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Comparative Effectiveness Review
Number 30

Pain Management Interventions for Hip Fracture

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Number 30

Pain Management Interventions for Hip Fracture

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting Comparative Effectiveness Reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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Pain Management Interventions for Hip Fracture

Structured Abstract

Objectives. To review and synthesize the evidence on pain management interventions in nonpathological hip fracture patients following low-energy trauma. Outcomes include pain management (short and long term), mortality, functional status, pain medication use, mental status, health-related quality of life, quality of sleep, ability to participate in rehabilitation, return to pre-fracture living arrangements, health services utilization, and adverse effects.

Data Sources. Comprehensive literature searches were conducted in 25 electronic databases from 1990 to present. Searches of the grey literature, trial registries, and reference lists of previous systematic reviews and included studies were conducted to identify additional studies.

Methods. Study selection, quality assessment, data extraction, and grading of the evidence were conducted independently and in duplicate. Discrepancies were resolved by consensus or third-party adjudication. Meta-analyses were conducted where data were available and deemed appropriate.

Results. In total, 83 studies were included (69 trials, 14 cohort studies). Most participants were females older than 75 with no cognitive impairment. The methodological quality of cohort studies was generally moderate; most trials were at high or unclear risk of bias. Included studies were grouped into eight intervention categories: systemic analgesia, anesthesia, complementary and alternative medicine, multimodal pain management, nerve blocks, neurostimulation, rehabilitation, and traction.

Most studies examined peri- and postoperative pain management, albeit from few perspectives such as reported pain, mortality, and adverse effects. Long-term pain was not reported, and other outcomes were reported infrequently. Nerve blockade was effective for relief of acute pain; however, most studies were limited to either assessing acute pain or use of additional analgesia and did not report on how nerve blockades may affect rehabilitation such as ambulation or mobility if the blockade has both sensory and motor effects. Acupressure, relaxation therapy, and transcutaneous electrical neurostimulation may be associated with potentially clinically meaningful reductions in pain, but further evidence is warranted before any firm conclusions are reached. While the strength of evidence is insufficient to make firm conclusions, postoperative physical therapy may improve pain control, andintravenous parecoxib, a systemic analgesic not available in North America, may be a possible alternative to traditional intramuscular injections of opiates and older nonsteroidal anti-inflammatory drugs (NSAIDs). Preoperative traction and spinal anesthesia (with or without additional agents) did not consistently reduce pain or complications in any demonstrable way compared with standard care. Although most studies reported on adverse effects, they were short term and not adequately powered to identify significant differences.

None of the included studies exclusively examined participants from institutional settings or with cognitive impairment, which reduces the generalizability of results to the overall hip fracture patient population.

Conclusion. For most interventions in this review there were sparse data available, which precludes firm conclusions for any single approach or for the optimal overall pain management following hip fracture.

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Executive Summary

Introduction

Hip fractures are a source of significant morbidity and mortality. Incidence increases substantially with age, rising for men and women, respectively, from 22.5 and 23.9 per 100,000 populations at age 50, to 630.2 and 1,289.3 per 100,000 populations by age 80. Short-term mortality rates are high and range from 25 percent for women to 37 percent for men in the first year following a hip fracture. Furthermore, a large proportion of those patients who survive never recover to their prefracture level of function, and approximately 25 to 50 percent of elderly patients with hip fractures have not returned home by 1 year postfracture. Up to 25 percent of hip fractures occur in continuing care facilities (i.e., long-term residential care for dependent people).

Pain following hip fracture has been associated with delirium, depression, sleep disturbance, and decreased response to interventions for other disease states. Therefore, it is important to treat and manage complaints of pain adequately during acute treatment for hip fracture. Furthermore, poorly managed postoperative pain is associated with delayed ambulation, pulmonary complications, and delayed transition to lower levels of care. The patient's self-report of pain is the gold standard for evaluating its character and intensity. However, those with dementia or acute delirium may have difficulty reporting pain levels. The potential for underreporting of pain has direct ramifications for the hip fracture population, as many patients are frail older people with postoperative confusion and an impaired ability to communicate.

Key Questions

Key Question (KQ) 1. In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions for controlling acute (up to 30 days postfracture) and chronic pain (up to 1 year postfracture) compared with usual care or other interventions in all settings?

KQ 2. In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions on other outcomes up to 1 year postfracture compared with usual care or other interventions in all settings? Other outcomes include:

a. Mortality (30-day and up to 1 year postfracture)
b. Functional status
c. Pain medication use; change in type and quantity
d. Mental status
e. Health-related quality of life
f. Quality of sleep in the hospital
g. Ability to participate in rehabilitation
h. Return to prefracture living arrangements
i. Health services utilization

KQ 3. In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the nature and frequency of adverse effects that are directly or indirectly associated with

pharmacologic and nonpharmacologic pain management interventions up to 1 year postfracture compared with usual care or other interventions in all settings?

KQ 4. In older adults (≥50 years) admitted to the hospital following acute hip fracture, how do the effectiveness and safety of pharmacologic and nonpharmacologic pain management interventions vary in differing subpopulations following acute hip fracture up to 1 year after fracture compared with usual care or other interventions in all settings?

Methods

Literature Search

The following bibliographic databases were searched systematically for studies published from 1990 to 2010: AMED (Allied and Complementary Medicine); Global Health; International Pharmaceutical Abstracts; BIOSIS Previews; CINAHL (Cumulative Index to Nursing & Allied Health Literature); Academic Search Elite; Health Source: Nursing and Academic Edition; Cochrane Complementary and Alternative Medicine and Pain Database; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; EBM Reviews – Cochrane Central Register of Controlled Trials; Embase; Global Health Library; MEDLINE; Pascal; PeDRO (The Physical Therapy Evidence Database); ProQuest Dissertations and Theses–Full Text; Scopus; Web of Science; and TOXLINE. Hand searches were conducted to identify literature from proceedings from the following scientific meetings: American Geriatric Society, American Physical Therapy Association, American Society of Regional Anesthesia and Pain Medicine, European Society of Regional Anesthesia, European Society of Anesthesiology, and International Anesthesia Research Society. Ongoing studies were identified by searching clinical trials registers in addition to contacting experts in the field. Reference lists of relevant reviews were searched to identify additional studies. No language restrictions were applied.

Study Selection

Two reviewers independently screened titles and abstracts using general inclusion criteria. The full-text publication of all articles identified as “include” or “unclear” were retrieved for formal review. Each full-text article was independently assessed by two reviewers using detailed a priori inclusion criteria and a standardized form. Disagreements were resolved by consensus or by third-party adjudication. Randomized controlled trials (RCTs), nonrandomized controlled trials (nRCTs), cohort studies (prospective or retrospective), and case-control studies were included if they were published in 1990 or later, focused on older adults (≥ 50 years) who were admitted to the hospital with acute hip fracture due to low-energy trauma, and examined any pharmacological or nonpharmacological pain management therapy, regardless of mode of administration or time point during the care pathway.

Quality Assessment and Rating the Body of Evidence

Two reviewers independently assessed the methodological quality of included studies, with disagreements resolved through discussion or third-party adjudication, as needed. The Cochrane Collaboration’s Risk of Bias tool was used to assess RCTs and nRCTs. Observational analytic studies were assessed using the cohort and case-control Newcastle Ottawa Scales. In addition, the source of funding was recorded for all studies.

The body of evidence was rated by two reviewers using the Agency for Healthcare Research and Quality GRADE approach (Grading of Recommendations, Assessment, Development, and Evaluation). The strength of evidence was assessed for outcomes identified by the clinical investigators to be most clinically important: acute pain (up to 30 days), chronic pain (up to 1 year), mortality (30-day), and the incidence of serious adverse effects (e.g., delirium, myocardial infarction, renal failure, stroke). The following four major domains were assessed: risk of bias (low, medium, high), consistency (no inconsistency, inconsistency present, unknown, or not applicable), directness (direct, indirect), and precision (precise, imprecise).

Data Extraction

Data were independently double-extracted by two reviewers using a standardized form; discrepancies were resolved by consensus or third-party adjudication. Extracted data included study characteristics, inclusion/exclusion criteria, participant characteristics, interventions, and outcomes.

Data Analysis

Evidence tables and qualitative description of results were presented for all included studies. Comparative studies were considered appropriate to combine in a meta-analysis if the study design, study population, interventions being compared, and outcomes were deemed sufficiently similar. Dichotomous outcomes were combined using the DerSimonian and Laird random-effects model, except in instances where the percentage of participants with an event was less than 1 percent, in which case Peto's odds ratio (OR) was calculated using a fixed-effect model. Continuous outcomes were combined using the mean difference (MD), or standardized mean difference (SMD), where appropriate. Statistical heterogeneity was quantified using the I-squared (I^2) statistic.

Results

Description of Included Studies

The search strategy identified 9,357 citations; 83 unique studies met the eligibility criteria and were included in the review. The studies included 64 RCTs, 5 nRCTs, and 14 cohort studies. The number of participants in the studies ranged from 14 to 1,333 (median = 60 [interquartile range (IQR): 40 to 90]). The mean age of study participants ranged from 59.2 to 86.3 years. Based on the interventions reported in each study, the studies were divided into eight groups: systemic analgesia (n = 3), anesthesia (n = 30), complementary and alternative medicine (CAM) (n = 2), multimodal pain management (n = 2), nerve blocks (n = 32), neurostimulation (n = 2), rehabilitation (n = 1), and traction (n = 11).

Methodological Quality of Included Studies

All but two of the RCTs were considered to have a high or unclear risk of bias. The most common sources of potential bias were inadequate description of the randomization procedure, allocation concealment, and external sources of funding. The methodological quality of the cohort studies was moderate, with a median score of 7 stars on a possible score of 9 (IQR: 6 to 8). Common weaknesses in the design of the studies included lack of independent blind outcome assessment and failure to adequately control for potential confounding factors.

Results of Included Studies

The results of the studies are presented by the type of intervention and by the key questions. A table with the summary of findings for outcomes for each intervention is presented at the end of the executive summary.

Systemic Analgesia

Three RCTs (n = 214) evaluated different types of systemic analgesia. The mean age ranged from 77.2 to 78.5 years; most patients were female.

