sensory level at L1-L2 (n = 30)
Outcomes	Urinary retention
Notes	No anaesthesia or local anaesthetic toxicity-related complications happened in two groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly divided"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned

Cao 2008 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No cross-over
Other bias	Low risk	Groups well balanced

Casati 2003

Methods	RCT Approval was obtained from our Institutional Ethics Committee and written informed consent from each participant
Participants	Orthopaedic hospital in Milan, Italy 30 patients of ASA grade II or III undergoing hemiarthroplasty for a proximal femoral fracture Mean age 84 years (range 67-94) Male: 7% Number lost to follow-up: 0
Interventions	Treatment group: Spinal anaesthesia at L3-4 with 7.5 mg of hyperbaric bupivacaine injected in lateral decubitus with the patient maintained in this position for 15 minutes (n = 15) Control group: General anaesthesia with sevoflurane inhalation and laryngeal mask airway. No neuromuscular blocking agent (n = 15) All patients received a standardized protocol for preoperative fluid resuscitation, including blood The day before surgery, all patients had a standard preoperative evaluation, including chest radiography, electrocardiography and routine laboratory tests. Preoperative analgesics consisted of IV ketorolac (30 mg every 8 h). Preoperative fluid resuscitation including transfusion if required to maintain haemoglobin concentration 9 G/L. Postoperative analgesia with tramadol and ketorolac Length of follow-up: 7 days & hospital discharge
Outcomes	Operative blood loss (taken as P value) Operative hypotension (20% decrease, period undefined). Numbers taken are those requiring a bolus of fluid Acute confusional state within 7 (defined as maximal number of patients with a decrease of 2 points or more on the Mini mental test and this occurred at 24 hours while patients were tested at 24 hours and 7 days)
Notes	Absence/presence of thromboprophylaxis unspecified

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomly allocated". Probably adequate considering the use of sealed envelopes although not clearly mentioned
Allocation concealment (selection bias)	Low risk	Sealed envelopes

Casati 2003 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Couderc 1977

Methods	RCT	
Participants	Orthopaedic hospital in Paris, France 100 patients with a proximal femoral fracture (nail and plate n = 56; hemiarthroplasty n = 44) Mean age 86 years. (Inclusion criterion: 80+ years; range not stated) Male: 14% Number lost to follow-up: not stated Operated within 24 hours after admission	
Interventions	Treatment group: Five to seven hundreds mL of fluid (LR or colloid). Neuraxial block (epidural anaesthesia) in lateral decubitus consisting of single shot or continuous infusion of 0.5% bupivacaine and adrenaline with or without lidocaine (n = 50) Control group: General anaesthesia with thiopentone, pancuronium or succinylcholine, dextromoramide or methoxyflurane, nitrous oxide/oxygen (n = 50) Premedicated with hydroxyzine and atropine	
Outcomes	Mortality at 3 months (cumulative) Operative hypotension (≥ 40 mm HG; number of patients at induction of anaesthesia) Myocardial infarction (serial preprogrammed EKGs and enzymes)	
Notes	In French Length of follow-up: 3 months Complete data for fatal myocardial infarction, congestive heart failure and pulmonary embolism not provided Early mobilization and anti-vitamin K from day 3	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized study: by 'drawing of lots'

Anaesthesia for hip fracture surgery in adults (Review)

Couderc 1977 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	EKG interpreted by a blinded cardiologist. Not blinded for the other outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed epidural reported
Other bias	Low risk	Groups well balanced

Davis 1981

Methods	Randomized trial: method not stated
Participants	<p>Orthopaedic hospital Christchurch, New Zealand 132 patients with a proximal femoral fracture (intertrochanteric, basicapital or subcapital) and coming within 72 hours of the injury Mean age 81/78 years (Inclusion criterion: 50+, range not given) Male: 15% Number lost to follow-up: 0</p> <p>Patients < 50 years of age, requiring arthroplasty or with cardiac heart failure were excluded</p>
Interventions	<p>Treatment group: Spinal anaesthesia in lateral decubitus on the fractured side using hyperbaric tetracaine 0.5% in 51 patients and hyperbaric 0.5% cinchocaine in 13 patients. Patients were retained in this position for 10 minutes. Ketamine also used for sedation in 8 patients (positioning for the spinal). Sedation also provided with diazepam (mean dose 9 mg). Supplemental oxygen or a mixture of nitrous oxide and oxygen during the surgery (n = 64)</p> <p>Control group: General anaesthesia with diazepam (2.5-30 mg) mean dose 9.5 mg, fentanyl 1-3 mcg/kg, nitrous oxide and oxygen, IPPV, pancuronium (mean dose 6 mg) (n = 68).</p> <p>Infusion of 200-400 mL of fluids before induction for all patients</p> <p>Length of follow-up : 1 month</p>
Outcomes	<p>Mortality - at 1 month Operative hypotension</p> <p>Number of patients transfused</p> <p>Pneumonia Cerebrovascular accident Congestive heart failure Acute kidney injury</p> <p>Deep vein thrombosis (fibrinogen) (available in 76 patients only)</p>

Davis 1981 (Continued)

Notes Presence/absence of thromboprophylaxis not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	High risk	Incomplete data for deep venous thrombosis (76/132)
Selective reporting (reporting bias)	Low risk	Eight failed spinal
Other bias	Low risk	Groups well balanced. Intention-to-treat analysis

Davis 1987

Methods	RCT Approved by the five Ethics Committee of the participating hospitals
Participants	Orthopaedic hospitals in New Zealand - multicentre study 549 (538 analysed) participants with a proximal femoral fracture Mean age 79.5 years (range not stated) Male: 22% Number lost to follow-up: 0, but 11 excluded 20% subcapital and 80% trochanteric fractures Excluded if < 55 years of age, arthroplasty required, pathological fracture or contraindication to one anaesthetic technique
Interventions	Treatment group: Spinal anaesthesia with sedation with diazepam. Hyper of isobaric tetracaine, nupercaine or bupivacaine for spinal (n= 259 analysed) Control group: General anaesthesia with pre-oxygenation, IV induction with thiopentone, IPPV maintained with nitrous oxide/oxygen, non-depolarizing neuromuscular blocker, fentanyl (n = 279 analysed)
Outcomes	Mortality at 1 month (28 days) Operative hypotension requiring vasopressor Length of hospital stay
Notes	There was 1 non fatal anaphylactoid reaction at induction of general anaesthesia

Anaesthesia for hip fracture surgery in adults (Review)

Davis 1987 (Continued)

Length of follow-up: 1 month

A longer duration of follow-up was available for a fraction of the patients only and therefore was not reported to decrease the chances of selective reporting

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized with stratification by sex and hospital
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	11 excluded out of 549. Exclusion were made on pre-defined criteria: age less than 55 years, multiple trauma, possible replacement or hemi-arthroplasty or pathological fractures
Selective reporting (reporting bias)	Low risk	30 failed spinal and 14 incomplete
Other bias	Low risk	Groups well balanced. Intention-to-treat

de Visme 2000

Methods	RCT Approved by the Research and Ethics Committees and written informed consent from all patients
Participants	Orthopaedic hospital in Brest, France 29 patients with a proximal femoral fracture (69% trochanteric and 31 % femoral neck) Mean age 85 years (range 68-97) Male: 17% Number lost to follow-up: none Evidence of cognitive deficit (MMSE lower than 5), contraindication to SA, or peripheral nerve block, resulted in exclusion Length of follow-up: not stated but probably 5 days
Interventions	Treatment group: Lumber plexus (30 mL Winnie's technique), sacral plexus (10 mL Mansour's technique) with 1.33% lidocaine and adrenaline (1:240,000) and 5 mL 1% lidocaine for the iliac crest block (for lateral cutaneous nerve) (n = 15). Neurostimulation at 0.8 mA accepted Control group: Spinal anaesthesia at L3-4 with 3 mL 0.5% plain bupivacaine (n = 14) All patients received 250 mcg alfentanil before being turned to the lateral position, with the operated side uppermost

Anaesthesia for hip fracture surgery in adults (Review)

de Visme 2000 (Continued)

The patients were given 5 mL/kg of Hartman solution before the 5 mL/kg/h of the same solution until transferred to the recovery room. Ephedrine for systolic < 90 mmHG or 30% decrease

Outcomes	Length of surgery Acute confusional state within 7 days
Notes	There were no complications that could be attributed to the techniques In both groups, adequate muscle relaxation was present for all patients to ensure manipulation for positioning of the injured extremity and fracture reduction Presence/absence of thromboprophylaxis not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients were randomly assigned by the hospital pharmacy just before transfer to the operating area to 2 groups
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Patients in the CPNB group required light adjunct of drugs (alfentanil 250 mcg) 3 times for the incision (anaesthesia was judged incomplete) and 1 patient received sedation repeatedly (anaesthesia was judged unsatisfactory). No conversion to GA
Other bias	Unclear risk	Groups well balanced

Eyrolle 1998

Methods	RCT Ethics Committee approval
Participants	Orthopaedic hospital in Paris, France 50 patients with a proximal femoral fracture Mean age 82 years (range not stated) Male: % not stated Number lost to follow-up: none probably

Eyrolle 1998 (Continued)

Interventions	<p>Treatment group: Lumber plexus block using equal volumes of 2% lidocaine and 0.5% bupivacaine with 1:200,000 epinephrine (n = 25)</p> <p>Control group: Spinal anaesthesia with 0.5% bupivacaine (n = 25) A light sedation with propofol intravenously, as required</p>
Outcomes	Operative hypotension (mean arterial blood pressure decrease > 20%)
Notes	<p>Conference abstract only</p> <p>presence/absence of thromboprphylaxis not mentioned</p> <p>In the PNB group, 19/25 patients required a propofol infusion > 1 mg/kg/h. A lumbar plexus block alone was considered insufficient to provide adequate anaesthesia for hip fracture repair</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized in two groups", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed block mentioned
Other bias	Low risk	Groups said to be equivalent

Heidari 2011

Methods	<p>RCT</p> <p>This study was approved by the Ethics Committee</p>
Participants	<p>Four hundred patients older than 30 years old (in class I, II, and III of ASA classification) who were scheduled for elective operative fixation of fractured hip</p> <p>Patients were included if they had no dementia or cognitive dysfunctions and no history of opioid or psychotic drugs use. Patients with hypersensitivity to blood transfusion, sever reaction to cement implantation, sever bleeding, hypotension needed interventions, prolonged operation changed surgical plan which impressed the study goals, were excluded</p>

Heidari 2011 (Continued)

54.5% trochanteric

20.9% femoral neck

9.8% subtrochanteric

Mean time of surgery > 72 hours after admission

Interventions

Treatment group: patients were given Ringer's lactate solution (15 mL/kg) prior to the induction of anaesthesia and received either spinal with plain bupivacaine 0.5% (3 mL) at L3-L4 or epidural anaesthesia with 25 mL of 0.5% bupivacaine with epinephrine 1:200,00 performed with a 18-G-Touhy needle at the L3-L4 (n = 190)

Control group: Patients were given Ringer's lactate solution (10 mL/kg), thiopental, fentanyl, nitrous oxide, halothane and pancuronium. Residual neuro-muscular block was antagonized (n = 197)

All patients were infused Ringer's lactate solution (4 mL/kg) on arrival at the operating room to all patients. postoperative analgesia with morphine

Outcomes

Operative hypotension (MAP < 70% of baseline or 65 mm HG)

Length of surgery

Length of hospital stay (after the surgery)

Mortality at 1 month

Acute confusional state in hospital

Myocardial infarction

Congestive heart failure

Pneumonia

Thrombosis

Pulmonary embolism

Cerebrovascular accident

Notes

"low dose of heparin as a DVT prophylaxis"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomly assigned into two groups using random-number table"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned

Heidari 2011 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"Three patients of the general anaesthesia group and 10 of the neuraxial block group were excluded because of change in anaesthetic or surgical plan"
Selective reporting (reporting bias)	Low risk	Recruitment ended with the completion of the protocol in the 387th patient.
Other bias	High risk	"Groups are similar regarding age, weight and gender ratio." Not in intention-to-treat: "Three patients of the GA group and 10 of the NA group were excluded because of change in anaesthetic or surgical plan"

Hoppenstein 2005

Methods	RCT Institutional review board-approved and written informed consent was obtained before patient inclusion into the study
Participants	Sixty ASA physical status I, II, and III geriatric patients at least 60 years of age, undergoing surgical fixation of the neck of femur Patients with known haemoglobinopathy, as well as those with a clinical history of cerebrovascular or carotid artery disease, were excluded from the study.
Interventions	Treatment group: spinal anaesthesia performed with the patient in the lateral decubitus position and 4 mg isobaric bupivacaine plus 25 mcg of fentanyl via a 25-gauge pencil-point needle (n = 30) Control group: General anaesthesia with thiopental, fentanyl, nitrous oxide, isoflurane and vecuronium (n = 30)
Outcomes	Length of surgery
Notes	Presence/absence of thromboprophylaxis not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were allocated via computer-generated randomization schedule to one of two treatment groups
Allocation concealment (selection bias)	Low risk	Randomized after enrolment
Blinding of participants and personnel (performance bias) All outcomes	High risk	"open label study"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"open label study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up

Hoppenstein 2005 (Continued)

Selective reporting (reporting bias)	Low risk	No conversion to general anaesthesia
Other bias	Low risk	Groups well balanced

Ibanez 1993

Methods	RCT
Participants	Patients undergoing hip fracture repair by Ender's fixation
Interventions	Treatment group: spinal anaesthesia (n = 30) Control group: general anaesthesia (n = 30)
Outcomes	Mortality Deep vein thrombosis
Notes	Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"at random"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up mentioned
Selective reporting (reporting bias)	Unclear risk	Standard deviation not provided
Other bias	Unclear risk	Few details, conference abstract

Juelsgaard 1998

Methods	RCT
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Juelsingaard 1998 (Continued)

Approved by the Ethics Committee

Participants	Orthopaedic hospital in Aarhus, Denmark 29 followed-up out of 54 patients with proximal femoral fracture and known coronary artery disease. Patients with a recent (< 6 months) myocardial infarction excluded For 29 patients included in this review: Age: mean 80.9 years (range 65-99) Male: 13% Number lost to follow-up: 0, but 11 excluded from original trial population
Interventions	<p>Treatment groups: Single shot (n = 15) with 2.5 mL of 0.5% bupivacaine or incremental doses (0.5 mL every 15 minutes) (n = 14) of the same drug. Considered as two subgroups of the same study</p> <p>Control group: General anaesthesia with fentanyl 1-2 mcg/kg, 1-4 mg/kg thiopentone, 0.5 mg/kg atracurium, nitrous oxide and oxygen and enflurane (n = 14). This group was split in half to be compared with each treatment group separately</p> <p>All patients were premedicated with pethidine 1 mg/kg and received supplemental oxygen for 12 hours after the surgery</p>
Outcomes	Mortality at 1 month Operative hypotension (number of patients with 33% reduction in systolic arterial blood pressure from baseline) Myocardial infarction (World Health Organization criteria)
Notes	Presenc/absence of thromboprophylaxis not mentioned Length of follow-up: 1 month

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The investigator was blinded to the treatment group" (ischemias)
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Kamitani 2003

Methods	RCT Oral informed consent
Participants	40 patients with a femoral neck fracture Mean age 82 years (range - not stated) Male: 10% Number lost to follow-up: 0 Patients who could not communicate well were excluded in this study
Interventions	Treatment group: Spinal anaesthesia with 3 mL of 0.5% isobaric bupivacaine (n = 19) Control group: General anaesthesia with propofol (0.5-1 mg), vecuronium (0.5-1 mg/kg), nitrous oxide, sevoflurane and fentanyl (0.1-0.2 mg/kg) and local field block with local anaesthesia (n = 21) Diclofenac for postoperative analgesia
Outcomes	Length of surgery Acute confusional state (maximal incidence within 7 days) (Inoue's "the confusion assessment method diagnosis algorithm" by the nurse on the floor)
Notes	In Japanese Length of follow-up: 4 days

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Maurette 1988

Methods	RCT
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Anaesthesia for hip fracture surgery in adults (Review)

Maurette 1988 (Continued)

Consent obtained from each patient.