KQ1: Acute pain management. All three trials reported acute pain. Acute pain was measured using the 10cm Visual Analogue Scale (VAS); the mean baseline measure was 6.5cm. One trial (n = 90) comparing parecoxib intravenous (IV) versus diclofenac intramuscular (IM) ± meperidine IM found a significant difference in favor of parecoxib IV (MD -0.70; 95% confidence interval [CI] -1.04, -0.36; p <0.0001). The second trial (n = 30) comparing intrathecal isotonic clonidine versus intrathecal hypertonic clonidine reported a significant difference in favor of isotonic clonidine (MD -1.69; 95% CI -2.01, -1.37; p <0.00001). The third trial (n = 94) comparing lysine clonixinate versus metamizole found no significant difference (MD -0.43; 95% CI -1.30, 0.44; p = 0.33). The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. Additional pain medication use was reported in one trial comparing lysine clonixinate versus metamizole and reported no significant difference between groups (OR 3.00; 95% CI 0.30, 29.94; p = 0.35). Delirium was reported in one trial comparing lysine clonixinate versus metamizole and found no significant difference (OR 0.96; 95% CI 0.06, 15.77; p = 0.98). The strength of the evidence was rated as insufficient.

KQ3: Adverse effects. One trial comparing lysine clonixinate versus metamizole reported the number of participants with any adverse event and found a significant difference in favor of metamizole (OR 3.50; 95% CI 1.04, 11.81; p = 0.04). Similarly, fewer patients in the metamizole group reported any gastrointestinal disturbance (OR 11.84; 95% CI 1.45, 96.75; p = 0.02). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Anesthesia

Twenty-one RCTs and one nRCT (n = 1,062) evaluated anesthesia including neuraxial (i.e., continuous vs. single administration) or neuraxial versus general anesthesia, or another form of anesthesia (i.e., spinal or regional); sample sizes ranged from 20 to 90. Additionally, eight cohort studies (n = 3,086) provided additional data. The mean age of participants ranged from 70 to 86 years; most were female. Acute pain was measured using different scales (numeric rating score (1–5) and 10cm VAS). The studies were grouped as follows: spinal versus epidural or general anesthesia (n = 10); neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil (n = 14); neuraxial anesthesia: different doses or modes of administration (continuous vs. single administration) (n = 13).

KQ1: Acute pain management**.** The average baseline VAS pain score was 4.7.

Spinal versus general anesthesia. One RCT (n = 30) reported a statistically significant difference of additional pain relief in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42; p = 0.0001). The strength of the evidence was rated as insufficient.

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Three RCTs compared additional fentanyl (n = 40), morphine (n = 40), and sufentanil (n = 50) versus standard spinal anesthesia. In the studies comparing the addition of fentanyl or sufentanil, no patients reported feeling pain following the procedure. In the study comparing the addition of morphine, there was no significant difference between groups (MD = -0.36; 95% CI -1.11, 0.39; p = 0.35). One RCT and one nRCT (n = 80) comparing additional fentanyl reported acute pain on day 1 and found no significant difference between groups (OR 1.24; 95% CI 0.34, 4.48; p = 0.75). The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. Spinal versus general anesthesia or spinal versus epidural anesthesia. Two RCTs reported 30-day mortality (n = 99) and found no statistically significant difference in mortality rates (OR 1.73; 95% CI 0.53, 5.68; p = 0.36). In two cohort studies (n = 650), pooling was not performed due to marked statistical heterogeneity and conflicting results between the studies. The strength of the evidence was rated as insufficient.

In one RCT (n = 30) that reported delirium there was no significant difference between groups (OR 0.76; 95% CI 0.18, 3.24; p = 0.71). The strength of the evidence was rated as insufficient.

Length of stay (LOS) for acute hospitalization was reported in two RCTs (n = 99). LOS was significantly less in the general anesthesia group (MD 1.69; 95% CI 0.38, 3.01; p = 0.01).

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Additional pain medication use was reported in six RCTs. In one RCT (n = 40) comparing the addition of clonidine versus standard spinal anesthesia, all participants required additional pain medication. The pooled estimate from three trials examining the addition of fentanyl (n = 102) showed no significant difference between groups (OR 5.51; 95% CI 0.25, 122.08; p = 0.28). There was no significant difference in additional pain medication use in one RCT (n = 40) that compared the addition of morphine (OR 0.27; 95% CI 0.07, 1.04; p = 0.06). Similarly, three RCTs (n = 132) that compared the addition of sufentanil found no difference between groups (Peto's OR 7.39; 95% CI 0.15, 372.38; p = 0.32).

Delirium was reported in one RCT (n = 40) comparing the addition of morphine and found no significant difference between groups (OR 3.15; 95% CI 0.12, 82.16; p = 0.49). The strength of the evidence was rated as insufficient.

Neuraxial anesthesia: different doses and modes of administration (continuous vs. single administration). Three RCTs (n = 163) reported 30-day mortality. In two, there were no deaths. In the third, there was no significant difference between groups (OR 0.46; 95% CI 0.07, 3.02; p = 0.42). Additionally, 30-day mortality was reported in one cohort study (n = 291) that found no

significant difference between groups (OR 0.96; 95% CI 0.30, 3.00; p = 0.94). The strength of the evidence was rated as low.

Additional pain medication use was reported in two RCTs (n = 134); there were no events in either group. LOS for acute hospitalization was reported in two RCTs (n = 89). There was no significant difference between groups (MD = -0.98; 95% CI -2.06, 0.10; p = 0.07). In two RCTs (n = 134) that reported delirium, there was no significant difference between groups (OR 1.27; 95% CI 0.32, 4.99; p = 0.73). The strength of the evidence was rated as low.

Spinal anesthesia (different doses). One cohort study (n = 182) reported that there was no significant difference in 30-day mortality rates between groups (OR 0.49; 95% CI 0.12, 2.02; p = 0.32). The strength of the evidence was rated as insufficient. Another cohort study (n = 60) reported no significant difference in the incidence of delirium (OR 0.46; 95% CI 0.08, 2.75).

In one RCT (n = 60) that reported on additional pain medication use, there was no significant difference between groups at different doses (4 vs. 5mg, 4 vs. 6mg, or 5 vs. 6mg).

KQ 3: Adverse effects. Spinal versus general anesthesia or spinal versus epidural anesthesia. Two RCTs (n = 73) and one cohort study (n = 335) reported adverse effects. Overall, the RCTs reported no significant differences in the occurrence of hypotension, myocardial infarction, or ST segment depression. The cohort study found no difference in the incidence of headaches and hypotension.

Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil. Eleven RCTs and one nRCT (n = 490) provided data on adverse effects.

(a) Addition of clonidine. One trial (n = 40) reported no damage to surrounding structures, headaches, or infections.
(b) Addition of fentanyl. There was no significant difference in the number of participants reporting an allergic reaction in four RCTs (n = 164). There was no significant difference in the number of participants reporting bradycardia in one RCT (n = 42). Seven trials (n = 284) reported the frequency of hypotension. Results were inconsistent across studies and the pooled results are not reported due to high heterogeneity. Five trials (n = 204) reported nausea or vomiting and found no significant difference between groups (OR 1.10; 95% CI 0.06, 20.73; p = 0.95). There were no reports of neurological complications in one RCT (n = 40); no reports of respiratory distress in three RCTs (n = 124); no reports of gastrointestinal symptoms in three RCTs (n = 140); and no reports of headaches in one trial (n = 40).
(c) Addition of meperidine. There were no reports of headaches in one RCT (n = 34).
(d) Addition of morphine. One RCT (n = 40) reported no significant difference in the number of participants reporting allergic reactions, gastrointestinal symptoms, or nausea or vomiting.
(e) Addition of sufentanil. There was no significant difference in the incidence of bradycardia in one trial. Three trials (n = 132) reported a significantly lower incidence of hypotension in participants receiving sufentanil (OR = 0.05; 95% CI 0.01, 0.34). In one RCT (n = 42) there were no reports of allergic reaction, nausea or vomiting, or respiratory distress.

Neuraxial anesthesia: different modes of administration. In one cohort study (n = 291), there were no reports of adverse effects. In one RCT (n = 60) there was no significant difference in the occurrence of gastrointestinal symptoms. In two trials (n = 103) that reported on hypotension there was a significant difference between groups in favor of continuous spinal anesthesia (OR 0.12; 95% CI 0.03, 0.51; p = 0.004). Similarly, in one cohort study (n = 291) there was a statistically significant difference in favor of continuous spinal anesthesia (OR 0.08; 95% CI 0.04, 0.14; p < 0.00001). There was no significant difference in myocardial infarction in one trial (n = 29). There was no significant difference in the occurrence ST depression in one trial (n = 29). In one RCT (n = 74) there were no reports of bradycardia, myocardial ischemia, or stroke, and no reports of headache in one trial (n = 60) or one cohort study (n = 291).

Neuraxial anesthesia: different doses. In one cohort study (n = 182), there were no reports of adverse effects. In one RCT (n = 60) there was no significant difference in the occurrence of allergic reaction for the different doses of bupivacaine. Bradycardia was reported in two trials (n = 120); there was no significant difference among the different doses of bupivacaine or levobupivacaine. Hypotension was reported in four RCTs (n = 190). There was a significant difference following 4mg versus 6mg of bupivacaine (OR 0.03; 95% CI 0.00, 0.58; p = 0.02), but not 5 versus 6mg of bupivacaine (OR 0.31; 95% CI 0.08, 1.13; p = 0.08). Three cohort studies reported hypotension (n = 267) and found a significant difference following 2.5mg versus 5mg of bupivacaine (OR 0.08; 95% CI 0.03, 0.23; p <0.00001), 4 versus 12mg of bupivacaine (OR 0.03; 95% CI 0.01, 0.15; p <0.00001), and 0.125 versus 0.5 percent of bupivacaine (OR 0.15; 95% CI 0.03, 0.87; p = 0.03). One cohort study reported a significant difference in the incidence of hypotension following 4mg versus 12mg (OR 0.03; 95% CI 0.01, 0.15; p <0.00001), but no difference in the incidence of *delirium*. There were no reports of nausea or vomiting in two trials (n = 100); no reports of residual sensory deficits or motor weakness, respiratory distress, sedation, or urinary retention in one RCT (n = 60); no reports of gastrointestinal symptoms in two trials (n = 100); and no reports of headache in one cohort study (n = 182).

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Complementary and Alternative Medicine

Two RCTs (n = 98) evaluated the administration of CAM interventions versus no or sham intervention. The mean age ranged from 76.8 to 86.3 years; most were female. One trial (n = 38) compared acupressure versus sham control delivered preoperatively. Acute pain was measured using the 10cm VAS; the baseline measure was 6.5cm. The second trial (n = 60) compared the Jacobson relaxation technique (a two-step process of contracting and relaxing specific muscles) versus no intervention. Pain was measured using a 10-point verbal scale; the baseline measure was not reported.