Participants	Orthopaedic hospital Bordeaux, France 35 patients with a proximal femoral fracture Garden's screw or Hender's nail Mean age 83 years (> 70 years) Male: % not stated Number lost to follow-up: not stated, but 2 excluded as they failed to participate in postoperative tests
Interventions	Treatment group: Spinal anaesthesia with 1.5 mg/kg prilocaine (n = 19 randomized; 18 analysed) Control group: General anaesthesia using thiopentone, spontaneous ventilation, nitrous oxide/oxygen, enflurane, dextromoramide (n = 16 randomized; 15 analysed) No premedication
Outcomes	Operative hypotension (number of patients with 20% decrease in MAP) Length of surgery
Notes	In French Length of follow-up: 3 days

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'random draw'
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient from each group did not participate in the test and was excluded from the analysis
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced (included similar results for mental tests before the surgery: 52.2 ± 8 and 52.5 ± 8.5 for spinal and GA respectively)

McKenzie 1984

Methods	Randomized trial: use of envelopes containing random numbers
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McKenzie 1984 (Continued)

Participants	Orthopaedic hospital in Glasgow, Scotland 150 patients with fractured neck of femur Nail/plate no hemiarthroplasty Mean age 75 years (range not stated) Male: % not stated Mean delay before the surgery 48 hours Number lost to follow-up: 0, but 2 excluded due to postponement of operation
Interventions	Treatment group: Spinal anaesthesia with 0.5% hyperbaric cinchocaine 1.3-1.5 mL at L3-4 or L4-5 . Supplemented by small doses of diazepam if required (n = 73) Control group: General anaesthesia induced with althesin 1-3 mL, suxamethonium 50 mg, nitrous oxide and oxygen, halothane and spontaneous respiration (n = 75)
Outcomes	Mortality at 1, 3, 6 and 12 months Length of surgery Operative blood loss Length of hospital stay Deep vein thrombosis (venography; subgroup of 40) Returned home
Notes	Additional information supplied by Dr McLaren indicated that all the references referred to one study. Additional data on mortality supplied Length of follow-up: 12 months The venography study for DVT detection involved a subgroup of 40 patients

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	" randomly allocated." No details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up. Over the period study, operation was postponed in only two patients (not included in the 150). In two patients, the subarachnoid space could not be identified and these patients received general anaesthesia and were excluded from the study.
Selective reporting (reporting bias)	Low risk	The authors provided results for all measurements for 148 patients.

McKenzie 1984 (Continued)

Other bias	High risk	Groups well balanced. Not in intention-to-treat: two patients randomized, excluded (surgery postponed)
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McLaren 1978

Methods	Randomized trial: method not stated
Participants	<p>Orthopaedic hospital in Glasgow, Scotland 116 patients with fractured neck of femur Mean age 76 years. Male: % not stated Number lost to follow-up: none for the original report of 55 cases. Loss to follow-up not reported in the later study report (1982) of 116 cases</p> <p>Nail and plate only, hemiarthroplasty excluded from the study</p>
Interventions	<p>No premedication</p> <p>Treatment group: Spinal anaesthesia with 0.5 mL hyperbaric cinchocaine 0.5% injected in lateral decubitus position with the patient lying on the fractured side. the patient was maintained in that position for 3 minutes. Patients sedated with 10% althesin in 5% dextrose during operation (n = 36/56)</p> <p>Control group: General anaesthesia with althesin 50 mcg/kg, pancuronium bromide 0.1 mg/kg, IPPV, nitrous oxide, oxygen and fentanyl 0.05 mg as needed, reversal of neuromuscular blocking drugs at the end (n = 39/60)</p>
Outcomes	<p>Mortality at 1 month Operative hypotension (decrease in systolic blood pressure greater than 50% of baseline)</p> <p>Pneumonia</p>
Notes	<p>The original paper in 1978 reported the results for 55 cases. A later report in 1982 of the same study gave the outcome for 116 patients. The latter report was used for the outcomes of mortality at one month. The original paper was used for the other outcomes for 55 patients. The methodology assessment was based on the 1978 report.</p> <p>Length of follow-up: 1 month minimum</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up

Anaesthesia for hip fracture surgery in adults (Review)

McLaren 1978 (Continued)

All outcomes

Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Unclear risk	Fourteen patients in the spinal group (54%) and ten patients in the general anaesthetic group (34%) had signs and/or symptoms of respiratory problems preoperatively

Messina 2013

Methods	RCT Approved by the Ethics Committee
Participants	Patients > 75 years of age admitted with fractured hips not scheduled for hip replacement
Interventions	<p>Treatment group: Spinal with 7.5 mg of levobupivacaine plus 5 mcg of sufentanil performed in the lateral position with the fractured side uppermost. Patients were kept in this position for 5 minutes (n = 10)</p> <p>Control group: General anaesthesia with propofol, sevoflurane, remifentanil and cisatracurium (n = 10)</p> <p>All patients received Ringer's Lactate solution 500 mL rapidly administered via the peripheral line before either spinal or general anaesthesia induction, Voluven[®], (hydroxyethylstarch 6%), 20 mL X BMI I3 was used to treat the first episode of hypotension in both groups</p>
Outcomes	Surgery (min) Operative hypotension (MAP decrease of 25% or more)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization list
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up

Messina 2013 (Continued)

Selective reporting (reporting bias)	Low risk	No failed spinal mentioned: "All patients in subarachnoid anaesthesia group had an effective intraoperative anaesthesia and analgesia"
Other bias	Low risk	Groups well balanced

Racle 1986

Methods	RCT Consent obtained from the family or the patient for the spinal anaesthesia group	
Participants	Orthopaedic hospital in Cedex, France 70 female patients with a proximal femoral fracture Mean age: 82 years (Inclusion criterion: 75+, range not given) Male: 0% Number lost to follow-up: not state Hemi- or total hip arthroplasty	
Interventions	Premedication with IM hydroxyzine and atropine Treatment group: 200-300 IV fluids before the spinal and 8 mL/kg after. Spinal anaesthesia with 3 mL 0.5% bupivacaine + adrenaline with the patients lying on the fractured side (n = 35). Flunitrazepam for sedation Control group: General anaesthesia using thiopentone, vecuronium, fentanyl, nitrous oxide/oxygen, enflurane (n = 35)	
Outcomes	Mortality at 1 and 3 months Length of surgery Operative hypotension (number of patients with > 20% decrease in systolic arterial blood pressure) Length of hospital stay Pneumonia Congestive cardiac failure Acute confusional state (maximal number observed) Pulmonary embolism Acute kidney injury Cerebrovascular accident	
Notes	Length of follow-up: 3 months In French Early mobilization and heparin for thromboprophylaxis	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization table Cochran and Cox"
Allocation concealment (selection bias)	Unclear risk	Not mentioned

Racle 1986 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed spinal
Other bias	Low risk	Groups well balanced

Spreadbury 1980

Methods	<p>RCT</p> <p>No specific consent "as not double-blind"</p> <p>Protocol changed to restrict the trial to patients > 80 years in view of poor surgical results in the Ketamine group</p>
Participants	<p>Orthopaedic hospital in Warwick, England</p> <p>60 previously ambulant female patients with a proximal femoral fracture</p> <p>Mean age 84 years (range not stated)</p> <p>Male: % not stated</p> <p>Nail/plate (45%) or arthroplasty (55%)</p> <p>Number lost to follow-up: none</p>
Interventions	<p>Atropine 0.6 mg, with analgesics and oral diazepam as required</p> <p>Treatment group: Ketamine anaesthesia with ketamine 2 mg/kg at induction then ketamine 1 mg/kg as required. Also optional diazepam (n = 30)</p> <p>Control group: General anaesthesia using drugs and method chosen by the anaesthetist. Twenty patients received neuromuscular blocking agents (n = 30)</p> <p>Postoperative analgesia with papaveretum or pethidine and supplemental oxygen for 24 hours</p>
Outcomes	<p>Mortality during hospital stay</p> <p>Length of hospital stay (for patients discharged home only)</p> <p>Returned home</p> <p>Unsatisfactory surgical results (unstable nail/plate or prosthesis dislocation)</p>
Notes	<p>Length of follow-up: not stated</p> <p>Presence/absence of thromboprophylaxis not mentioned</p> <p>Total number of patients taken as the denominator for the outcome "return home"</p>

Risk of bias
Anaesthesia for hip fracture surgery in adults (Review)

Spreadbury 1980 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not double-blind
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up mentioned up to 14 days.
Selective reporting (reporting bias)	Low risk	The authors provided results for all measurements, no evidence of selective reporting.
Other bias	High risk	More certified (versus in training) surgeons for the older patients in the ketamine group Unclear exactly how many patients came from home. Not in intention-to-treat for all results

Svarting 1986

Methods	RCT Approved by the Ethics Committee and informed consent obtained from each patient
Participants	University hospital in Helsinki, Finland 30 patients with a proximal femoral fracture treated with a Thompson prosthesis. (ASA grade II OR III) Mean age 77 years (range not stated) Male: 13% Thompson's prosthesis Number lost to follow-up: none likely
Interventions	Both groups premedicated with pethidine and atropine Treatment group : Spinal anaesthesia using 3 mL of 0.5% isobaric bupivacaine into the subarachnoidal space. Patients maintained for 3 min in the lateral decubitus position Balanced salt solution 10 mL/kg (n = 15) Control group : General anaesthesia using fentanyl, thiopental, pancuronium bromide, nitrous oxide/oxygen, then atropine and neostigmine (n = 15)
Outcomes	Operative hypotension Length of surgery Number of patients transfused

Svarting 1986 (Continued)

Notes	Length of follow-up: not stated
	Emphasis in the article on the connection of the results with the use of methylmethacrylate cement for the Thompson prosthesis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups well balanced

Tasker 1983

Methods	RCT
Participants	<p>Orthopaedic hospital in Leicester, England 100 patients with a proximal femoral fracture Mean age not stated. Male: % not stated</p> <p>Subcapital fractures</p> <p>Thompson's prosthesis Number lost to follow-up: not stated</p>
Interventions	<p>Treatment group : Spinal</p> <p>Control group: General anaesthesia Exact method of anaesthesia not stated. The number of participants attributed to each treatment group is unspecified. For the purpose of this review, we counted them as 50 participants in each group</p>
Outcomes	Mortality. This result was not included in the analysis: time point unknown
Notes	Conference abstract only

Tasker 1983 (Continued)

Length of follow-up: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"random selection", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not mentioned, conference abstract
Selective reporting (reporting bias)	Unclear risk	Few details, conference abstract only
Other bias	Unclear risk	No details

Ungemach 1993

Methods	RCT
Participants	Orthopaedic hospital in Mannheim, Germany 114 patients with a proximal femoral fracture Mean age 79 years (range not stated). Male: 16% Number lost to follow-up: not stated
Interventions	Treatment group: spinal anaesthesia with 3-4 mL of 0.5% hyperbaric bupivacaine (n = 57) Control group: general anaesthesia with isoflurane, fentanyl, nitrous oxide/oxygen (n = 57)
Outcomes	Mortality at 2 weeks only. This result was not included in the analysis
Notes	Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized", no details

Ungemach 1993 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unlikely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up mentioned
Selective reporting (reporting bias)	Low risk	No failed spinal mentioned
Other bias	Low risk	Groups said to be comparable

Valentin 1986

Methods	<p>RCT</p> <p>"It was decided not to obtain informed consent from the patients as to participation in the study because a large proportion of patients with hip fractures are old, and mentally unable to reach a logical decision." "Human research committees were not established in Denmark at the start of this investigation"</p>
Participants	<p>Orthopaedic hospital in Hellerup, Denmark 662 patients (578 analysed) with a proximal femoral fracture Mean age 79 years (range 50 - 100) Male: 20%</p> <p>internal fixation (63%) or hemiarthroplasty (37%) (Moore) Number lost to follow-up: 2 (0.3%), 84 patients excluded patients who received heparin treatment were excluded</p>
Interventions	<p>No premedication was given to poor-risk patients; in the others, premedication consisted of pethidine 25-75 mg, often supplemented with promethazine 12.5-25 mg, both administered IM, approximately 30 min before the induction of anaesthesia</p> <p>Treatment group: Spinal anaesthesia with 3-4 mL isobaric bupivacaine injected in the lateral decubitus position. It is unclear whether the fractured side was up or down. Patients were left in that position for 5-15 minutes until a sensory level to the lower thoracic segments was achieved. Patients were sedated with fentanyl 0.05-0.1 mg IV and midazolam and some received supplemental oxygen. (n = 281) Control group: General anaesthesia with enflurane and nitrous oxide/oxygen with or without thiopentone at induction or neurolept anaesthesia with droperidol, fentanyl and nitrous oxide/oxygen. All patients having neurolept anaesthesia, and the majority of the patients receiving enflurane received gallamine to provide neuromuscular blockade during the surgical procedure. (n = 297)</p>
Outcomes	Mortality at 1 month, 3, 6 and 12 months (read from graphs)
Notes	<p>Length of follow-up: 24 months</p> <p>Mobilization on postoperative day 2 or 3</p>

Anaesthesia for hip fracture surgery in adults (Review)

Valentin 1986 (Continued)

Antiembolic stockings were provided, but anticoagulant therapy was not given routinely

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	84 patients excluded from the analysis. Their allocation is not mentioned
Selective reporting (reporting bias)	Low risk	Not in intention-to-treat: "Of the 662 patients admitted to the study, 84 were later excluded by the authors for the reasons listed in table II, leaving data from 578 patients for consideration"
Other bias	High risk	"the two anaesthetic groups were comparable with respect to age, sex, type of fracture and surgical procedure. Classification according to the ASA criteria was applied to 508 patients: there were more patients in ASA group III in the general anaesthesia group, and more of group IV in the spinal anaesthesia group (P value < 0.02) (table IV). Not in intention-to-treat: "Of the 662 patients admitted to the study, 84 were later excluded by the authors for the reasons listed in table II, leaving data from 578 patients for consideration"

Wajima 1995

Methods	RCT Informed consent of this studies were obtained from the patients and families
Participants	Hospital in Higashine, Japan 41 (randomized) patients with a femoral neck fracture Mean age 80 (range: inclusion criteria ages 70-90 years) Male: 22% Number lost to follow-up: Probably none Operated with a mean delay of 7 and 10 days after the surgery
Interventions	Treatment group: Epidural anaesthesia with continuous infusion of bupivacaine and butorphanol for 72 hours postoperatively (n = 16; 8 between 70 and 80 years of age and 8 > 80 years of age) Control group: General anaesthesia with thiopental, succinylcholine, nitrous oxide and sevoflurane. Postoperative analgesia with diclofenac. (n = 25; 10 between 70 and 80 years of age and 15 > 80 years of age)

Wajima 1995 (Continued)

Outcomes Mental tests (Hasegawa dementia scale scores) at 7 days (a high score means good mental function).
Not retained in the analysis

Notes In Japanese

Length of follow-up: 1 week

The study contains participants with abdominal and hip fracture surgery (41 randomized and 9 not randomized) for a total of 98 participants. Results in tables are provided for 40 participants (19 for neuraxial blockade and 21 for general anaesthesia). These tables contain results for delirium after the surgery. A letter was sent to authors on January 27, 2016 to obtain number of participants with hip surgery who experienced acute confusional state within seven days. We did not receive any reply so far.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"randomly allocated", no details and size of the groups unequal (16 versus 25)
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed epidural mentioned
Other bias	Unclear risk	Patients of the GA group in the 70s had higher preoperative scores while those in the 80s had lower ones

White 1980

Methods RCT

"consent was sought for inclusion in the trial"

Participants Orthopaedic hospital in Cape Town, South Africa
40 of 60 patients in trial with a proximal femoral fracture of less than 8 days

Operated at a mean of 3.5 days from the fracture

Zimmer sliding screw (64%) or Moore prosthesis (36%)
Mean age 79 years (> 60 years [range not stated])
Male: 8%
Number lost to follow-up: 0

White 1980 (Continued)

Interventions	<p>All patients received diazepam 10 mg orally 2 hours before surgery</p> <p>Treatment group 1: Spinal anaesthesia with 0.6-0.8 mL hyperbaric cinchocaine and 'light' general anaesthesia with althesin, fentanyl, nitrous oxide/oxygen. Injection in the lateral decubitus position and maintained lying on the fractured side for 5 minutes (n = 20)</p> <p>Treatment group 2: Psoas nerve block with 30 mL 2% mepivacaine and 'light' general anaesthesia with fentanyl and althesin (n = 20 randomized; n = 16 analysed). Chayen's technique with the fracture side uppermost. This group was not retained (outside the scope of the present review)</p> <p>Control group: General anaesthesia with thiopentone, suxamethonium, nitrous oxide/oxygen, halothane, fentanyl. Competitive neuromuscular blocking drugs were not used. This group (n = 20) was split in two for comparison with the two treatment groups</p>
Outcomes	<p>Mortality at 1 month</p> <p>Length of surgery</p> <p>Pneumonia</p> <p>Acute confusional state</p> <p>Deep vein thrombosis</p> <p>Total medical complications (pneumonia, deep vein thrombosis)</p>
Notes	<p>Length of follow-up: minimum 4 weeks</p> <p>presence/absence of thromboprophylaxis not mentioned</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated", no details
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No failed block mentioned
Other bias	Unclear risk	Groups well balanced except possibly for a lower number of preoperative pneumonia in the Psoas compartment block group

Abbreviations

AMT: Abbreviated mental test; ASA: American Society of Anesthesiologists (ASA) physical status; BIS: bispectral index monitor; b.p.m.: beats per minute; CHF: cardiac heart failure; CPNB: continuous peripheral nerve block; DVT: deep venous thrombosis; EKG: electrocardiogram; GA: general anaesthesia; h: hour; IM: intramuscular; IPPV: intermittent positive pressure ventilation; IV: intravenous; kg: kilogram; L: Lumbar; MAP: mean arterial blood pressure; mg: milligram; MI: myocardial infarction; mL: millilitres; mm HG: millimetre of mercury; MMSE:

mini mental state examination; n: number; PE: pulmonary embolism; PNB:; peripheral nerve block; RCT: randomized controlled trial; SA: spinal anaesthesia; T: Thoracic; ug: microgram

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Adams 1990	Quasi-randomized: allocated according to the day of surgery (even or uneven)
Darling 1994	No outcome of interest
Lattermann 2005	Different population: elective surgery for primary total hip arthroplasty
Messaoudi 2009	No outcome of interest
Ungemach 1987	A randomized trial of 50 hip fracture patients using either enflurane or enflurane and fentanyl. The trial was excluded as it was a comparison of different drugs within one type of anaesthesia (general anaesthesia) and not a comparison of different anaesthetic techniques
Yao 1997	Different intervention. Study on two different speeds of injection of the local anaesthetic for spinal anaesthesia

Characteristics of studies awaiting assessment [ordered by study ID]

[Neuman 2016](#)

Methods	RCT Institutional review board approval obtained Written informed consents obtained Between July 2014 and March 2015
Participants	12 participants aged 18 or older, femoral neck or pertrochanteric hip fracture requiring surgery, and ability to speak English and provide written informed consent. Exclusion criteria were pathological or periprosthetic fracture, concurrent conditions requiring surgery (e.g., multitrauma, acute cholecystitis), Montreal Cognitive Assessment ⁴ score less than 16, delirium at time of screening, known contraindications to spinal anaesthesia or volatile general anaesthetics, and pregnancy.
Interventions	Intervention: spinal anaesthesia with sedation (n = 6) Control: general anaesthesia (n = 6)
Outcomes	<ul style="list-style-type: none"> Primary outcome: New diagnosis of delirium assessed with the Montreal Cognitive Assessment, and a delirium screen using the Confusion Assessment Method during postoperative day 1 through 5 or discharge whichever came first (blinded assessment)
Notes	ClinicalTrials.gov identifier NCT02190903

[Parker 2015](#)

Methods	RCT (sealed opaque envelope) Approval from Research and Development Committee obtained
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Anaesthesia for hip fracture surgery in adults (Review)

Parker 2015 (Continued)

	<p>Written informed consent obtained</p> <p>No external source of funding</p> <p>Between June 2007 and November 2012</p>
Participants	<p>322 participants aged over 49 years of age presenting to one hospital with an acute hip fracture. Patients with dementia were included if their next was willing to allow their relative to participate in the trial. Patients with more than one injury were also included if spinal anaesthesia was suitable.</p> <p>Exclusion criteria: patients who expressed a preference to a particular method of anaesthesia or for whom the surgeon considered one of the anaesthetic technique being more appropriate</p>
Interventions	<p>Intervention: spinal anaesthesia (n = 158 randomised, 13 switched to general anaesthesia and one lost to follow-up at 68 days)</p> <p>Control: general anaesthesia (n = 164 randomised, 6 switched to spinal anaesthesia)</p>
Outcomes	<ul style="list-style-type: none"> • Mortality (unblinded at 30, 90 and 120 days and at one year) • Myocardial infarction • Pneumonia • Thromboembolic complications (pulmonary embolism or deep venous thrombosis) • Cerebrovascular accident • Acute kidney injury • Urine retention • Number of blood units transfused • Intraoperative hypotension • Gastrointestinal bleeding • Pressure sores • Wound infection • Congestive heart failure • Cardiac arrhythmia • Length of hospital stay • Discharge to same residence
Notes	<p>Participants were assessed at 6 weeks and by a telephone interview at one year.</p> <p>ISRCTN36381516</p>

Characteristics of ongoing studies [ordered by study ID]

NCT00590707

Trial name or title	Post-operative delirium in elderly surgical patients (STRIDE)
Methods	RCT; double-blind (subject, caregiver, outcomes assessor); parallel assignment
Participants	65 years of age or older at admission; has surgical treatment of a traumatic hip fracture; has Mini-Mental Status Exam score of 15 or higher; able to read/write/speak/hear/understand English; receives spinal anaesthesia
Interventions	Patients randomly assigned to this arm will receive enough sedative drugs to keep their level of awareness during the hip fracture repair at a BIS score of 50-60. This is the "deeper sedation" arm. versus patients randomly assigned to this arm will receive enough sedative drugs to keep their lev-

NCT00590707 (Continued)

el of awareness during the hip fracture repair at a BIS score of 70-80. This is the "moderate sedation" arm

Outcomes	<p>Primary outcome measures: Presence of delirium (time frame: postoperative days 1-5; 1 month after surgery; and 1 year after surgery). Memory/thinking testing</p> <p>Secondary outcome measures: Change in functional status (time frame: 1 month and 1 year after surgery). Ability to perform Activities of Daily Living; strength and walking testing</p>
Starting date	January 2005
Contact information	Frederick E. Sieber, MD: fsieber1@jhmi.edu and Michael D. Sklar, MA: msklar1@jhmi.edu
Notes	

NCT02213380

Trial name or title	Effect of Anesthesia on Post-operative Delirium in Elderly Patients Undergoing Hip Fracture Surgery (RAGADelirium)
Methods	RCT; open label; parallel assignment
Participants	Older patients (≥ 65 years with hip fracture and planned hip fracture surgery)
Interventions	General anaesthesia versus regional anaesthesia
Outcomes	<p>Primary Outcome Measures: the incidence of postoperative cognitive dysfunction (POD) in 7 days postoperation [Time Frame: in 7 days postoperation POD diagnosed with CAM</p> <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • The type of delirium diagnosed in 7 days postoperation (time frame: 7 days postoperation). The type of delirium diagnosed with the Delirium Rating Scale-Revised-98 (DRS-R-98) • Acute pain score using visual analogue scale (VAS) (time frame: 7days postoperation) • Postoperative morbidity (time frame: up to hospital discharge or mortality postoperation) including chest infection, myocardial infarction, renal failure, gastrointestinal ileus and so on • Length of hospital stay (time frame: on the day of discharge from hospital) • Severity of delirium (time frame: 7 days postoperation). Severity of delirium was diagnosed with the DRS-R-98 • Duration of delirium (time frame: 7 days postoperation) diagnosed with CAM • 30-day mortality (time frame: 30 days after surgery) • 6 months incidence of delirium (time frame: 6 months after discharge) in clinic or at their residence, diagnosed with CAM • 12 months incidence of delirium (time frame: 12 months after discharge) in clinic or at their residence, diagnosed with CAM • 6 months quality of life (time frame: 6 months after discharge) using SF-36 questionnaire • 12 months quality of life (time frame: 12 months after discharge) using SF-36 questionnaire
Starting date	October 2014
Contact information	Contact: Ting LI, M.D.: liting1021@aliyun.com and Contact: Sishi Chen: chenshiwz@163.com
Notes	

NCT02507505

Trial name or title	Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN): protocol for a pragmatic, international multicentre trial Ethics boards approval obtained
Methods	RCT, multicenter
Participants	1600 previously ambulatory participants aged 50 and older with a clinically or radiographically diagnosed intra- or extracapsular hip fracture and planned surgical treatment via hemiarthroplasty, total hip arthroplasty or appropriate fixation procedure Exclusion criteria: planned concurrent surgery not amenable to spinal anaesthesia, contraindications to spinal anaesthesia, known susceptibility to malignant hyperthermia, periprosthetic fracture, prior participation to this trial, prisoner status or not being suitable for randomisation
Interventions	Intervention: spinal anaesthesia Control: general anaesthesia
Outcomes	<ul style="list-style-type: none"> • Composite of death, new inability to walk 10 feet or across room at 60 days (blind assessor) • Delirium (in-hospital) • Major inpatient hospital complication (in-hospital) • Mortality (in-hospital, 60, 180 and 365 days) • Acute postoperative pain (in-hospital) • Patient satisfaction (in-hospital) • Length of hospital stay (in-hospital) • Disease-free survival (60, 180 and 365 days) • Chronic pain (60, 180 and 365 days) • Return to pre-fracture residence (60, 180 and 365 days) • Need for new assistive device for ambulation (60, 180 and 365 days) • Cognitive impairment (60, 180 and 365 days)
Starting date	Recruitment began in February 2016 and will continue until the end of 2019
Contact information	Mark D Neuman
Notes	Expected results late 2020