KQ1: Acute pain. Acupressure reduced pain versus a sham intervention (MD -3.01; 95% CI -4.53, -1.49; p <0.0001). Relaxation also showed a reduction in pain versus no relaxation (MD -1.10; 95% CI -1.43, -0.77; p <0.00001). The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. In the RCT that examined relaxation, fewer patients in the relaxation group required additional pain medication (e.g., meperidine or morphine) versus the control group (MD -8.43; 95% CI -15.11, -1.75; p = 0.01).

KQ3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Multimodal Pain Management

Two cohort studies (n = 226) evaluated multimodal pain management versus standard care. These studies described the use of multiple pain management strategies (sequential or in parallel) as part of the clinical pathway for patients with hip fractures. The mean age was not reported; most participants were female. One study compared a formal postoperative protocol of IV-administered and oral tramadol plus acetaminophen versus standard care. The second compared a formal preoperative protocol of skin traction, morphine, and acetaminophen versus standard care.

KQ1: Acute pain. No data were reported.

KQ2: Other outcomes. Mortality was reported in one study (n = 106). There was no significant difference between groups after 30 days (OR 0.54; 95% CI 0.16, 1.77; p = 0.31), or at 1 year (OR 0.60; 95% CI 0.25, 1.47; p = 0.26). Both studies reported delirium and found no significant difference between groups. The strength of the evidence for both outcomes was rated as insufficient.

KQ 3: Adverse effects. Data were reported in one study (n = 106). There were no significant differences between groups.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Nerve Blocks

Twenty-nine RCTs (n = 1,757) evaluated nerve blocks, including 3-in-1 (neurostimulation [NS]/ultrasound-guided [US]), combined lumbar/sacral plexus, fascia iliaca compartment, femoral, lumbar plexus plus sciatic nerve, posterior lumbar plexus, psoas compartment, obutarator, and epidural nerve blocks. These were compared with placebo/standard care, or a different method of nerve blocks. Additionally, three cohort studies (n = 696) evaluated 3-in-1, femoral, and lumbar plexus plus sciatic nerve blocks versus analgesia, or comparing different analgesic medications in femoral lumbar plexus plus sciatic blocks. The mean age of participants ranged from 59.2 to 85.9 years; most were female. Acute pain was measured using different scales (i.e., numeric rating scales and 10cm VAS). Eight studies using the VAS reported mean baseline scores from 1.4cm to 7.3cm. The studies were grouped as follows: nerve blocks versus standard care/placebo; nerve blocks versus neuraxial anesthesia; nerve blocks–ropivacaine versus bupivacaine; nerve blocks–addition of clonidine; and nerve blocks–ultrasound versus neurostimulation.

KQ1: Acute pain management. Nerve blocks versus no block. Acute pain was reported in 13 RCTs (n = 942). There was significant heterogeneity between the study results (I^2 = 92 percent) and so pooled results are not reported. Even so, subgroup analyses showed significant results in favor of individual nerve blocks, except 3-in-1 block. Also preoperative nerve blocks seemed to be more effective than postoperative administration. One trial (n = 50) reported a significant difference in postoperative pain on day 1 favoring nerve blocks (OR 0.10; 95% CI 0.03, 0.36; p = 0.0005). The strength of the evidence was rated as moderate.

Nerve blocks versus neuraxial anesthesia. Acute pain was reported in three RCTs (n = 109). There was no significant difference between groups (MD -0.35; 95% CI -1.10, 0.39; p = 0.35). The strength of the evidence was rated as low.

KQ 2: Other outcomes. Nerve blocks versus no block. Four RCTs (n = 228) evaluated 30-day mortality; there was no significant difference between groups (OR 0.28; 95% CI 0.07, 1.12; p = 0.07). The strength of the evidence was rated as low. There was no significant difference in 1-year mortality in two RCTs (n = 112) (OR 0.82; 95% CI 0.25, 2.72; p = 0.74), or in one cohort study (n = 535) (OR 0.73; 95% CI 0.48, 1.10; p = 0.14). Seven RCTs (n = 378) evaluated additional pain medication use and found a significant difference favoring nerve blocks (OR 0.32; 95% CI 0.14, 0.72; p = 0.006). Similarly, one cohort study (n = 99) reported a significant difference favoring nerve blocks (OR 0.03; 95% CI 0.00, 0.44; p = 0.01). Pooled results for four RCTs (n = 461) and two cohort studies (n = 634) that provided data on delirium showed a significant difference favoring nerve blocks (OR 0.33; 95% CI 0.16, 0.66; p = 0.002 [RCTs]; OR 0.24; 95% CI 0.08, 0.72; p = 0.01[cohort studies]). The strength of the evidence was rated as moderate. LOS for acute hospitalization (days) was reported in two cohort studies (n = 634), but the pooled results are not reported due to marked heterogeneity between the original study results. Quality of sleep was reported in one RCT (n = 77) that found no significant difference (MD 0.30; 95% CI -0.46, 1.06; p = 0.44).

Nerve blocks versus neuraxial anesthesia. Additional pain medication use was reported in one RCT (n=30); there was no significant difference between groups (OR 2.00; 95% CI 0.38, 10.51; p = 0.41). Delirium was reported in one RCT (n = 29); there was no significant difference between groups (OR 1.20; 95% CI 0.27, 5.40; p = 0.81). The strength of the evidence was rated as insufficient.

Ropivacaine versus bupivacaine. Additional pain medication use and delirium were reported in one cohort study (n=62). There was no significant difference between groups for either outcome (OR 1.25; 95% CI 0.42, 3.76; p=0.69; OR 1.93; 95% CI 0.17, 22.50; p=0.60, respectively). The strength of the evidence for delirium was rated as insufficient.

KQ3: Adverse effects. *Nerve blocks versus no block. Respiratory infection* was reported in five RCTs (n=268) and found no significant difference (OR 0.43; 95% CI 0.18, 1.04; p=0.06). There were no significant differences between groups for the following adverse effects: *cardiac complications* (2 RCTs, n=128; 1 cohort study, n=99); *damage to surrounding structures* (3 RCTs, n=224); *deep venous thrombosis* (2 RCTs, n=100); *myocardial infarction* (2 RCTs, n=145; 1 cohort study, n=535); *nausea/vomiting* (6 RCTs, n=421); *pulmonary embolism* (2 RCTs, n = 128); *surgical wound infection* (2 RCTs, n = 110); *urinary retention* (2 RCTs, n = 62;

1 cohort study, n = 535). There were no reports of infection in two RCTs (n = 184). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

Nerve blocks versus neuraxial anesthesia, ropivacaine versus bupivacaine and addition of clonidine. The reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

US versus NS. Two RCTs (n = 100) reported no significant difference in damage to surrounding structures (OR 0.16; 95% CI 0.02, 1.30; p = 0.09). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. One RCT recruited patients with pre-existing heart disease. There was a significant reduction in pain favoring nerve blocks (MD -0.55; -0.81, -0.29; p <0.0001). There was no significant difference in 30-day mortality (OR 0.10; 95% CI 0.01, 1.90; p = 0.12) or adverse effects. One RCT recruited participants that were independent prior to their hip fracture. There was no significant difference between nerve blocks versus standard care for 30-day mortality (OR 1.00; 95% CI 0.06, 16.76; p = 1.00).

Neurostimulation

Two RCTs (n = 123) evaluated transcutaneous electrical neurostimulation (TENS) versus sham control. One trial administered the TENS preoperatively, and the other postoperatively. The mean age of participants ranged from 71.2 to 80.5 years; most were female. Pain was measured using the VAS; the mean baseline measure was 8.4 to 8.8.

KQ1: Acute pain. Two RCTs (n = 123) found a significant difference in additional pain relief in favor of TENS (MD -2.79; 95% CI -4.95, -0.64; p = 0.01). Pain on movement was reported in one trial (n = 60) and found a significant difference in favor or TENS (MD -3.90; 95% CI -6.22, -1.58; p = 0.001). The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. One RCT (n = 60) provided data on *health-related quality of life (*HRQOL) and quality of sleep. TENS provided significant improvement in HRQOL (MD -4.30; 95% CI -6.86, -1.74; p = 0.001) and quality of sleep (MD -3.60; 95% CI -575, -1.45; p = 0.001).

KQ3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Rehabilitation

One RCT (n = 37) evaluated physical therapy (stretching and strengthening of spinal and psoas muscles) versus standard care. The mean age was 67.1; all participants were female. Pain was measured using the 10cm VAS; the mean baseline measure was 7.9cm.

KQ1: Acute pain. There was a significant difference in additional pain relief following physical therapy (MD -1.39; 95% CI -2.27, -0.51; p = 0.002). The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. No other outcomes were reported.

KQ3: Adverse effects. No data were reported.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. All participants were female.

Traction

Nine RCTs, four nRCTs, and one cohort study evaluated skin or skeletal traction versus no intervention or other interventions. Sample sizes ranged from 60 to 311. The mean age ranged from 74.0 to 81.0; most participants were female.

KQ1: Acute pain management. Acute pain was measured using the 10cm VAS; the mean baseline measure ranged from 0.3 to 6.9cm. Eight trials compared skin traction (n = 498) versus no traction (n = 594) and found no significant difference between groups. The strength of the evidence was rated as low. One trial (n = 78) compared skin traction versus skeletal traction and found no difference between groups. The strength of the evidence was rated as insufficient.

KQ2: Other outcomes. LOS for acute hospitalization was reported in two trials (n = 326) comparing skin traction versus no traction and no significant difference was found. Thirty-day mortality was reported in one RCT (n = 80) that found no difference between skin and skeletal traction versus no traction. Additional pain medication use was reported in one RCT and one nRCT (n = 352). There was no significant difference between groups.

KQ3: Adverse effects. Seven RCTs (n = 1,043) and one cohort study (n = 134) provided data on adverse effects. The reported adverse effects were from one to two studies, and did not demonstrate any significant statistical differences between the pain management interventions.

KQ 4: Efficacy, effectiveness, and safety in subpopulations. No data were reported.

Rating the Body of Evidence

Most of the evidence for the key outcomes (acute pain, chronic pain, mortality [30-day]), and the incidence of serious adverse effects (i.e., delirium, myocardial infarction, renal failure, stroke) came from single trials and cohort studies precluding any conclusions. The strength of evidence was low to moderate to support the use of some interventions for alleviating acute pain, preventing delirium, and decreasing the 30-day mortality rate (see Table A). The strength of evidence for the remaining outcomes was classified as insufficient due to lack of an adequate number of studies and study power.

Future Research

Multicenter research studies. Adequately powered multicenter research studies are needed to provide a comprehensive assessment of safe, effective, and appropriate pain management

following a hip fracture. Studies need to be large enough to allow subgroup analyses by age, sex, comorbidities, or functional groups (e.g., independent vs. dependent in ambulation). In addition, researchers need to consider inclusion of common subpopulations of hip fracture patients. In particular, those with altered cognition who make up a substantial proportion of the overall hip fracture patient population should be included in future studies of pain management following hip fracture.

Outcomes. Standardization of outcomes and outcome measures will allow easier and meaningful comparisons across different interventions and among studies. The types of outcomes reported do not reflect the multidimensional nature of pain. Relevant outcomes should include validated pain scores, prescription of opiates and other agents, and adverse effects or complications attributable or related to the intervention. Associated outcomes of pain such as function, quality of life, and time to recovery should also be evaluated. The evaluation of pain should include long-term followup of outcomes beyond the acute hospital setting to determine the pattern of pain recovery and whether early effective pain management techniques affect ultimate recovery levels.

Methods. Future research should seek to minimize bias by blinding outcome assessors, use of validated and standardized outcome assessment instruments, adequate allocation concealment (where applicable), and appropriate handling and reporting of missing data.

Conclusions

For the majority of interventions, sparse data are available, which precludes firm conclusions for any single approach or for the optimal overall pain management following nonpathological hip fracture due to low energy trauma. The dearth of evidence related to long-term outcomes and the fact that the majority of the data is derived from studies of low methodological quality or from study designs associated with higher risk of bias (i.e., cohort studies) further weaken any conclusions. Overall, the evidence shows that most interventions result in improvements in short-term pain scores; however, few differences of long-term clinical importance are noticeable when comparisons between interventions are available. The rates of complication were generally low, and the majority of complications were not significantly different among the interventions. Well-designed and -powered, long-term trials are needed in order to determine the relative effectiveness of pain interventions for hip fracture patients. Until then, pain management in this population will rely heavily on availability of the interventions, staff skills, and training and pre-existing patient comorbidities.

Table A. Summary of evidence for key outcomes for pain management following hip fracture

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Systemic analgesia			
Acute pain	Parecoxib IV vs. diclofenac ± meperidine IM (1 RCT) Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine (1 RCT) Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	Significant effect in favor of parecoxib IV (MD = -0.70; 95% CI -1.04, -0.36) Significant effect in favor of intrathecal isotonic clonidine (MD = -1.69; 95% CI -2.01, -1.37) No significant difference
Acute pain at rest	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal vs. general anesthesia			
Acute pain	Spinal vs. general anesthesia (1 RCT)	Insufficient	Significant effect in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42)
Chronic pain	None	Insufficient	No data
30-day mortality	Spinal vs. general anesthesia (2 RCTs, 2 cohort studies)	Low	No significant difference
Delirium	Spinal vs. general anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	Spinal vs. general anesthesia (2 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – continuous vs. single administration			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	Continuous vs. single administration (3 RCTs, 1 cohort study)	Low	No significant difference
Delirium	Continuous vs. single administration (2 RCTs)	Low	No significant difference
Myocardial infarction	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Anesthesia: spinal – addition of other medications			
Acute pain	Addition of fentanyl vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of sufentanil vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – different doses			
Acute pain	Bupivacaine 2.5mg vs. 5mg (1 cohort study)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Bupivacaine 4mg vs. 12mg (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Complementary and alternative medicine			
Acute pain	Acupressure vs. standard care (1 RCT)	Insufficient	No significant difference
	Relaxation vs. standard care (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Multimodal pain management			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Delirium	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Nerve blockade			
Acute pain	Nerve block vs. no nerve block (11 RCTs)	Moderate	Significant effect in favor of nerve block in subgroup analyses
Pain on movement	Nerve block vs. no nerve block (4 RCTs)	Low	Significant effect in favor of nerve block in subgroup analyses
Pain at rest	Nerve block vs. no nerve block (3 RCTs)	Low	Data inconsistent for conclusions to be made
Day 1 pain	Nerve block vs. no nerve block (1 RCTs)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	Nerve block vs. no nerve block (4 RCTs)	Low	No significant difference
Delirium	Nerve block vs. no nerve block (3 RCTs, 2 cohort studies)	Moderate	Significant effect in favor of nerve block (OR_{RCT} = 0.36; 95% CI 0.17, 0.74) (OR_{Cohort} = 0.24; 95% CI 0.08, 0.72)
Myocardial infarction	Nerve block vs. no nerve block (2 RCTs, 1 cohort study)	Insufficient	No significant difference
Stroke	Nerve block vs. no nerve block (1 RCT, 1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Nerve blockade vs. regional anesthesia			
Acute pain	Nerve block vs. regional anesthesia (3 RCTs)	Low	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Nerve block vs. regional anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data

Table A. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of Evidence	Summary
Nerve Blocks: ropivacaine vs. bupivacaine			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Ropivacaine vs. bupivacaine (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Neurostimulation			
Acute pain	Neurostimulation vs. standard care (2 RCTs)	Insufficient	Significant effect in favor of neurostimulation (MD = -2.79; 95% CI -4.95, -0.64)
Pain on movement	Neurostimulation vs. standard care (1 RCT)	Insufficient	Significant effect in favor of neurostimulation (MD = -3.90; 95% CI -6.22, -1.58)
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Rehabilitation			
Acute pain	Physical therapy vs. standard care (1 RCT)	Insufficient	Significant effect in favor of physical therapy (MD = -1.39; 95% CI -2.27, -0.51)
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Traction			
Acute pain	Skin traction vs. no traction (7 RCTs) Skin traction vs. skeletal traction (1 RCT)	Low Insufficient	No significant difference No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	Skin traction vs. no traction (1 RCT) Skeletal traction vs. no traction (1 RCT)	Insufficient Insufficient	No significant difference No significant difference
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data

CI = confidence interval; IM = intramuscular; IV = intravenous; MD = mean difference; OR = odds ratio; RCT = randomized controlled trial

Introduction

Background

Hip fractures are a source of significant morbidity and mortality. Incidence increases substantially with age, rising for men and women, respectively, from 22.5 and 23.9 per 100,000 population at age 50, to 630.2 and 1,289.3 per 100,000 population by age 80.[1-4] The impact of hip fractures is far reaching. Short-term mortality rates are high and range from 25 percent for women to 37 percent for men in the first year following a hip fracture.[5] Furthermore, a large proportion of those patients who survive never recover to their prefracture level of function,[6-8] and approximately 25 to 50 percent of elderly patients with hip fractures have not returned home by 1 year postfracture.[9] Up to 25 percent of hip fractures occur in continuing care facilities (long-term residential care for dependent people).[10,11] Because of poor functional recovery, health service utilization associated with recovery is substantially increased for at least 1 year, with much of the health care cost attributable to subsequent long-term care.[1,12-14]

Pain following hip fracture has been associated with delirium, depression, sleep disturbance, and decreased response to interventions for other disease states.[15-17] Therefore, it is important to treat and manage complaints of pain adequately during acute treatment for hip fracture. Furthermore, poorly managed postoperative pain is associated with delayed ambulation, pulmonary complications, and delayed transition to lower levels of care.[18]

Hip fracture patients require a continuum of pain management from the time of prehospital admission through the completion of final rehabilitation. Therefore the interventions administered to relieve pain in this population can be divided according to both the timing of the intervention (e.g., pre-, peri-, and postoperative) and according to their classification (e.g., systemic analgesia, nerve blocks, etc.).

According to the timing of the intervention, preoperative pain management has traditionally been achieved using systemic analgesia and in some cases, lower limb traction. Recently, nerve blocks, which block the nerve impulses from reaching the sensory cortex, have been introduced.

Intra-operative pain management has also traditionally been achieved with systemic analgesia in association with general anesthesia. Even so, neuraxial anesthesia is gaining momentum as a replacement for general anesthesia.

Postoperative pain management is usually accomplished by a more diverse array of interventions including systemic analgesia, nerve blocks, physical therapy, and transcutaneous electrical nerve stimulation (TENS).

Interventions

Pain management interventions can be divided into pharmacological and nonpharmacological interventions. Pharmacological interventions include systemic analgesia and medications used in nerve blocks and neuraxial anesthesia (e.g., bupivacaine). Nonpharmacological interventions include TENS, acupressure, or stabilization of the fracture using traction. The following broad categories represent the interventions covered by this report.

Systemic Analgesia

This classification of intervention is broad and encompasses both narcotic and non-narcotic medications. The general goal is to provide pharmacologic analgesia although some also have anti-inflammatory properties.

Opiates (e.g., morphine) can be used at all stages of pain management to treat mild to severe pain.[19] Fentanyl, primarily targets the *mu* receptors in the brain and spinal cord and, is used in the treatment of severe pain. Sufentanil is 5–10 times more potent than fentanyl and, due to its immediate onset of action and its limited accumulation, it is ideal for short, quick action.

Nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., diclofenac) are used for their analgesic properties and act by inhibiting both cyclooxygenase (COX) isoenzymes (COX-1 and COX-2).[20] Acetaminophen, a commonly used analgesic, has minimal inhibition of COX-1 and COX-2, with appreciable inhibition of central COX-3, but its precise mechanism for analgesia has not been confirmed. The use of COX-II selective inhibitors (coxibs) has fluctuated since their introduction on the U.S. market in the 1990s with the current use of coxibs in decline.

Anesthesia

Anesthesia can generally be divided into general and neuraxial, with the latter constituting spinal and epidural anesthesia. Pain management during general anesthesia is usually accomplished by the use of pharmacological systemic analgesia (e.g., opioids). During neuraxial anesthesia, injection of a local anesthetic into the epidural or subarachnoid space (e.g., spinal anesthesia) causes pain relief and often does not require additional pain medications.

Complementary and Alternative Medicine (CAM)

Complementary and alternative medicine (CAM) has been defined as a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine (i.e., medicine as practiced by holders of M.D. (medical doctor) and D.O. (doctor of osteopathy) degrees and by allied health professionals, such as physical therapists, psychologists, and registered nurses).[21] CAM practices are often grouped into broad categories, such as natural products, mind-body medicine, and manipulative and body-based practices. In this report, two CAM practices were identified as having been used with hip fracture patients: acupressure and the Jacobson relaxation technique.