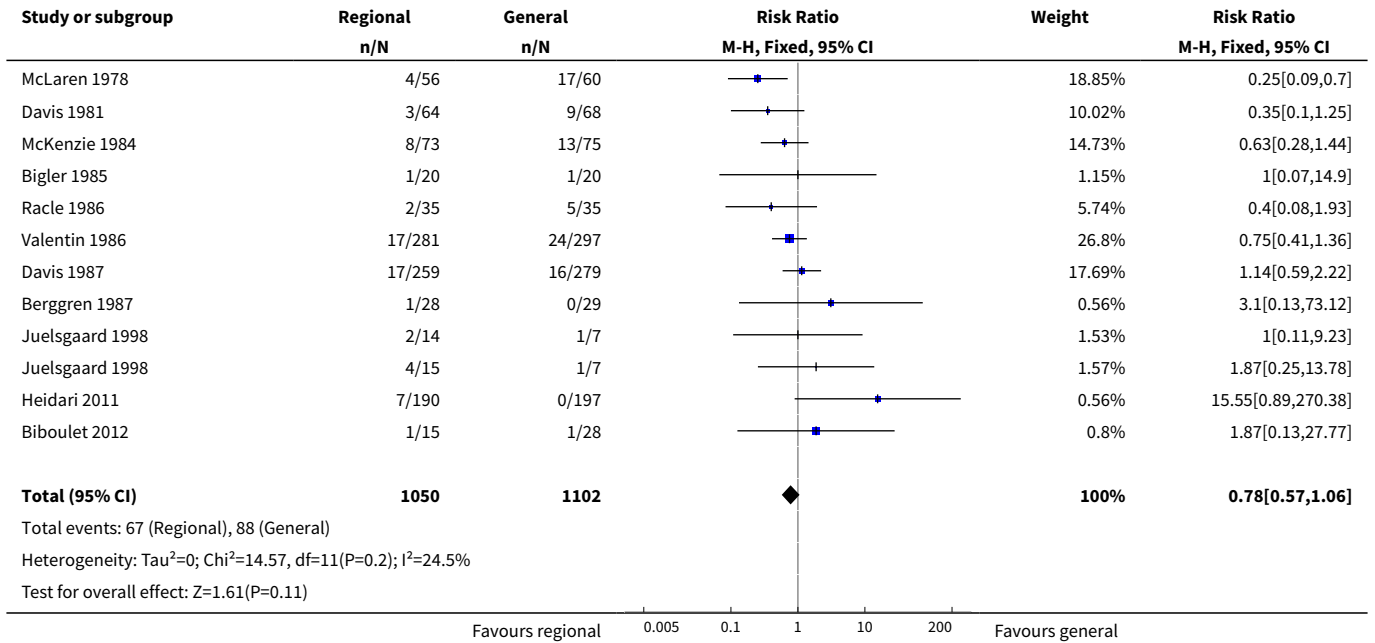
BIS: bispectral index; CAM: Confusion Assessment Method ; mcg/kg: micrograms per kilogram of body weight; mL; millilitres; RCT: randomized controlled trial

DATA AND ANALYSES
Comparison 1. Neuraxial block (spinal or epidural) versus general anaesthesia

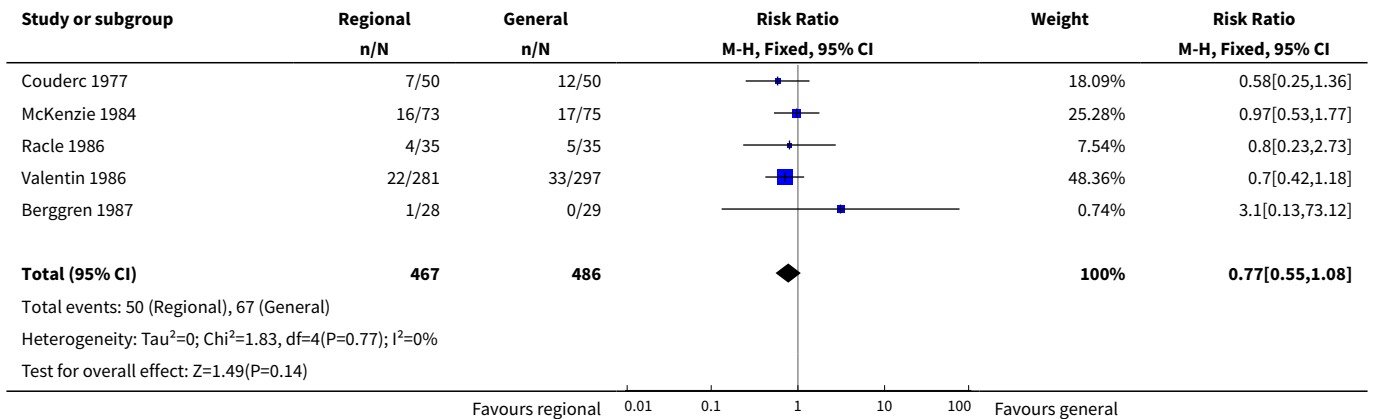
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality - 1 month	11	2152	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.57, 1.06]
2 Mortality - 3 months	5	953	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.55, 1.08]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Mortality - 6 months	2	726	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.73, 1.37]
4 Mortality - 12 months	2	726	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.81, 1.39]
5 Pneumonia	6	761	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.45, 1.31]
6 Myocardial infarction	4	559	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.22, 3.65]
7 Cerebrovascular accident	6	729	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.46, 4.83]
8 Acute confusional state	6	624	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.51, 1.40]
9 Deep vein thrombosis	4	591	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.45, 0.91]
9.1 No prophylaxis or early mobilization only	2	116	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.41, 0.78]
9.2 Low molecular weight heparin	1	88	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.52, 1.84]
9.3 Standard heparin	1	387	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Congestive cardiac failure	6	729	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.31, 1.96]
11 Acute kidney injury	2	202	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.18, 5.83]
12 Pulmonary embolism	5	642	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.51 [1.51, 37.38]
13 Number of patients transfused	3	202	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.49, 1.66]
13.1 Fixation	2	172	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.76, 1.15]
13.2 Arthroplasty	1	30	Risk Ratio (M-H, Random, 95% CI)	0.2 [0.03, 1.51]
14 Length of hospital stay	4	1143	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.05, 0.65]
15 Length of surgery (minutes)	12	973	Mean Difference (IV, Random, 95% CI)	-2.73 [-8.50, 3.04]
16 Operative hypotension	12	1056	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.64, 1.35]
16.1 Unilateral	2	50	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.37, 0.89]
16.2 Bilateral, incremental doses	1	21	Risk Ratio (M-H, Random, 95% CI)	0.2 [0.05, 0.78]
16.3 Bilateral single shot	8	828	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.87, 1.95]
16.4 Epidural	2	157	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.50, 2.07]

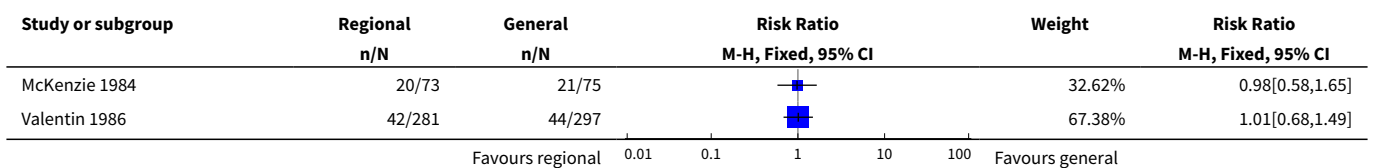
Analysis 1.1. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 1 Mortality - 1 month.

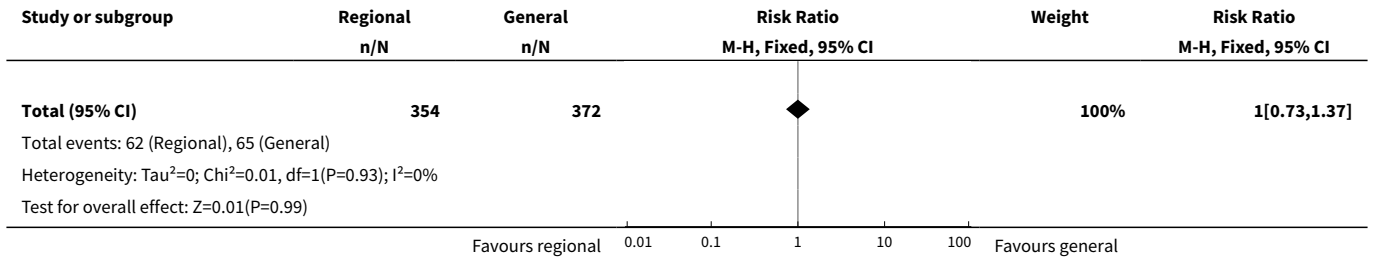


Analysis 1.2. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 2 Mortality - 3 months.

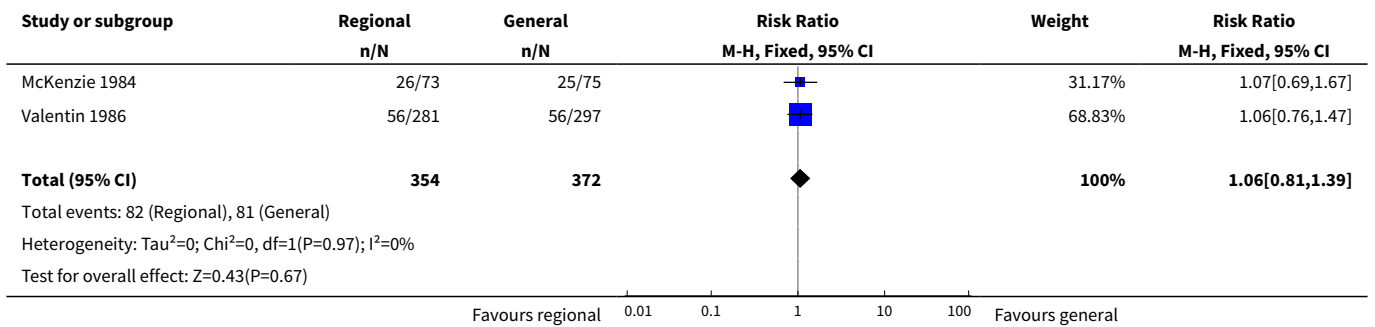


Analysis 1.3. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 3 Mortality - 6 months.

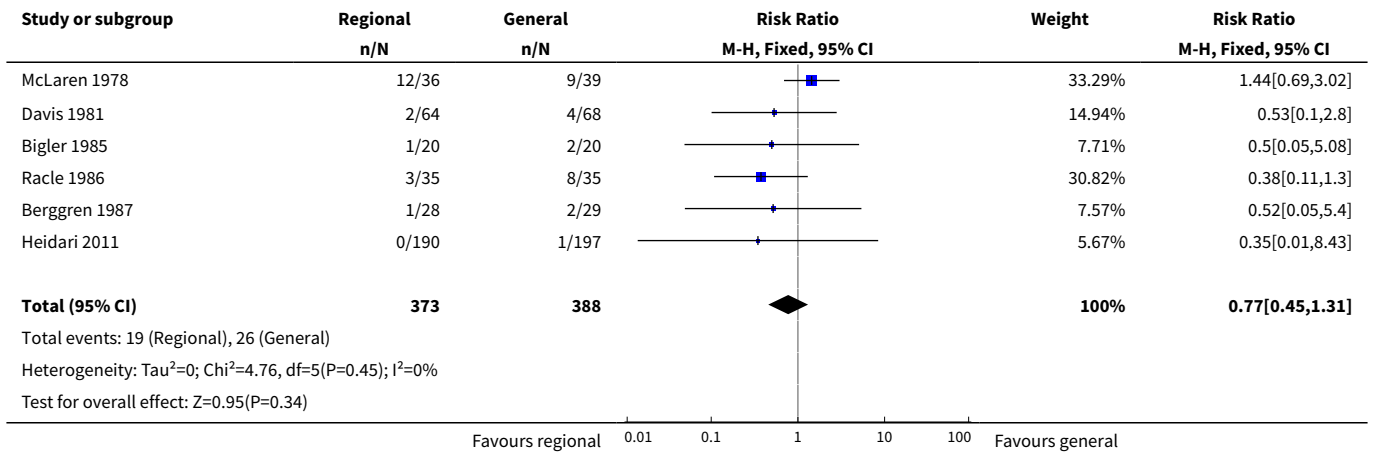




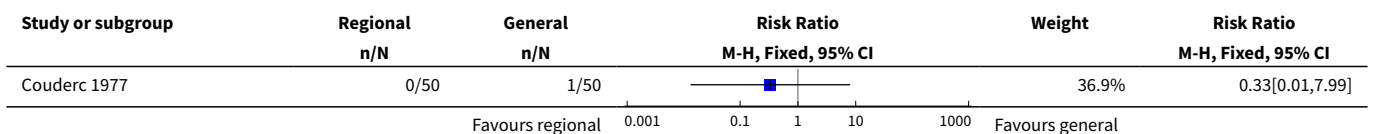
Analysis 1.4. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 4 Mortality - 12 months.

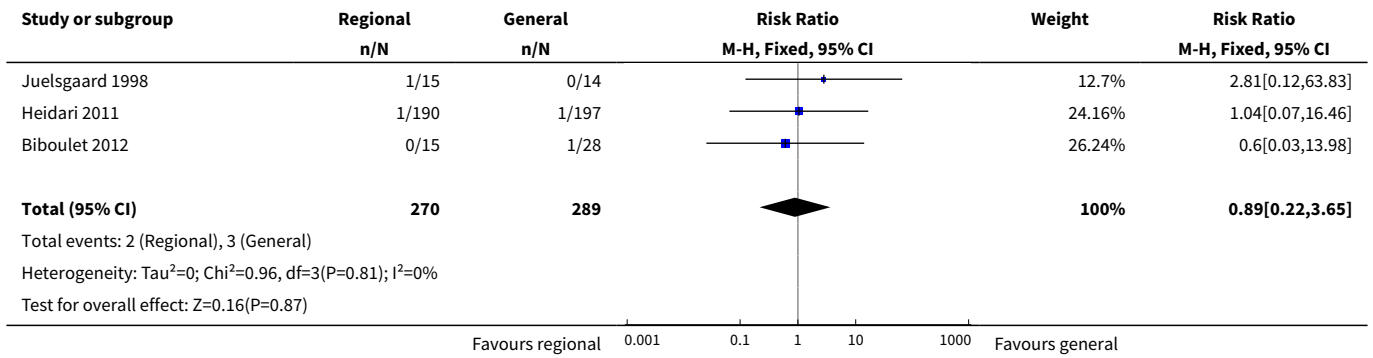


Analysis 1.5. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 5 Pneumonia.