According to traditional Chinese acupuncture, auricular acupressure involves the placing of tiny beads onto the outer ear at acupuncture points, thereby stimulating the corresponding acupuncture points. Bilateral auricular acupressure can be performed at sites known to decrease pain and anxiety (e.g., shenmen, hip, valium point).[22] Using these body points, areas can be stimulated to direct energy flow.

Another CAM procedure used for hip fracture patients is the Jacobson relaxation technique. This involves a two-step process of contracting and relaxing specific muscles. With practice the patient learns which muscles are related to pain and relaxes them.

Multimodal Pain Management

Multimodal pain management is the use of multiple pain management strategies (consecutively or in parallel) as part of the clinical pathway for patients with hip fractures. The goal is to decrease pain to a greater extent than with one intervention alone.

Nerve Blocks

Nerve blocks include the lateral cutaneous nerve of the thigh, femoral nerve, sciatic nerve, 3-in-1 nerve block (femoral, obturator, and sciatic nerves), psoas (lumbar plexus), or continuous epidural block.[23] Local anesthetics (e.g., bupivacine) are used in regional nerve blocks to prevent the generation and conduction of nerve impulses to the spinal column and brain.[24] Additional medications used with nerve blocks include clonidine, morphine, fentanyl, and sulfetanil.

Rehabilitation

Rehabilitation is a standard part of postoperative care in patients with hip fractures to increase mobility and reduce pain. The goal is to increase muscle strength and range of motion as soon as possible following hip fracture. One of the major factors that can limit patient participation in rehabilitation is the degree of delirium and pain that the patient may be experiencing.

Traction

Preoperative skin or skeletal traction was traditionally standard care in this patient population. The theory is that by maintaining the lower limb stretched, using 5 to 10 pounds, intracapsular pressure and pain is decreased, and fracture reduction is made easier. However, a recent Cochrane systematic review of 10 randomized controlled trials (1,546 participants) reported no benefits for traction use.[25]

Skin traction is used to stabilize a fractured leg and to decrease pain and the risk of surgical complications prior to any operation. Skin traction is applied by using adhesive tape, bandaging the limb, and placing it on a traction sled with an appropriate weight hung from it.[20,26] Foam boot traction, a form of skin traction, uses a foam boot strapped around the leg and placed on a traction sled with an appropriate weight attached.[26] Skeletal traction involves passing a metal pin through the proximal tibia or distal femur, under local anesthesia. Traction is applied using ropes and weights attached to the end of the pin.[20]

Transcutaneous Electrical Nerve Stimulation (TENS)

TENS uses electrodes to apply electrical energy to peripheral nerves to treat acute and chronic musculoskeletal pain. Electrical stimulation can be administered at varying amplitudes and frequencies, depending on the indication.[27]

Outcomes

The patient's self-report of pain is the gold standard for evaluating its character and intensity.[15] However, those with dementia or acute delirium may have difficulty reporting pain levels. Acute delirium, or confusion, following hip fracture may be a complication of the fracture, the resulting pain due to tissue trauma and/or the pain management interventions used. The potential for underreporting of pain has direct ramifications for the hip fracture population, as many patients are frail older people with postoperative confusion and an impaired ability to communicate.[28-31]

The most commonly used measure of pain in clinical settings is the visual analogue scale (VAS).[32] It consists of a 100mm unmarked line printed where the patients are instructed to point to the position on the line to indicate how much pain they are currently feeling. The far left end

of the line indicates “No pain” and the far right end of the line indicates “Worst pain ever.” Its ease of use, especially with older patients, reproducible results and extensive use in clinical practice makes it one of the first choices among pain measurement scales.[33] Additionally, it has been shown not to be biased by the severity of pain.[34]

Other commonly used scales include numerical, verbal, and facial pain scales. The numerical scales usually consist of a number between zero and 10, and the patients are instructed to give a number relating to how much pain they are currently feeling, with the higher numbers indicating greater pain intensity. Many variations of this scale exist including a numerical scale of zero to three, one to five, etc. Numerical scales have been shown to have a linear correlation with the VAS and don’t require the use of any printed material.[35,36]

With regard to clinically important effect size differences for pain measurements, no exact cutoff has been defined in the medical literature; however, it has been widely accepted as ranging from 20 to 30 percent absolute pain reduction. This would reflect an additional 30mm of absolute difference on the VAS.

Most research to date has focused on the management of acute pain, the expected sensory and emotional response to injury, which lasts for the duration of the injury and healing (i.e., up to 30 days post hip fracture). It is possible that pain following a hip fracture has longer-term effects on recovery as has been seen in recovery from hip replacement surgery.

The need to improve recovery after hip fracture, particularly among frail elderly patients, is a pressing worldwide problem that will only increase in the future as the population ages.[37] Synthesized data are lacking regarding pain management after hip fracture; therefore, our review will be of interest to patients and families, the medical community and health care decisionmakers. The review will also elucidate evidence on important subgroups of patients and interventions for which further research is needed.

Scope and Key Questions

We have focused the key questions using the PICOTS framework (population, intervention, comparison, outcome, timing, and setting) as follows:

Key Question 1

In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions for controlling acute (up to 30 days postfracture) and chronic pain (up to 1 year postfracture) compared with usual care or other interventions in all settings?

Key Question 2

In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the effectiveness of pharmacologic and/or nonpharmacologic pain management interventions on other outcomes up to 1 year postfracture compared with usual care or other interventions in all settings? Other outcomes include:

a. Mortality (30-day and up to 1 year postfracture)
b. Functional status
c. Pain medication use; change in type and quantity
d. Mental status
e. Health-related quality of life
f. Quality of sleep in the hospital

g. Ability to participate in rehabilitation
h. Return to prefracture living arrangements
i. Health services utilization

Key Question 3

In older adults (≥50 years) admitted to the hospital following acute hip fracture, what is the nature and frequency of adverse effects that are directly or indirectly associated with pharmacologic and nonpharmacologic pain management interventions up to 1 year postfracture compared with usual care or other interventions in all settings?

Key Question 4

In older adults (≥50 years) admitted to the hospital following acute hip fracture, how do the effectiveness and safety of pharmacologic and nonpharmacologic pain management interventions vary in differing subpopulations following acute hip fracture up to 1 year after fracture compared with usual care or other interventions in all settings?

Important refinement points regarding the key questions:

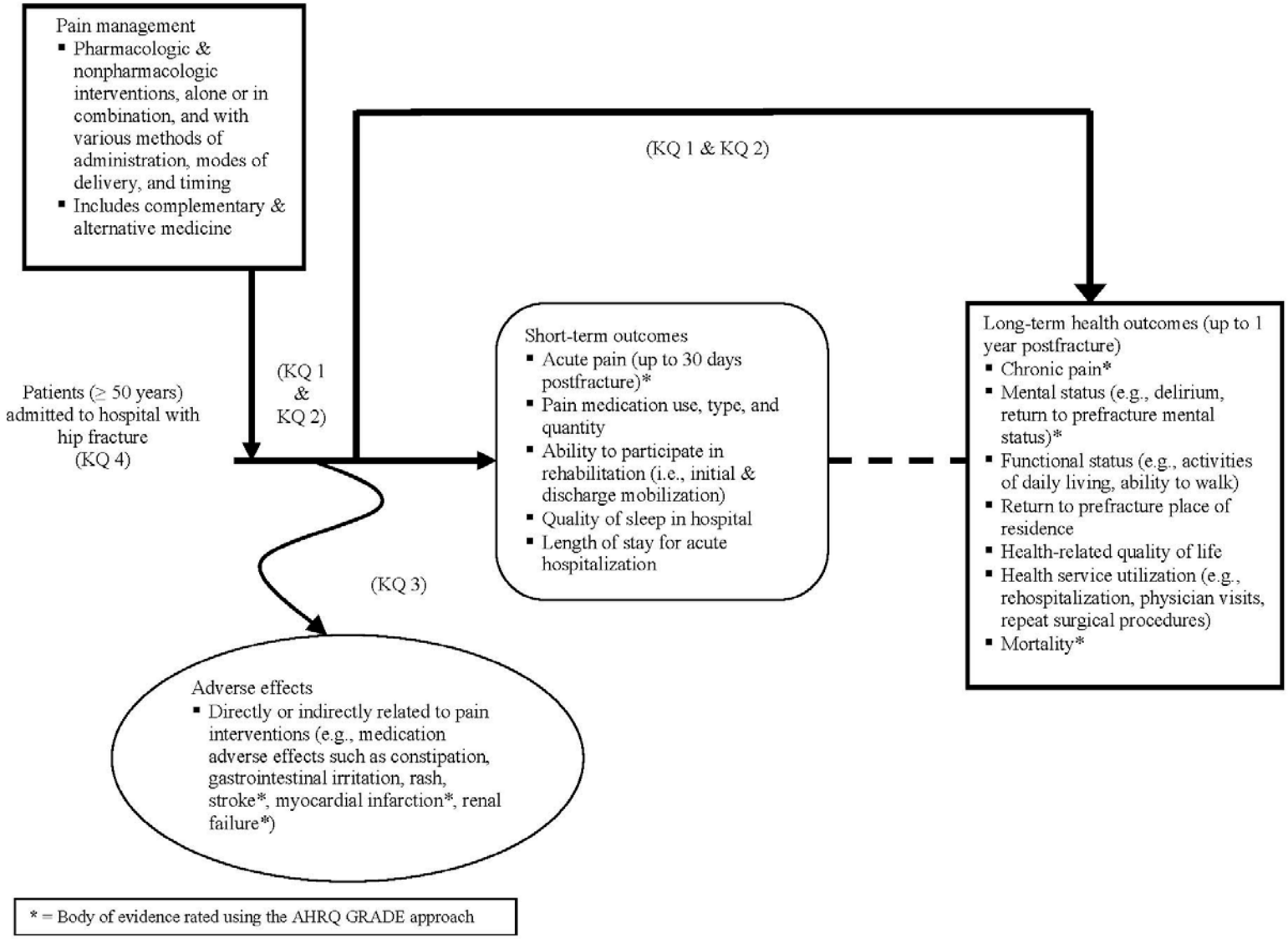
- **Population(s):**
  Older adults of either sex who were diagnosed as having an acute hip fracture resulting from low-energy trauma (e.g., slip and fall) were included. This includes patients with intracapsular (e.g., subcapital and femoral neck) and extracapsular (e.g., basal, trochanteric, intertrochanteric, and subtrochanteric) fractures regardless of whether surgical repair was performed. There were no restrictions on comorbidities or baseline functionality.
  Patients with hip fracture due to the following etiologies were not considered: pathologic hip fractures (e.g., metastatic fractures, Paget's disease); femoral head fractures; periprosthetic fractures (i.e., post-hip replacement fractures/arthroplasty population); fractures resulting from high energy trauma (e.g., motor vehicle crashes, falls from heights, etc.).
- **Interventions:**
  We considered all interventions, alone or in combination, with various methods of administration and modes of delivery, and at various time points during the care pathway (e.g., preoperative, intra-operative, postoperative, rehabilitation, and following discharge from acute care). The same intervention may be administered at different time points (e.g., epidural block for preoperative analgesia and intra-operatively for anesthesia). Interventions included traditional and nontraditional medications/interventions (e.g., natural health products). Interventions that were directly related to surgical/nonsurgical treatment of the hip fracture (e.g., reduction, fixation, hemiarthroplasty, total hip replacement) were not considered.
- **Comparators:**
  Comparators of interest were defined in the primary studies. This included, but was not limited to, opioid, nonopioid, or NSAIDS, and nonpharmacological comparators.
- **Outcomes for each question:**
  For KQ1, pain had to be assessed using a validated pain measurement tool—either patient defined or proxy reported.
  For KQ2, all reported outcomes that were directly or indirectly related to the intervention for pain management were investigated.

For KQ3, all reported adverse effects that were directly or indirectly associated to the intervention for pain management (e.g., medication complications such as constipation or gastrointestinal bleeding; pain interventions (e.g., femoral blocks) that may delay ambulation) were investigated. Adverse effects of interventions directly related to surgical/nonsurgical/medical treatment of the hip fracture (e.g., wound infection, etc.) were not investigated.
For KQ4: Subgroups to be investigated included sex, age, race, marital status, comorbidities, body mass index, prefracture functional status, and family distress.

- **Timing:**
  We included all followup time points from the time of the trauma leading to the hip fracture and thereafter.
- **Settings:**
  Settings included, but were not limited to, emergency department, hospital, rehabilitation facilities, skilled nursing facility, subacute care facility, and place of residence.

Figure 1 provides an analytic framework to illustrate the population, interventions, and outcomes that guided the literature search and synthesis. The figure depicts the key questions within the context of the PICOTS described in the previous section. In general, the figure illustrates how pharmacologic and nonpharmacologic pain management interventions, alone or in combination, may result in (1) intermediate outcomes such as control of acute pain, pain medication use, the ability to participate in rehabilitation, the quality of sleep in hospital, and length of stay, and (2) long-term outcomes such as chronic pain, changes in the mental status, the functional status (e.g., activities of daily living), the ability to return to prefracture place of residence, health-related quality of life, health service utilization, and mortality. Also, adverse effects may occur at any point after the treatment is received (e.g., medication adverse effects such as constipation, gastrointestinal irritation, rash).

Figure 1. Analytic framework for pain management interventions



Methods

This chapter describes the prospectively designed protocol that the University of Alberta Evidence-based Practice Center (UAEPC) used to synthesize the evidence on pain management interventions following hip fracture. The topic refinement process for developing the key questions is described. We outline the literature search strategy, the selection process for identifying relevant articles, the process for extracting data from eligible studies, the methods for assessing the methodological quality of individual studies and for rating the overall body of evidence, and our approach to data analysis and synthesis.

Topic Development

The UAEPC was commissioned to conduct a preliminary literature review to gauge the availability of evidence and to draft the key research questions for a full comparative effectiveness review (CER). In consultation with the Agency for Healthcare Research and Quality (AHRQ) and the Scientific Resource Center, a Technical Expert Panel (TEP) was invited to provide input in the development of the key questions and scope of the report. Initial questions were posted on the AHRQ Web site, and the public was invited to comment on these questions. After reviewing the public comments, the key questions were finalized and submitted to AHRQ for approval.

The TEP was subsequently invited to provide high-level content and methodological expertise throughout the development of the CER. The names of technical experts are available in Appendix A.

Search Strategy

The research librarian, in collaboration with the research team, developed and implemented search strategies designed to identify evidence relevant to the key questions (Appendix B).

For the questions on efficacy and effectiveness, we conducted comprehensive searches in the following electronic databases: AMED (Allied and Complementary Medicine); Global Health; International Pharmaceutical Abstracts; BIOSIS Previews; CINAHL (Cumulative Index to Nursing & Allied Health Literature); Academic Search Elite and Health Source: Nursing and Academic Edition; Cochrane Complementary Alternative Medicine and Pain Database; Cochrane Database of Systematic Reviews; Database of Abstracts of Reviews of Effects; EBM Reviews – Cochrane Central Register of Controlled Trials; Embase; Global Health Library; MEDLINE; Pascal; PeDRO (The Physical Therapy Evidence Database); ProQuest Dissertations and Theses–Full Text; Scopus; Web of Science. For the questions on adverse effects, in addition to the above databases, we also searched TOXLINE (Appendix B-1 to B-15).

In order to identify literature from symposia proceedings, we searched Conference Papers Index (1982 to 2010), OCLC PapersFirst (1993 to 2010), and ScienceDirect Tables of Contents for select journals (Appendix B). We also hand searched proceedings for the following associations: American Geriatric Society, American Physical Therapy Association, American Society of Regional Anesthesia and Pain Medicine, European Society of Regional Anesthesia, European Society of Anesthesiology, and International Anesthesia Research Society (Appendix B-16 to B-19).

Unpublished studies and studies in progress were identified by searches of clinical trials registers (ClinicalStudyResults.org; ClinicalTrials.gov; Current Controlled Trials; ICTRP Search

Portal; IFPMA Clinical Trials Portal; UMIN-CTR Clinical Trials) (Appendix B-20 to B-25), by contacting experts in the field, and by contacting authors of relevant studies.

The reference lists of reviews and guidelines were reviewed to help identify potential studies for inclusion. Original studies that met the inclusion criteria for this review were searched for citing studies using Scopus Citation Tracker.

Search terms were selected by scanning search strategies of systematic reviews on similar topics and by examining index terms of potentially relevant studies. A combination of subject headings and text words were adapted for each electronic resource. This included terms for hip fracture (fracture* and (hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck")) and pain terms (pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological or acupunct* or acupress* or traction or "electrical stimulation" or "passive motion" or morphine or acetaminophen or paracetamol or tylenol or anesth* or analges*). All searches were restricted to studies published from 1990. No language or study design restrictions were applied. The detailed search strategies for each database are presented in Appendix B. The original searches were conducted between July 9 and July 27, 2009. On May 6, 2010 and December 16, 2010, the searches were updated using the original search strategies in Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, PASCAL, CINAHL, Scopus, DARE and ClinicalTrials.gov.

Results from the literature searches were entered into Reference Manager 11.0.1 (Thomson Reuters, Carlsbad, CA).

Study Selection

The results of the electronic literature searches, hand searches, and expert nominated records were screened using a two-step process. We included studies published as full-text manuscripts, conference abstracts, or other grey literature with no language restrictions. Research published prior to 1990 was not considered based on the rationale that surgical procedures and medical care in North America (particularly as related to aggressive postsurgery mobilization) for this patient population has changed and the earlier research may not be applicable to current care.

Study selection was based on an a priori set of criteria for inclusion and exclusion of studies including study design, patient population, interventions, and outcome measures (Table 1). First, two reviewers independently screened the titles and abstracts (level I screening) to determine if an article met the broad inclusion/exclusion criteria for study design, population, and intervention. Each article was rated independently as: include, exclude or unclear. Records rated as “include” or “unclear” by at least one reviewer were advanced to level II screening. The full-text versions of all potentially relevant articles were retrieved for independent formal review by two reviewers, applying a priori eligibility criteria and using a standardized screening form that was developed and piloted by the review team. Discrepancies regarding inclusion/exclusion of a study were resolved through discussion and consensus or by third-party adjudication if consensus could not be reached. Reviewers were not masked to the study authors, institution, or journal.[38]

Table 1. Inclusion and exclusion criteria

(A) Inclusion criteria

Study design	Randomized controlled trials , nonrandomized controlled trials (e.g. quasi-randomized trials), cohort studies (prospective or retrospective), case-control studies
Participants	Older adults (≥50 years old) of either sex admitted to hospital with acute hip fracture due to low energy trauma
Interventions	Pharmacological and/or nonpharmacological pain management monotherapy or combination therapy, regardless of mode of administration or time point during the care pathway
Comparator	Usual care (as defined by study authors) or another intervention(s) for pain management, administered as monotherapy or combination therapy
Outcomes	Primary outcomes: • Acute pain • Chronic pain Secondary outcomes: • Mortality • Functional status • Pain medication use; change in type and quantity Adverse effects: • Adverse effects related to the pain management intervention • Mental status • Health-related quality of life • Quality of sleep in hospital • Ability to participate in rehabilitation • Return to prefracture place of residence • Length of stay for acute hospitalization, skilled nursing facility, subacute care facility • Health service utilization
Timing	From time of trauma leading to acute hip fracture and thereafter
Setting	All settings

(B) Exclusion criteria

Study design	Observational study designs with no comparison group (case reports, case series, cross-sectional studies)
Participants	Majority (>80%) of participants <50 years, as stated by the study investigators or evident from the study characteristics (e.g., mean/SD of patient population); participants with underlying pathological conditions that may directly lead to fracture; acute hip fractures due to high energy trauma
Interventions	Interventions directly related to surgical/nonsurgical treatment of the hip fracture and not a pain management intervention
Comparator	Initial care for patients is substantially different than the current practices in North America (e.g., based on time to discharge from acute care to subacute care)
Outcomes	None of the aforementioned outcomes were available from the trial report or through communication with the study's corresponding author

Assessment of Methodological Quality of Individual Studies

The risk of bias of the included trials was assessed using the Cochrane Collaboration's Risk of Bias (RoB) tool[39] for randomized controlled trials (RCTs) and nonrandomized controlled trials (nRCTs). The methodological quality of cohort and case-control studies was assessed using the Newcastle-Ottawa Scale (NOS)[40] for cohort and case-control studies, respectively. Decision rules regarding application of the tools were developed a priori by the research team. For RCTs and nRCTs, we performed a domain-based risk of bias assessment according to the principles of the RoB tool. The domains were: (1) sequence generation (e.g., was the allocation sequence adequately generated?); (2) allocation concealment (e.g., was allocation adequately concealed?); (3) blinding of participants, personnel and outcome, assessors (e.g., was knowledge of the

allocated intervention adequately prevented during the study?); (4) incomplete outcome data (e.g., were incomplete outcome data adequately addressed?); (5) selective outcome reporting (e.g., were reports of the study free of suggestion of selective outcome reporting?); and (6) other sources of bias (e.g., was the study apparently free of other problems that could put it at a high risk of bias?). Other sources of bias included baseline imbalances, source of funding, early stopping for benefit, appropriateness of crossover design. For cohort and case-control studies, the NOS uses a "star system" in which a study is judged on three broad perspectives: (1) the selection of the study groups; (2) the comparability of the groups; and (3) the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively.