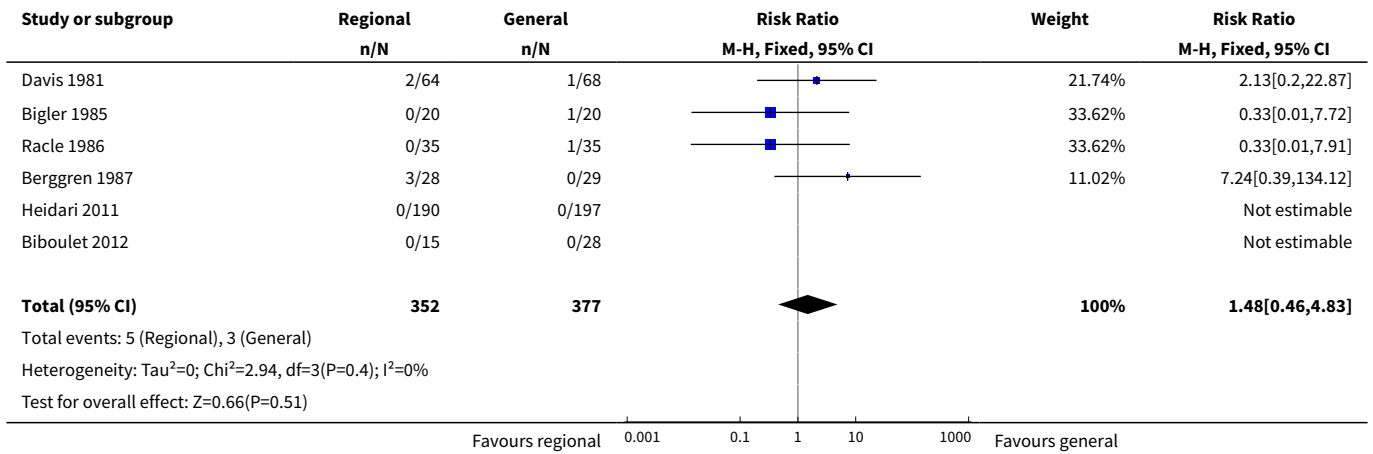


Analysis 1.6. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 6 Myocardial infarction.

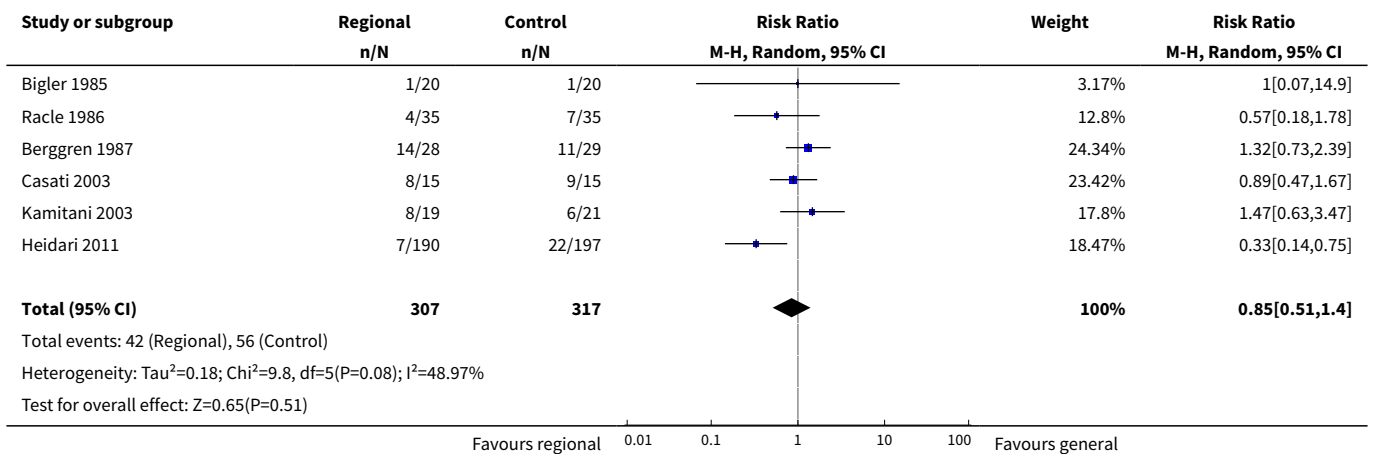




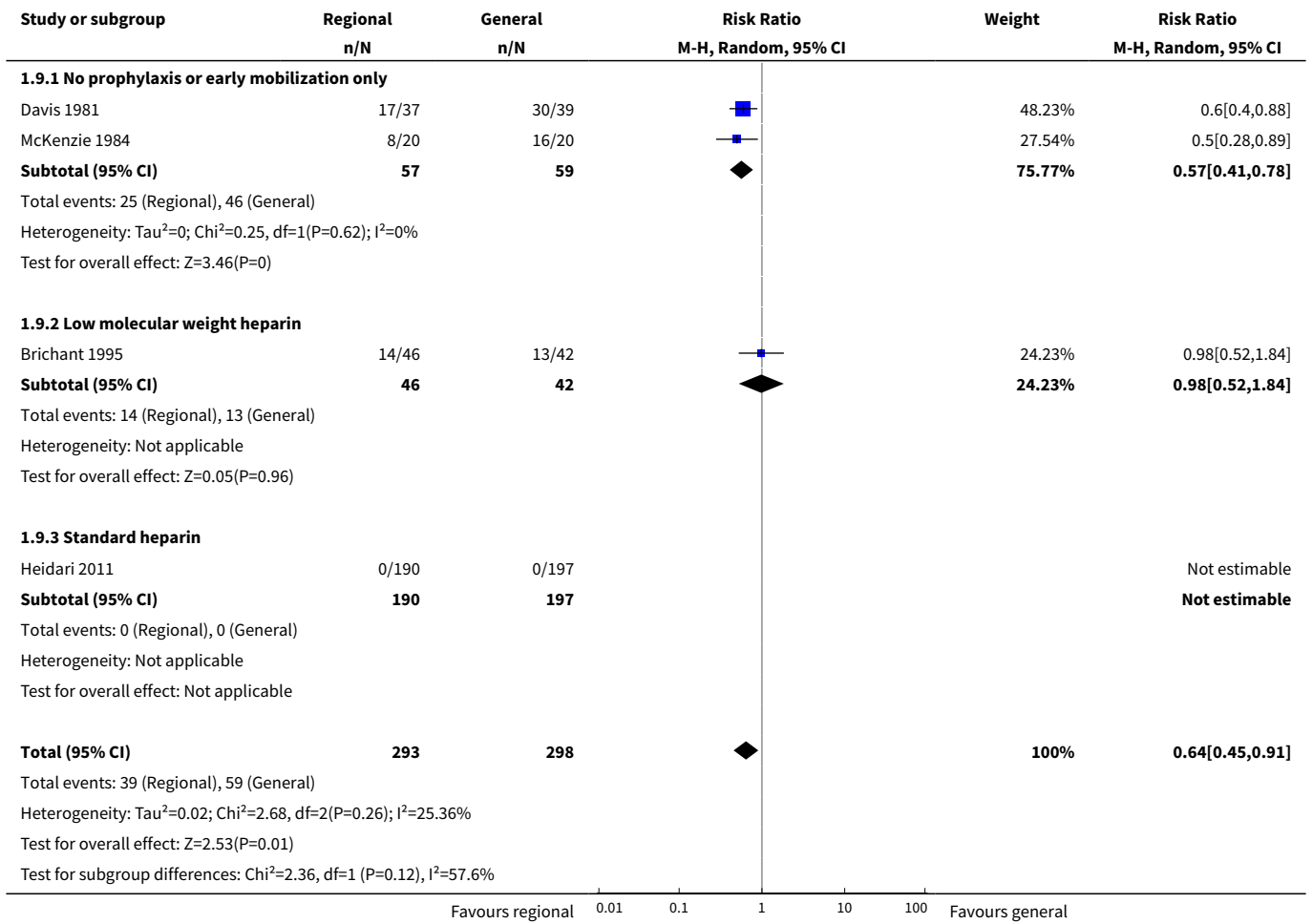
Analysis 1.7. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 7 Cerebrovascular accident.



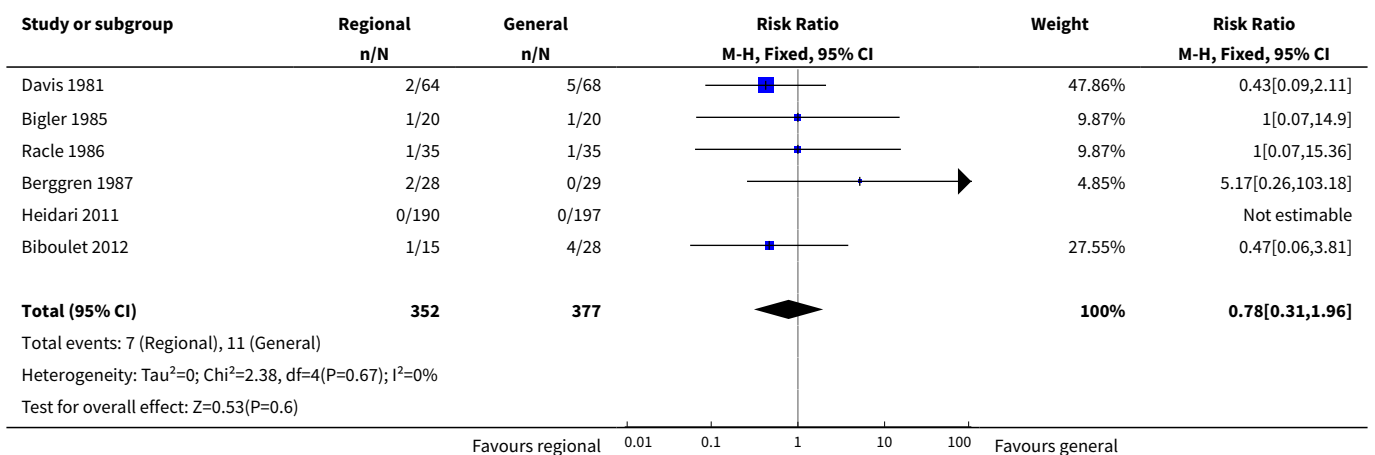
Analysis 1.8. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 8 Acute confusional state.



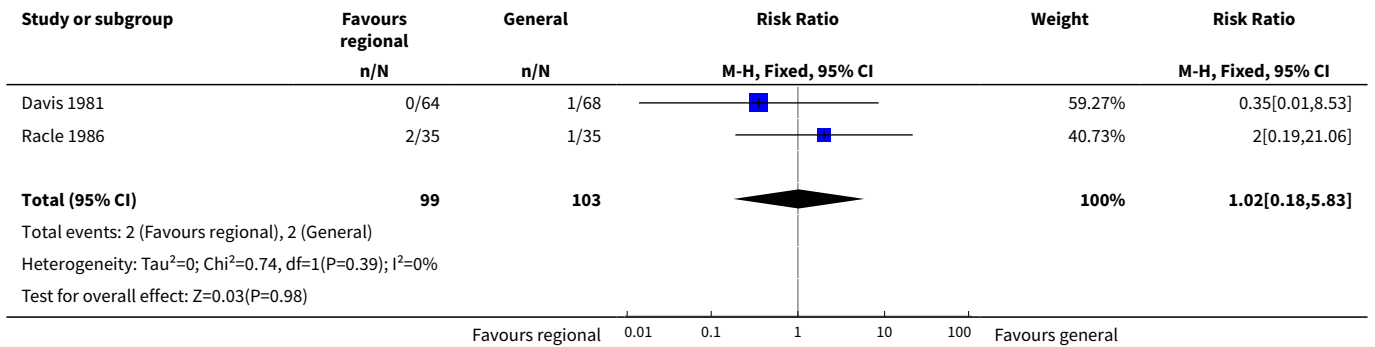
Analysis 1.9. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 9 Deep vein thrombosis.



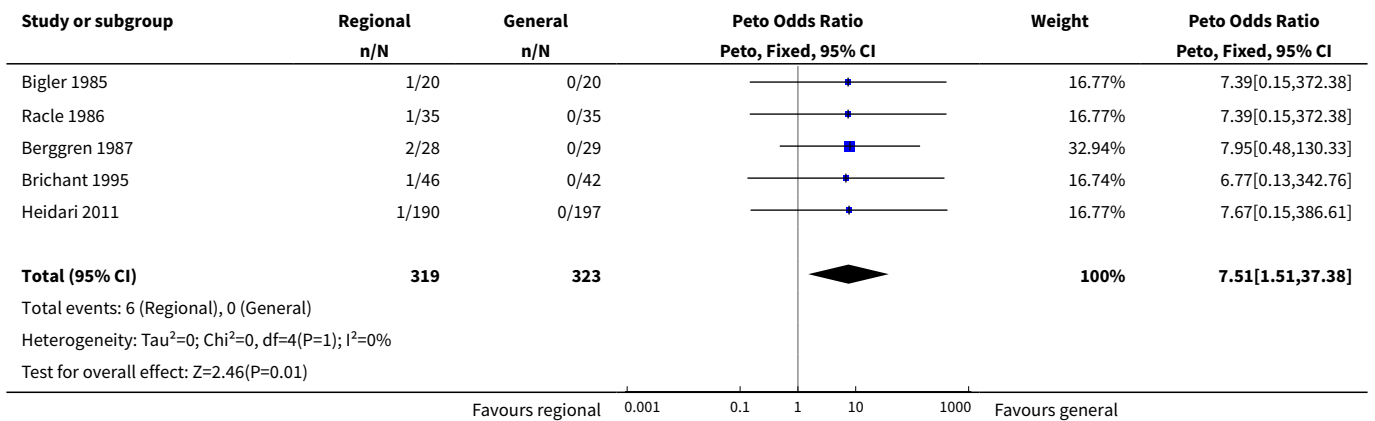
Analysis 1.10. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 10 Congestive cardiac failure.



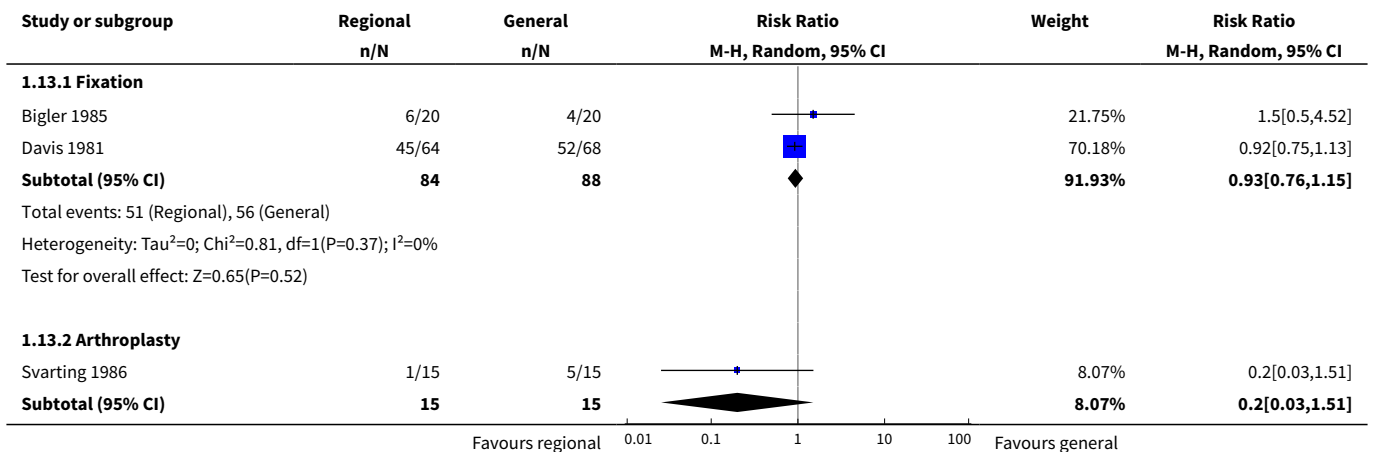
Analysis 1.11. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 11 Acute kidney injury.