Two reviewers in a four-person team (AMAS, MH, MK, KW) independently performed quality assessment of the included studies with disagreements resolved through discussion or third-party adjudication, as needed.

Data Extraction

Published data were independently double-extracted by members of the research team (AMAS, MH, MK, KW, SM). Standardized data extraction forms were developed in Microsoft Word (Microsoft Corporation, Redmond, WA; Appendix C). Data extraction forms were piloted with three studies[41-43] and identified issues were resolved. We extracted data on the following: general study characteristics (e.g., study design); population characteristics (e.g., age, sex); interventions and dosing regimens; numbers of patients allocated into relevant treatment groups; outcomes measured, method of ascertainment, and the results of each outcome, including measures of variability, by relevant intervention arm. Funding source, if reported, was also recorded.

When there were multiple reports of the same study we referenced the primary or most relevant study, and extracted only additional data from companion reports. Corresponding authors were contacted for data clarification and missing data. All data were imported into Microsoft Excel (Microsoft Corporation, Redmond, WA) for data management.

Dichotomous data were extracted as the number (n) of participants with events and the total number of participants (N). Continuous outcomes were extracted as the mean with the accompanying measure of variance for each treatment group, or as a mean difference (MD) between treatments based on the method of outcome measurement (e.g., scale, score system). Continuous data were analyzed as post-treatment score or absolute difference (or change score) from baseline.[44] Multiple scales and scoring systems were used to measure the outcomes (e.g., pain scores). Therefore, in addition to summary data and measure of variance, the scale and the type of analysis used in the study were extracted (Appendix C). For all outcomes (e.g., delirium, hypotension) we used the definitions as reported by the authors of individual studies.

When data were available only in a graphical format, data were extracted from the available graphs using the distance measurement tool in Adobe Acrobat 8 Professional (Adobe Systems Inc., San Jose, CA). When data were not available for the measure of variability for continuous outcomes, the variability was calculated from the computed p-value or, if not available, it was imputed from other studies in the same analysis. When relevant data for multiple followup/observation periods were reported, only the followup data for the reported period that demonstrated the greatest improvement for the intervention arm was extracted. When studies incorporated multiple relevant treatment arms, data from all were extracted. We noted the specific intervention, dosage and intervals of each intervention to determine if arms were

clinically appropriate for pooling. For the purpose of this review, acute outcomes (mortality, acute pain, and delirium) occurred up to 30 days postfracture.

Data Analysis

Evidence tables and qualitative description of results are presented for all included studies. Where appropriate, we conducted meta-analyses to answer the key questions. Meta-analyses were performed in Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark). For dichotomous outcomes, the Review Manager software allows pooling with one of the following statical methods: Mantel-Haenszel (MH), inverse variance (IV) or the Peto's modified Mantel-Haenszel (Peto). For continous outcomes, pooling is performed using IV. Additionally, for the aforementioned methods both fixed-effects or random-effects models are available, except for Peto, which uses only a fixed-effect model. For the purpose of this review, we pooled binary data using the MH and a random-effects model (DerSimonian and Laird),[45] except in instances where the percentage of participants with an event was less than one percent, in which case Peto's odds ratio was calculated using a fixed-effects model.[46] For continuous outcomes, we used the IV and a random-effects model (DerSimonian and Laird).[45] Chi-square tests were used to test for significant heterogeneity reduction in partitioned subgroups. A chi-square test of $p < 0.1$ was considered to be significant. Forest plots were generated and presented for the primary outcomes as long as at least two trials contributed to the synthesis. For secondary outcomes, forest plots were presented only if there were at least five included studies.

In the meta-analyses, RCTs and nRCTs were combined. Cohort studies were synthesized separately, as meta-analysis including both trials and cohort studies is controversial.[47] For continuous summary estimates where the same measure of analysis was used the MD was calculated with 95 percent confidence intervals (CI). When different measures of analysis (e.g., different scales) were used, the standardized mean difference was used. Dichotomous summary estimates were reported as odds ratios with accompanying 95 percent CI.

Heterogeneity was tested using an I^2 statistic,[48] with an I^2 value 75 percent or greater considered to be substantial, thereby precluding pooling of studies. In the case of substantial statistical heterogeneity, if there were at least 10 studies in the analysis, we proposed to explore heterogeneity through meta-regression, subgroup analyses, and sensitivity analyses. If the number of included studies was less than 10, we explored heterogeneity qualitatively through subgroup and sensitivity analyses. Effect modifiers that were considered important to explain heterogeneity included specific intervention details (e.g., type and quantity), study design, and risk of bias. In addition, we conducted sensitivity analyses on studies with imputed data to determine if the imputations had any effect on the effect estimate or heterogeneity. A priori subgroup analyses included sex, age, race, body mass index, marital status, comorbidities, prefracture functional ability, and family distress.

Almost one-fourth (22.1 percent) of the trials had multiple intervention arms comparing different doses or concentrations of the same intervention, or drugs of the same class. When appropriate, data from the available arms were pooled before being included in the meta-analysis. Dichotomous arms were pooled by simple addition, while pooling of continuous arms was performed using generic inverse variance.

Dichotomous data with zero values (i.e., no participant experienced an event) were not included in meta-analyses because summary trial results were not estimable, but the results from these studies were reported in the narrative synthesis for the relevant intervention.

Potential publication bias was explored graphically through funnel plots for comparisons for which meta-analyses were conducted and when there were at least 10 studies in the analysis. Additionally, if bias was suspected, publication bias was quantitatively assessed using the Begg adjusted rank correlation test and Egger regression asymmetry test.[49]

Applicability

Applicability of evidence distinguishes between effectiveness studies conducted in primary care or office-based settings that use less stringent eligibility criteria, assess health outcomes, and have longer followup periods than most efficacy studies.[50] The results of effectiveness studies are more applicable to the spectrum of patients in the community, than efficacy studies, which usually involve highly selected populations. The applicability of the body of evidence was assessed following the PICOTS (population, intervention, comparator, outcomes, timing of outcome measurement, setting) format used to assess study characteristics. Clinically important outcomes and participant characteristics are reported in the results.

Rating the Body of Evidence

We evaluated the overall strength of the evidence for key outcomes. We used the AHRQ GRADE[51] approach, which is based on the standard GRADE approach developed by the Grading of Recommendation Assessment, Development and Evaluation (GRADE) Working Group.[52] The strength of evidence was assessed for outcomes identified by the clinical investigators to be most clinically important: acute pain, chronic pain, mortality (30-day), and the incidence of serious adverse effects (e.g., stroke, myocardial infarction, delirium, renal failure). The following four major domains were examined: risk of bias (low, medium, high), consistency (inconsistency not present, inconsistency present, unknown or not applicable), directness (direct, indirect), and precision (precise, imprecise).

Each key outcome on each comparison of interest was given an overall evidence grade based on the ratings for the individual domains. The overall strength of evidence was graded as “high” (indicating high confidence that the evidence reflects the true effect and further research is very unlikely to change our confidence in the estimate of effect); “moderate” (indicating moderate confidence that the evidence reflects the true effect and further research may change our confidence in the estimate of effect and may change the estimate); “low” (indicating low confidence that the evidence reflects the true effect and further research is likely to change our confidence in the estimate of effect and is likely to change the estimate); and “insufficient” (indicating that evidence is either unavailable or does not permit estimation of an effect). When no studies were available for an outcome or comparison of interest, the evidence was graded as insufficient. A detailed explanation of the parameters used to grade the evidence and their operationalization are summarized in Appendix J. The GRADEprofiler (GRADEpro), software (GRADE Working Group) was used and the results modified in accordance with the AHRQ GRADE model. The body of evidence was graded independently by two reviewers (AMAS, DD); disagreements were resolved through discussion.

Peer Review

Ten experts in the field (Appendix A) agreed to peer review the draft report and provide comments. Reviewer comments were considered by the UAEPC in preparation of the final

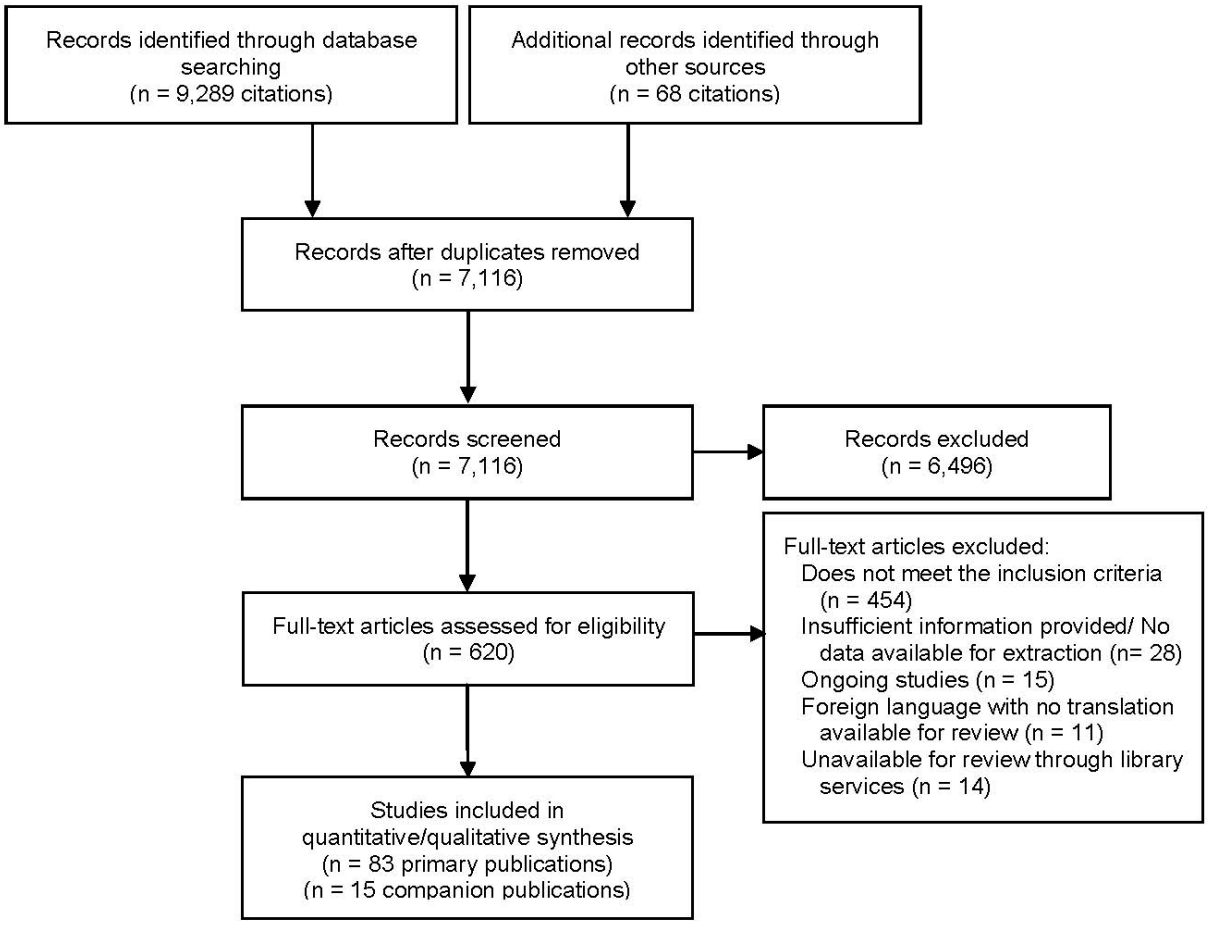
report. All peer reviewer comments and the UAEPC disposition of comments were submitted to AHRQ for assessment and approval.