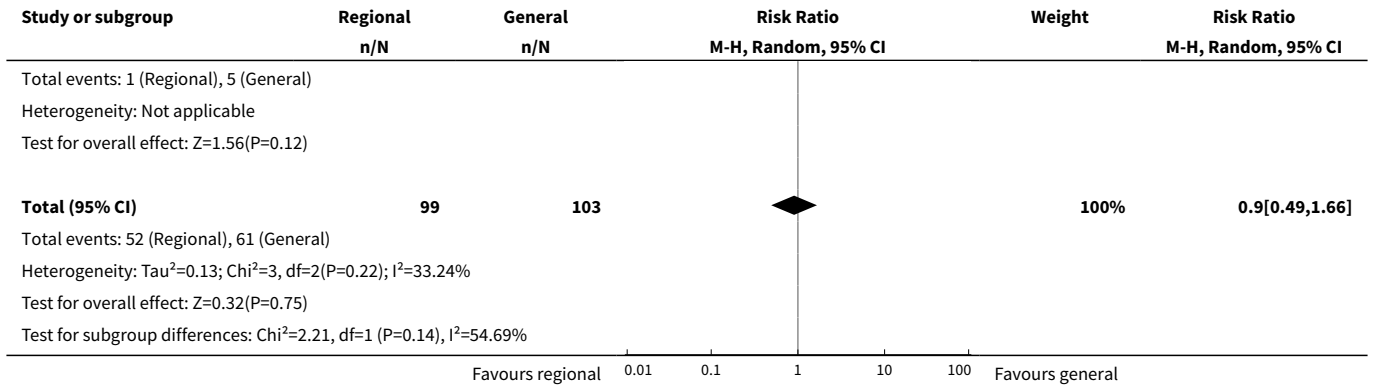


Analysis 1.12. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 12 Pulmonary embolism.

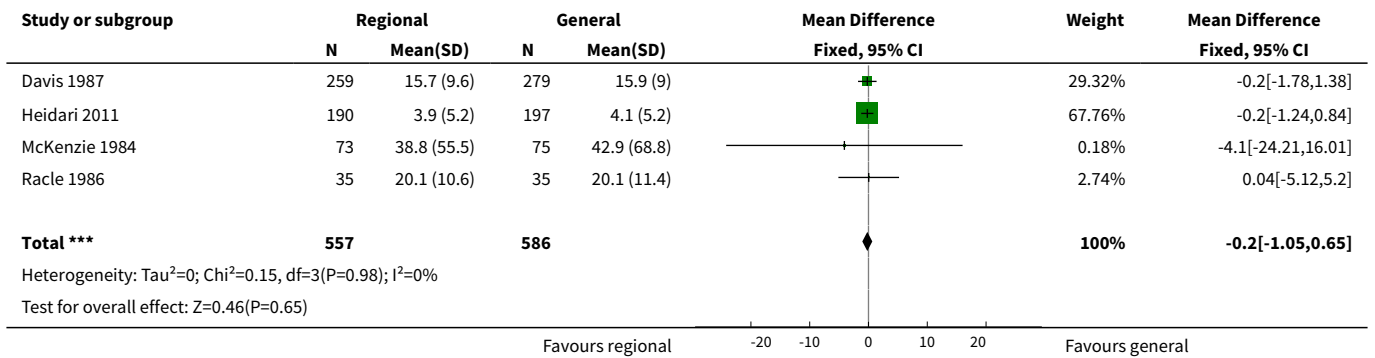


Analysis 1.13. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 13 Number of patients transfused.

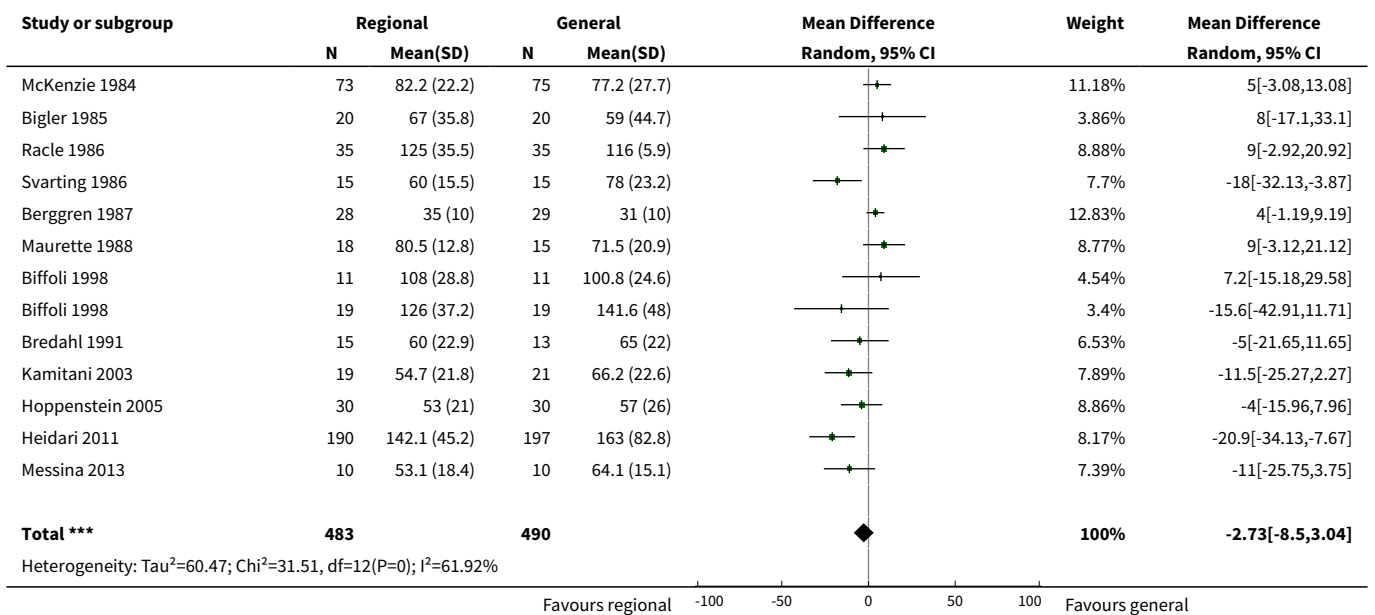


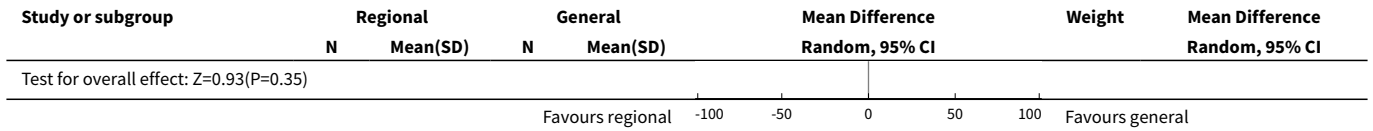


Analysis 1.14. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 14 Length of hospital stay.

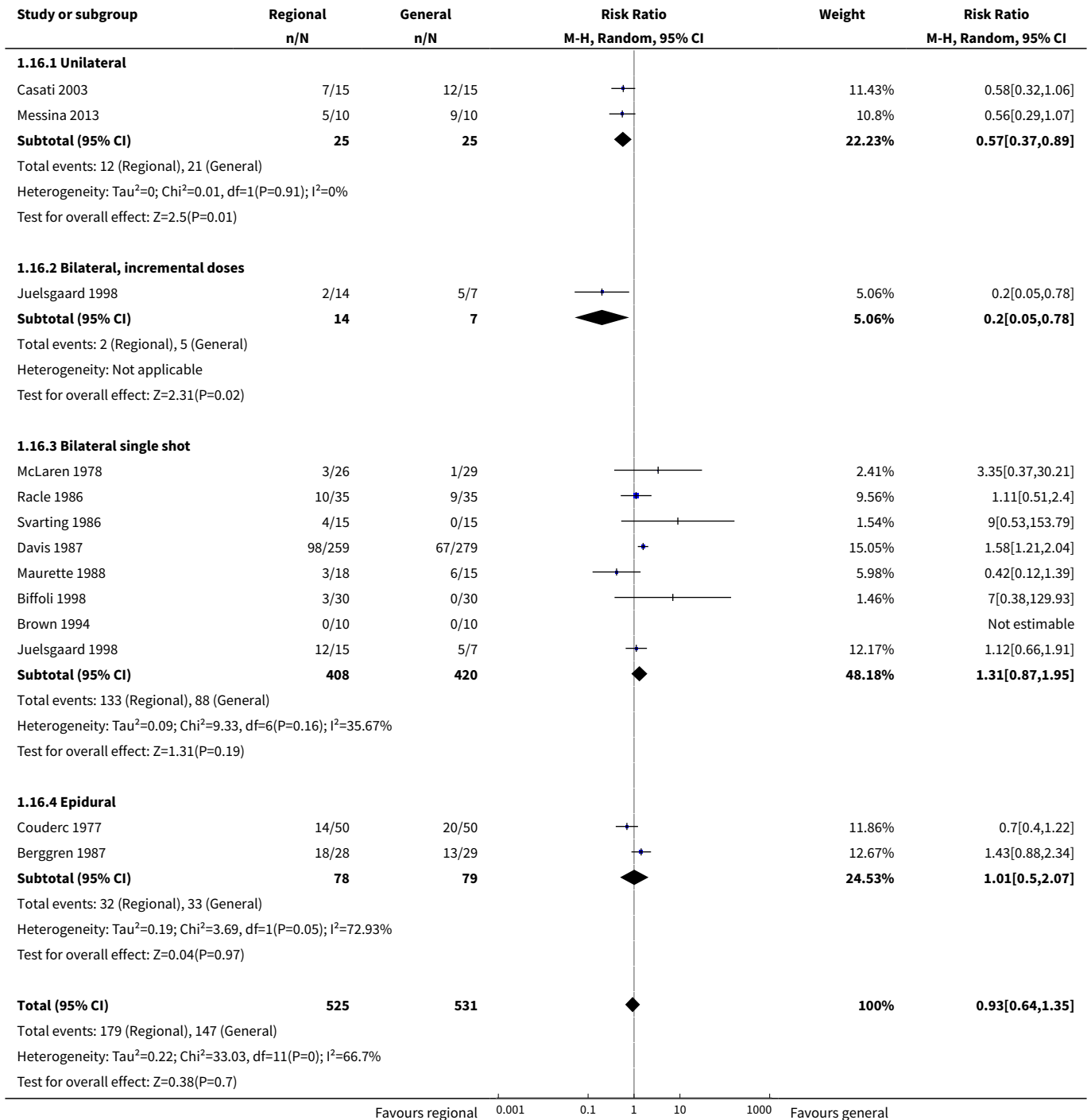


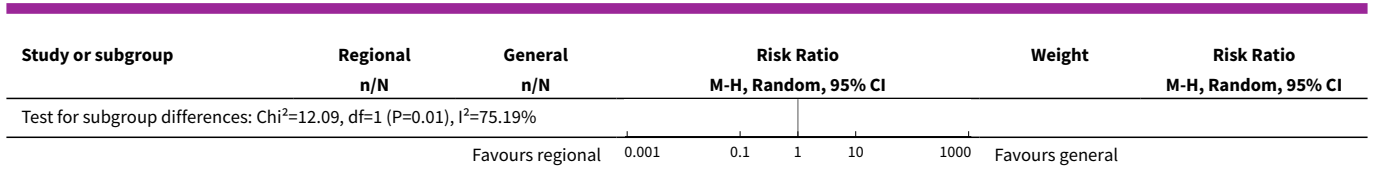
Analysis 1.15. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 15 Length of surgery (minutes).





Analysis 1.16. Comparison 1 Neuraxial block (spinal or epidural) versus general anaesthesia, Outcome 16 Operative hypotension.

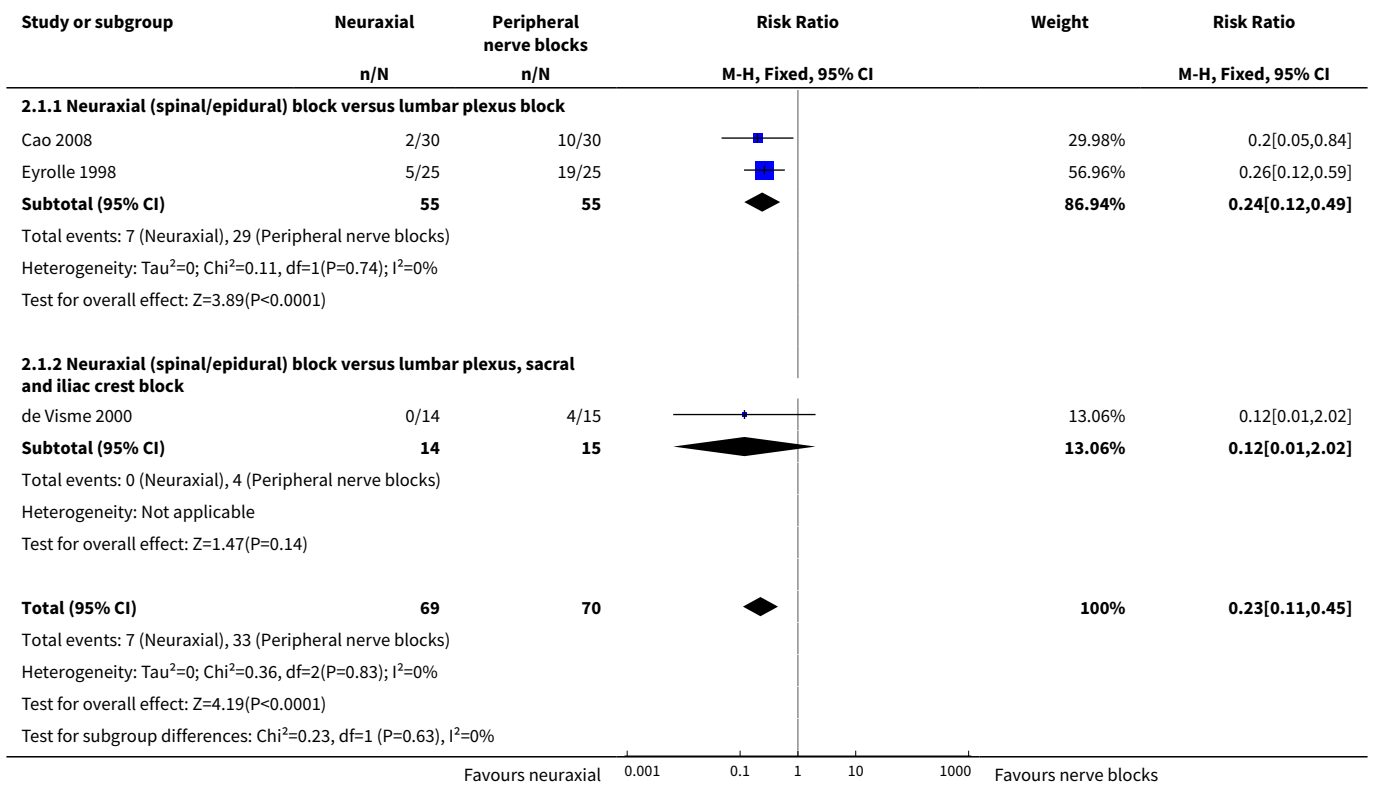




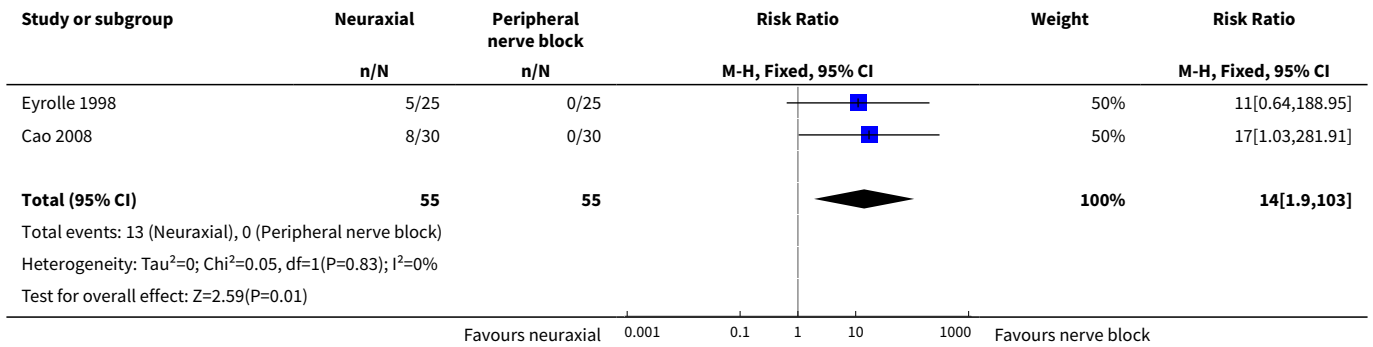
Comparison 2. Regional (spinal or epidural) versus lumbar plexus nerve blocks

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incomplete or unsatisfactory analgesia	3	139	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.11, 0.45]
1.1 Neuraxial (spinal/epidural) block versus lumbar plexus block	2	110	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.12, 0.49]
1.2 Neuraxial (spinal/epidural) block versus lumbar plexus, sacral and iliac crest block	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.01, 2.02]
2 Urine retention	2	110	Risk Ratio (M-H, Fixed, 95% CI)	14.0 [1.90, 103.00]

Analysis 2.1. Comparison 2 Regional (spinal or epidural) versus lumbar plexus nerve blocks, Outcome 1 Incomplete or unsatisfactory analgesia.



Analysis 2.2. Comparison 2 Regional (spinal or epidural) versus lumbar plexus nerve blocks, Outcome 2 Urine retention.



ADDITIONAL TABLES

Table 1. Outcomes: Definitions and time points

Outcome	Study	Definition	Time point
Pneumonia	Berggren 1987	"treated for"	"during the postoperative period"
	Bigler 1985	Unspecified	"postoperatively"
	Davis 1981	Chest X-Ray in clinical suspicion	Up to four weeks
	Heidari 2011	"diagnosed by the consultant specialist"	"postoperative"
	McLaren 1978	"The clinical criteria adopted as indicating respiratory problems were productive cough, the presence of rhonchi or crepitations on auscultation or abnormalities on chest X-ray." However the criteria adopted for the diagnosis of a pneumonia ("respiratory infection") are not clearly mentioned	Up to four weeks
	Racle 1986	"clinical and radiological criteria"	"in hospital"
	White 1980	Unspecified	Within four weeks
Myocardial infarction	Biboulet 2012	EKG and troponin measurement daily for three days, no definition provided	Within one month
	Couderc 1977	Serial preprogrammed EKGs up to postoperative day 10 interpreted by a blinded cardiologist. Q wave	In hospital
	Heidari 2011	"diagnosed by the consultant specialist"	"postoperative"
	Juelsgaard 1998	World Health Organization criteria applied by a blinded investigator	Within one month

Table 1. Outcomes: Definitions and time points (Continued)

Congestive cardiac failure	Berggren 1987	"treated for"	"during the postoperative period"
	Biboulet 2012	"acute heart failure"	Within one month
	Bigler 1985	"cardiac decompensation"	"postoperatively"
	Davis 1981	"life-threatening complications" "congestive heart failure"	Within four weeks
	Heidari 2011	"diagnosed by the consultant specialist"	"postoperative"
Cerebrovascular accident	Racle 1986	"episode of congestive heart failure"	In hospital
	Berggren 1987	"stroke"	All patients developed their stroke on postoperative day one
	Biboulet 2012	"stroke"	Within one month
	Bigler 1985	"Neurological sequelae", apoplexy for the sole event reported	"postoperatively"
	Davis 1981	"cerebrovascular accident"	Within four weeks
Acute confusional state	Heidari 2011	"cerebrovascular accident" "diagnosed by the consultant specialist"	"postoperative"
	Racle 1986	"cerebrovascular accident"	In hospital
	Berggren 1987	Diagnostic and Statistical Manual of Mental Disorders (DSM-III) as criteria for acute confusional state	Within seven days (the period 0-8 hours after the surgery was excluded)
	Bigler 1985	"Mental confusion"	"postoperatively"
	Casati 2003	Mini Mental State Examination test decreased 2 points from baseline	Within seven days
Renal failure (or acute kidney injury)	de Visme 2000	Mini Mental Status Examination lower than 5	Between the third and fifth postoperative day
	Heidari 2011	Cognitive dysfunction based on time, person, and place disorientation	Up to postoperative day two
	Kamitani 2003	Delirium was judged by floor nurse, using the Inoue's confusion assessment method diagnosis algorithm	Up to postoperative day four
	Racle 1986	Confusion with agitation	In hospital
	White 1980	Unspecified	Within four weeks
Renal failure (or acute kidney injury)	Davis 1981	"acute renal failure"	Within four weeks
	Racle 1986	Blood creatinine > 135 micromol/Liter	In hospital

Table 1. Outcomes: Definitions and time points (Continued)

Deep vein thrombosis	Brichant 1995	Systematic bilateral contrast venography	Postoperative day ten
	Davis 1981	125-iodine fibrinogen uptake test performed daily for seven days	Within seven days
	Heidari 2011	"deep veins thrombosis" "diagnosed by the consultant specialist"	"postoperative"
	Ibanez 1993	"thrombosis"	Within seven days
	McKenzie 1984	Systematic venography	Between postoperative day seven and ten
	White 1980	"deep vein thrombosis"	Within four weeks
Pulmonary embolism	Berggren 1987	"pulmonary embolism"	"postoperatively"
	Bigler 1985	"pulmonary embolus"	"postoperatively"
	Brichant 1995	Pulmonary venous angiogram or ventilation-perfusion lung scanning on clinical suspicion	Unclear
	Heidari 2011	"pulmonary emboli" "diagnosed by the consultant specialist"	"postoperatively"
	Racle 1986	Clinical suspicion confirmed with angiography	In hospital
Unsatisfactory surgical results	Spreadbury 1980	Either an unstable fixation of the fracture by nail and plate or the dislocation of a prosthesis, which required bedrest on traction and prevented early mobilization	In hospital
Operative hypotension	Berggren 1987	Decrease > 30% from baseline for systolic arterial blood pressure	Intraoperative
	Biffoli 1998	Decrease of 30% from baseline for arterial blood pressure	Intraoperative
	Brown 1994	Requiring the administration of a sympathomimetic	Intraoperative
	Casati 2003	Decrease in systolic arterial pressure 20% from baseline	Intraoperative
	Couderc 1977	Decrease of 40 mmHG in systolic arterial blood pressure	Intraoperative
	Davis 1987	Decrease in systolic arterial blood pressure > 20% from baseline	Intraoperative
	Eyrolle 1998	Decrease in mean arterial blood pressure > 20% from baseline	Intraoperative
	Juelsgaard 1998	Decrease in systolic arterial blood pressure > 33% from baseline	Intraoperative
	Maurette 1988	Decrease in mean arterial blood pressure > 20% from baseline	Intraoperative

Table 1. Outcomes: Definitions and time points (Continued)

	McLaren 1978	Decrease in systolic arterial blood pressure > 50% from baseline	Intraoperative
	Messina 2013	Decrease in mean arterial blood pressure of 25% from baseline	Intraoperative
	Racle 1986	Decrease in systolic arterial blood pressure of 20% from baseline	Intraoperative
	Svarting 1986	Decrease in systolic arterial blood pressure > 30% from baseline	Intraoperative
Urine retention	Berggren 1987	"urinary retention"	"postoperative"
	Cao 2008	"that required catheterization"	In hospital

EKG: electrocardiogram

Table 2. Anaesthetic agents for sedation or to produce general anaesthesia

Study	Sedative drugs for participants of the regional blockade group	Anaesthetic agents for general anaesthesia
Berggren 1987	Premedication: Meperidine No other sedative drugs mentioned as routinely administered for the surgery.	Premedication: Meperidine Induction: Thiopental and atropine Maintenance: Nitrous oxide, halothane and succinylcholine infusion
Biboulet 2012	None mentioned	Subgroup 1 Induction: Propofol Maintenance: Propofol infusion (for a bispectral index value of 50) and remifentanyl Subgroup 2 Induction: Sevoflurane Maintenance: Sevoflurane (for a bispectral index value of 50) and remifentanyl
Biffoli 1998	None mentioned	Induction: Propofol Maintenance: Nitrous oxide, isoflurane, fentanyl (intermittent injections) plus an atracurium infusion
Bigler 1985	Premedication: Pethidine Small amounts of diazepam if needed	Premedication: Pethidine Induction: Diazepam and atropine Maintenance: Nitrous oxide, fentanyl and pancuronium
Bredahl 1991	Premedication: Pethidine Diazepam for mild sedation	Premedication: Pethidine Induction: Thiopental

Table 2. Anaesthetic agents for sedation or to produce general anaesthesia (Continued)

		Maintainance: Nitrous oxide, thiopental and pethidine
Brichant 1995	Not mentioned	According to local practice
Brown 1994	Premedication: Tamazepam or pethidine No drug supplementation during the surgery	Premedication: Tamazepam or pethidine Induction: Thiopental or propofol Maintainance: Nitrous oxide, isoflurane or enflurane and atracurium 0.5 mg/kg one dose
Cao 2008	Midazolam and fentanyl if required	
Casati 2003	One dose of fentanyl before the block No other sedative drug routinely administered for the surgery.	Induction: Sevoflurane Maintainance: Nitrous oxide, sevoflurane
Couderc 1977	Premedication: Hydroxyzine and atropine None mentioned for the surgery	Premedication: Hydroxyzine and atropine Induction: Thiopental Maintainance: Nitrous oxide plus 1) Thiopental and dextromoramide or 2) methoxyflurane. One dose of pancuronium in some participants
Davis 1981	Ketamine 20-25 mg (for eight participants) before the spinal Ketamine at unspecified total doses during the surgery (two participants) or 25 mg at skin closure (two participants) Diazepam (mean dose 9 mg; range 0-35 mg)	Induction: Diazepam (mean dose 9.5 mg; range 2.5 to 30 mg) Maintainance: Nitrous oxide, fentanyl and pancuronium
Davis 1987	Benzodiazepine (optional)	Induction: Thiopental Maintainance: Nitrous oxide, fentanyl and non-depolarizing neuromuscular blocking agent
de Visme 2000	Alfentanil before the block and as required during the surgery. No mandatory sedative drugs mentioned. One patient in the continuous peripheral nerve block received "sedation repeatedly".	
Eyrolle 1998	Propofol as required	
Heidari 2011	None mentioned	Induction: Thiopental Maintainance: Nitrous oxide, fentanyl, halothane and one dose of pancuronium
Hoppenstein 2005	None mentioned	Induction: Thiopental Maintainance: Nitrous oxide, isoflurane, fentanyl and vecuronium

Table 2. Anaesthetic agents for sedation or to produce general anaesthesia (Continued)

Ibanez 1993	Not reported	Not reported
Juelsgaard 1998	Premedication: Pethidine None mentioned for the surgery	Premedication: Pethidine Induction: Thiopental Maintainance: Nitrous oxide, enflurane, fentanyl and one dose of atracurium
Kamitani 2003	No sedative drug	Induction: Propofol Maintainance: Nitrous oxide, fentanyl, sevoflurane and one dose of vecuronium
Maurette 1988	None mentioned	Induction: Thiopental Maintainance: Nitrous oxide, dextromoramide and enflurane
McKenzie 1984	Small doses of diazepam	Induction: Althesin Maintainance: Nitrous oxide and halothane
McLaren 1978	Althesin and nitrous oxide; arousable by ear lobe pressure	Induction: Althesin Maintainance: Nitrous oxide, fentanyl and pancuronium one dose
Messina 2013	None mentioned	Induction: Propofol Maintainance: Sevoflurane, remifentanil and one dose of cisatracurium
Racle 1986	Premedication: Hydroxyzine and atropine Flunitrazepam, verbal contact possible	Premedication: Hydroxyzine and atropine Induction: Thiopental Maintainance: Nitrous oxide, enflurane, fentanyl and one dose of vecuronium
Spreadbury 1980	No group with regional anaesthesia alone	Ketamine group Induction and maintenance: Ketamine and diazepam (2.5 to 10 mg) Relaxant group Technique at the discretion of the attending anaesthesiologist
Svarting 1986	Premedication: Pethidine and atropine None mentioned for the surgery	Premedication: Pethidine and atropine Induction: Thiopental Maintainance: Nitrous oxide, fentanyl (repeated injections) and one dose of pancuronium
Tasker 1983	Not reported	Not reported
Ungemach 1993	Not reported	Induction: Not reported Maintainance: Nitrous oxide, isoflurane and fentanyl

Table 2. Anaesthetic agents for sedation or to produce general anaesthesia (Continued)

Valentin 1986	Premedication: Pethidine and promethazine in some of the participants	Premedication: Pethidine and promethazine in some of the participants
	Small doses of diazepam and fentanyl	Subgroup 1 Induction: Thiopental or not Maintenance: Nitrous oxide, enflurane and gallamine (not all participants) Subgroup 2 Induction: Not clearly mentioned Maintenance: Nitrous oxide, droperidol, fentanyl and gallamine
Wajima 1995	None mentioned	Induction: Thiopental Maintenance: Nitrous oxide and sevoflurane
White 1980	Premedication: Diazepam	Premedication: Diazepam
	Althesin, nitrous oxide and fentanyl (spontaneous breathing) for the two subgroups	Induction: Thiopental Maintenance: Nitrous oxide, halothane and fentanyl

Table 3. Results for outcomes from single studies

Comparison: Neuraxial block versus general anaesthesia						
Study	Outcome	Number of patients	Type of effect size	Effect size	Lower 95% CI	Upper 95% CI
McKenzie 1984	Patient returned to their own home	130	RR	0.84	0.61	1.16
Berggren 1987	Urine retention	57	RR	0.86	0.30	2.51
Comparison: Neuraxial block added to general anaesthesia compared to general anaesthesia alone						
Study	Outcome	Number of patients	Type of effect size	Effect size	Lower 95% CI	Upper 95% CI
White 1980	Pneumonia	30	RR	0.80	0.20	3.20
White 1980	Acute confusional state	30	RR	1.00	0.16	6.09
White 1980	Deep vein thrombosis	30	RR	0.17	0.01	3.94
White 1980	Length of surgery (minutes)	30	MD	0.00	-17.96	17.96.
Comparison: Neuraxial block versus peripheral nerve block						
Study	Outcome	Number of patients	Type of effect size	Effect size	Lower 95% CI	Upper 95% CI
de Visme 2000	Acute confusional state	29	RR	0.89	0.35	2.28

Table 3. Results for outcomes from single studies (Continued)

Eyrolle 1998	Operative hypotension	50	RR	6.00	2.02	17.83
de Visme 2000	Length of surgery (minutes)	29	MD	17.00	-0.76	34.76
Comparison: Intravenous ketamine alone (without neuromuscular blocking agent) versus general anaesthesia						
Study	Outcome	Number of patients	Type of effect size	Effect size	Lower 95% CI	Upper 95% CI
Spreadbury 1980	Unsatisfactory surgical results defined as unstable fixation or prosthesis dislocation	60	RR	2.33	0.67	8.18
Spreadbury 1980	Mortality	60	RR	1.00	0.46	2.17
Spreadbury 1980	Patient returned home	60	RR	0.95	0.66	1.38
Spreadbury 1980	Length of hospital stay	39*	MD	12.00	5.63	18.37

CI: confidence interval; MD: mean difference; RR: risk ratio

*: Mean duration of admission refers only to those patients who were discharged home

APPENDICES

Appendix 1. CENTRAL (Cochrane Library) search strategy

#1 MeSH descriptor: [Hip Fractures] explode all trees

#2 ((hip* or fem?r* or trochant* or pertrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) and fracture*)

#3 #1 or #2

#4 MeSH descriptor: [Anesthesia] explode all trees

#5 (an?est* near (regional* or local* or general or spinal or epidural or intravenous)) or (endotracheal or laryngeal mask* or ((nerv or neuraxial) near block*)):ti,ab

#6 #4 or #5

#7 #3 and #6

Appendix 2. MEDLINE (Ovid SP) search strategy

1. exp Hip Fractures/ or ((hip* or fem?r* or trochant* or pertrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj5 fracture*).mp.

2. exp Anesthesia/ or (an?est* adj4 (regional* or local* or general or spinal or epidural or intravenous)).mp. or (endotracheal or laryngeal mask* or ((nerv or neuraxial) adj3 block*)):ti,ab.

3. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.

4. 1 and 2 and 3

Appendix 3. EMBASE (Ovid SP) search strategy

1. exp hip fracture/ or ((hip* or fem?r* or trochant* or pertrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj5 fracture*).mp.

2. exp anesthesia/ or (an?est* adj4 (regional* or local* or general or spinal or epidural or intravenous)).mp. or (endotracheal or laryngeal mask* or ((nerv or neuraxial) adj3 block*)):ti,ab.

3. (randomized-controlled-trial/ or randomization/ or controlled-study/ or multicenter-study/ or phase-3-clinical-trial/ or phase-4-clinical-trial/ or double-blind-procedure/ or single-blind-procedure/ or (random* or cross?over* or multicenter* or factorial* or placebo* or volunteer*).mp. or ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)):ti,ab. or (latin adj square).mp.) not (animals not (humans and animals)).sh

4. 1 and 2 and 3

Appendix 4. Modified strategy used when the search was reran in February 2017

Central

#1 MeSH descriptor: [Hip Fractures] explode all trees 1287
 #2 ((hip* or fem?r* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) and fracture*) 5605
 #3 #1 or #2 5605
 #4 MeSH descriptor: [Anesthesia] explode all trees 17293
 #5 (an*est* near (regional* or local* or general or spinal or epidural or intravenous)) or (endotracheal or laryngeal mask* or ((nerv* or neuraxial) near block*)):ti,ab 45561
 #6 #4 or #5 48386
 #7 #3 and #6 452
 #8 #7 Publication Year from 2014 to 2017, in Trials 55

Medline

1 Hip Fractures/ or ((hip* or fem?r* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj5 fracture*).mp. (47583)
 2 exp Anesthesia/ or (an?est* adj4 (regional* or local* or general or spinal or epidural or intravenous)).mp. or (endotracheal or laryngeal mask* or ((nerv* or neuraxial) adj3 block*)):ti,ab. (269134)
 3 ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh. (3450527)
 4 1 and 2 and 3 (321)
 5 limit 4 to yr="2014 -Current" (94)

Embase

1 exp hip fracture/ or ((hip* or fem?r* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj5 fracture*).mp. (67218)
 2 exp anesthesia/ or (an?est* adj4 (regional* or local* or general or spinal or epidural or intravenous)).mp. or (endotracheal or laryngeal mask* or ((nerv* or neuraxial) adj3 block*)):ti,ab. (392401)
 3 (randomized-controlled-trial/ or randomization/ or controlled-study/ or multicenter-study/ or phase-3-clinical-trial/ or phase-4-clinical-trial/ or double-blind-procedure/ or single-blind-procedure/ or (random* or cross?over* or multicenter* or factorial* or placebo* or volunteer*).mp. or ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)):ti,ab. or (latin adj square).mp.) not (animals not (humans and animals)).sh. (6637043)
 4 1 and 2 and 3 (657)
 5 limit 4 to yr="2014 -Current" (233)

WHAT'S NEW

Date	Event	Description
15 February 2017	Amended	We reran the search to February 2017.

HISTORY

Protocol first published: Issue 4, 1997

Review first published: Issue 4, 1999

Date	Event	Description
26 January 2016	New search has been performed	We reran the search to March 2014
26 January 2016	New citation required and conclusions have changed	Compared to the previous version (Parker 2004), we withdraw one study (Adams 1990 ; quasi-randomized trial) and added five new studies (Biboulet 2012 ; Cao 2008 ; Heidari 2011 ; Hoppenstein 2005 ; Messina 2013).

Date	Event	Description
		<p>Compared to general anaesthesia, using a neuraxial block for the surgery decreases the rate of thrombosis only if a prophylaxis with low molecular weight heparin is not used. We did not find a difference for mortality, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state or chances of returning home after the surgery.</p> <p>Change in authors: Helen HG Handoll and Richard Griffiths left the review. Joanne Guay, Pushpaj R Gajendragadkar and Sandra Kopp joined the review for this update.</p>
23 January 2014	Amended	This review has been transferred from the Bone, Joint and Muscle Trauma Group to the Cochrane Anaesthesia Group.
4 September 2008	Amended	Converted to new review format.
11 June 2004	New citation required and conclusions have changed	<p>For the third update, first appearing in Issue 4, 2004, the trial search was updated to February 2004. The following changes were made.</p> <p>(1) Five studies comparing spinal versus general anaesthesia were newly included (Biffoli 1998; Casati 2003; Kamitani 2003; Svarting 1986; Wajima 1995).</p> <p>(2) Additional data were obtained for McLaren 1978 resulting in the number of patients being increased from 55 to 116 for some of the outcomes.</p> <p>(3) Seven studies were newly excluded and two added to 'Studies awaiting assessment'.</p> <p>(4) Format changes to conform to the revised Cochrane Style Guide.</p> <p>(5) There were substantive changes to the conclusions of the review, reflecting new findings on postoperative acute confusional state and in response to editorial comments.</p>

CONTRIBUTIONS OF AUTHORS

Conceiving this update: Martyn Parker (MP), Joanne Guay (JG)

Co-ordinating the review: JG, MP

Screening search results: JG and PRG

Organizing retrieval of papers: JG

Screening retrieved papers against inclusion criteria: JG and Sandra Kopp (SK)

Appraising quality of papers: JG and SK

Abstracting data from papers: JG and SK

Writing to authors of papers for additional information: JG

Data management for the review: JG

Entering data into Review Manager (RevMan 5.3): JG

RevMan statistical data: JG

Other statistical analysis not using RevMan: JG

Interpretation of data: JG, MP, PRG and SK

Anaesthesia for hip fracture surgery in adults (Review)

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Statistical inferences: JG

Writing the review: JG, MP, PRG and SK

Securing funding for the review: Departmental resources only

Performing previous work that was the foundation of the present study: JG and MP

Guarantor for the review (one author): JG

Person responsible for reading and checking review before submission: JG, MP, PRG and SK

DECLARATIONS OF INTEREST

Joanne Guay: I am the editor of a multi authors textbook on anaesthesia (including notions on general and regional anaesthesia).

Martyn J Parker has received expenses and honorarium from a number of commercial companies and organizations 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. This implant and fracture type is not considered in this review and none of these payments related directly to this review. He is the author of one ongoing trial (ISRCTN36381516).

Pushpaj R Gajendragadkar: none known.

Sandra Kopp: none known.

SOURCES OF SUPPORT

Internal sources

- University of Teesside, Middlesbrough, UK.
- Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following changes to the published protocol ([Parker 1997](#))

Change in title: The first review ([Urwin 2000](#)), and update ([Parker 2001](#)), were published under the title: "General versus spinal/epidural anaesthesia for surgery for hip fractures in adults". The title was changed in the second update to reflect an expansion in the scope of the review to include comparisons of all forms of anaesthesia ([Parker 2004](#)).

Changes made in 2016 updated version

Background was updated

Objectives were reformulated from:

The following null hypotheses were tested within the trials included so far in this review:

- (1) There is no difference in outcome between regional anaesthesia (spinal or epidural) and general anaesthesia.
- (2) There is no difference in outcome between regional anaesthesia (spinal or epidural) supplemented with a 'light' general anaesthetic and general anaesthesia alone.
- (3) There is no difference in outcome between regional anaesthesia (spinal or epidural) and regional nerve blocks alone.
- (4) There is no difference in outcome between anaesthesia using ketamine (with or without a benzodiazepine) and inhalation general anaesthesia.

To:

The main focus of this review is the comparison of regional versus general anaesthesia for hip fracture repair. More precisely we tried to determine whether there are any major advantages in using regional anaesthesia compared to general anaesthesia for hip fracture repairs. The scope of this review, originally published in 2000 ([Urwin 2000](#)), was expanded in the second update to also cover other methods of anaesthesia ([Parker 2001](#)). We did not consider supplementary regional blocks in this review as they have been studied in another review ([Parker 2002](#)).

Study selection was changed from:

Anaesthesia for hip fracture surgery in adults (Review)

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Types of interventions

- (1) Regional anaesthesia (if necessary supplemented by sedatives) achieved by injection of local anaesthetic into the epidural or subarachnoid spaces. This type of anaesthesia is also referred to as 'spinal' or 'epidural'
- (2) General anaesthesia using intravenous or inhalation agents to render the patient unconscious. Unless otherwise stated, general anaesthesia refers to general anaesthesia using inhalation agents in this review.
- (3) Intravenous ketamine.
- (4) Local nerve blocks (if necessary supplemented by sedatives) when used as the primary method of anaesthesia.

Trials testing other methods of anaesthesia as the primary method of anaesthesia were considered for inclusion. Trials comparing the use of local nerve blocks in conjunction with general anaesthesia and the use of nerve blocks preoperatively, are evaluated in another Cochrane review (Parker 2001). Also not considered in this review were trials comparing different types of drugs or techniques of individual methods of anaesthesia.

To:

Types of interventions

We included studies that compared any combination of the following interventions:

1. Neuraxial blocks: epidural (single shots or continuous), spinals (single shots or continuous), or combined spinal/epidural (single shots or continuous) with or without intravenous sedation;
2. Peripheral nerve blocks: posterior lumbar (psoas) plexus blocks with or without sacral plexus blocks or any other peripheral nerve blocks with or without sedation;
3. General anaesthesia based on inhalational agents (with or without opioids and/or neuromuscular blocking agents), or on total intravenous anaesthesia (ketamine-based technique or other). Any technique where an endotracheal tube or a laryngeal mask airway was used was considered as general anaesthesia.

Outcomes: the number was reduced.

Method: methods were brought up to date.

NOTES

January 2014: This review has been transferred from the Bone, Joint and Muscle Trauma Group to the Cochrane Anaesthesia Group.

INDEX TERMS

Medical Subject Headings (MeSH)

*Anesthesia, Conduction [adverse effects] [mortality]; *Anesthesia, General [adverse effects] [mortality]; *Postoperative Complications [mortality]; Hip Fractures [*surgery]; Length of Stay; Nerve Block [adverse effects] [methods]; Randomized Controlled Trials as Topic

MeSH check words

Aged; Female; Humans; Male