Results

Search Results

All citations generated from electronic or hand searching and expert nominated studies were pooled into a single database (Figure 2).[53] Of these 9,357 citations retrieved, 2,241 were duplicates and 7,116 were considered to be unique study reports. Following level I screening, 6,496 were excluded and 620 were further evaluated for inclusion. Of these, 83 primary publications[26,41-43,54-132] passed level II screening and were included in this Comparative Effectiveness Review. An additional 15 companion publications[133-146] were identified and also included. The characteristics of the publications excluded at level II screening are presented in Appendix D. The main exclusion criteria were publication type (e.g., case-report, observational study, review), population characteristics (e.g., average age below 50, fractures other than hip fractures), no details of pain management intervention, and no extractable data related to outcomes of importance to the review (e.g., ongoing studies).

Figure 2. Flow diagram for study retrieval and selection



Description of Included Studies

Based on the interventions reported in each study, the primary publications were divided into eight groups: systemic analgesia (n = 3),[41,42,55] anesthesia (n = 30),[56-73,75-85,145] complementary and alternative medicine (CAM) (n = 2),[43,54] multimodal pain management (n = 2),[86,87] nerve blocks (n = 32),[88-119] neurostimulation (n = 2),[120,121] rehabilitation (n = 1),[122] and traction (n = 11).[26,123-132] The studies were published between 1990 and 2010 (median = 2003 [interquartile range (IQR): 1998 to 2007]). The majority of the studies were RCTs performed in single university settings in Europe, investigated pre- or intra-operative pain management interventions for hip fracture patients, and were published in peer-reviewed journals (Table 2).

Table 2. Characteristics of included studies

Publication type	Published manuscript	75
	Conference proceedings	7
	Dissertation	1
Study design	RCT	64
	nRCT	5
	Retrospective cohort study	8
	Prospective cohort study	6
Setting	General hospital	28
	Orthopedic hospital	1
	University hospital	54
Country	Asia/Australia	9
	Europe	56
	Middle East/North Africa	11
	North America	5
	South America	2
Number of centers	Single center	78
	Two centers	4
	Multicenter	1
Timing of intervention	Preoperative	32
	Intra-operative	36
	Postoperative	15

nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Methodological Quality of Included Studies

The risk of bias (RoB) of each included randomized and nonrandomized trial was assessed using the RoB tool by two independent reviewers and the consensus ratings are presented in Appendices G and H. The methodological quality of each included cohort study was assessed using the Newcastle Ottawa Scale (NOS) by two independent reviewers and the consensus ratings are presented in Appendix I. A summary of the overall quality trends by study design is presented below.

Randomized and Nonrandomized Controlled Trials

Of the 69 randomized controlled trials (RCTs) and nonrandomized controlled trials (nRCTs), 30 trials[26,54,56,60,64,68,77,88,90,92-94,98,106,110,112,114,116,120-131] were rated as having high risk of bias (RCTs = 24; nRCTs = 5), 37 RCTs[41-43,55,57-59,61-63,65-67,69-73,75,76,89,91,97,99-105,107-109,111,113,115,145] were rated as having an unclear risk of bias, and 2 RCTs[95,96] were considered to have a low risk of bias.

Cohort Studies

Data were prospectively collected in six cohort studies[78,79,85-87,132] and retrospectively in eight.[80-84,117-119] Overall, the methodological quality of the cohort studies was moderate (median score =7 stars; IQR: 6 to 8).

Results of Included Studies

This section is organized by intervention category (i.e., systemic analgesia, anesthesia, etc.). Within each intervention category, the results are presented for the four key questions addressed in this report: KQ1: Acute and chronic pain management; KQ2: Other outcomes; KQ3: Adverse effects; and, KQ4: Effectiveness and safety in differing subpopulations. For each category, we provide a description of the characteristics and findings of the individual trials and cohort studies and a summary of key findings. Appendixes E and F present detailed evidence tables on each of the included studies.

Systemic Analgesia

Overview of Included Studies

Three RCTs[41,42,55] evaluated the efficacy and/or harms of different types of systemic analgesia, in a total of 214 participants; sample sizes ranged from 30 to 94. See Table E-1 (Appendix E) for details of the study characteristics. Two RCTs[41,42] compared different parenteral analgesics (parecoxib IV vs. diclofenac ± meperidine IM, and intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine, respectively). The third RCT[55] compared different oral analgesics (lysine clonixinate vs. metamizole). See Table F-1 (Appendix F) for details of the interventions. The mean age of participants in the trials ranged from 77.3 to 78.5 years. Most were female (74.5 percent). Acute pain was measured using the 10cm Visual Analogue Scale (VAS) and the mean baseline pain measure was 6.5cm. All three trials had an unclear risk of bias (Appendix G). Summary of the evidence from these trials is provided in Table 3.

Table 3. Evidence addressing key questions: Systemic analgesia

Key Question	Outcome	Evidence availability	Summary of Evidence
KQ1	**Acute pain***	Yes	2 RCTs reported statistically significant effects in favor of parecoxib IV and intrathecal isotonic clonidine vs. diclofenac ± meperidine IM and intrathecal hypertonic clonidine, respectively. 1 RCT reported no statistically significant difference between lysine clonixinate vs. metamizole. The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	No	
	Functional status	No	
	Pain medication use; change in type and quantity	Yes	1 RCT comparing lysine clonixinate vs. metamizole reported no statistically significant difference.
	Mental status* (e.g., delirium, confusion)	Yes	1 RCT comparing lysine clonixinate vs. metamizole reported no statistically significant difference. The strength of the evidence was rated as insufficient.
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	No	
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	Yes	1 RCT comparing intrathecal isotonic vs. hypertonic clonidine reported no events of damage to surrounding structures, headaches, or infections. 1 RCT comparing lysine clonixinate vs. metamizole reported a statistically significant higher incidence of adverse effects and gastrointestinal disturbances in the lysine clonixinate group; other adverse effects were not significant.
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

Acute pain (post-treatment means) was reported in all three RCTs[41,42,55] (Table 4). One RCT[41] compared parecoxib intravenous (IV) (n = 35) vs. diclofenac intramuscular (IM) ± meperidine IM (n = 55). There was a statistically significant effect difference in additional pain relief in favor of parecoxib IV (mean difference [MD] -0.70; 95% confidence interval [CI] -1.04, -0.36; p <0.0001). This was not considered clinically significant.

The second RCT[42] compared intrathecal isotonic clonidine (n = 15) versus intrathecal hypertonic clonidine (n = 15). There was a statistically significant effect difference in additional

acute pain relief (post-treatment means) in favor of isotonic clonidine (MD -1.69; 95% CI -2.01, -1.37; p <0.00001). This was not considered clinically significant.

The third RCT[55] compared lysine clonixinate (n = 48) versus metamizole (n = 46), but no evidence of a significant effect difference (post-treatment means and at rest) was noted (MD -0.43; 95% CI -1.30, 0.44; p = 0.33).

The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Key Question 2. Other outcomes

Pain medication use. Additional pain medication use was reported in one RCT[55] comparing lysine clonixinate (n = 48) versus metamizole (n = 46). There was no statistically significant difference in the number of participants requiring additional pain medication (odds ratio [OR] 3.00; 95% CI 0.30, 29.94; p = 0.35) (Table 4).

Mental status. The incidence of delirium was reported in one RCT[55] comparing lysine clonixinate (n = 48) versus metamizole (n = 46). There was no statistically significant difference in the number of participants developing delirium (OR 0.96; 95% CI 0.06, 15.77; p = 0.98) (Table 4). The strength of the evidence was rated as insufficient to make any firm conclusions regarding this intervention.

Key Question 3. Adverse effects

Data on adverse effects associated with the administration of different types of systemic analgesia were available from two RCTs.[42,55] One RCT[55] comparing lysine clonixinate (n = 48) versus metamizole (n = 46) reported the number of participants with any adverse event and found a statistically significant difference in the number of patients experiencing any adverse event, in favor of metamizole (OR 3.50; 95% CI 1.04, 11.81; p = 0.04) (Table 4). Similarly, fewer patients in the metamizole group reported any gastrointestinal disturbance (OR 11.84; 95% CI 1.45, 96.75; p = 0.02) (Table 4). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

Key Question 4: Efficacy, effectiveness, and safety in subpopulations

No data were reported on subpopulations.

Table 4. Evidence summary table (randomized controlled trials): Systemic analgesia

	Outcome or subgroup	Studies (N)	Participants (N)	Statistical method	Effect estimate	I^2
KQ1	**Acute pain (post-treatment means)**					
	Parecoxib IV vs. diclofenac ± meperidine IM[41]	1	90	MD (95% CI)	**-0.70 (-1.04, -0.36)***	NA
	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine[42]	1	30	MD (95% CI)	**-1.69 (-2.01, -1.37)***	NA
	Lysine clonixinate vs. metamizole[55]	1	94	MD (95% CI)	-0.43 (-1.30, 0.44)	NA
	Acute pain (at rest)					
	Lysine clonixinate vs. metamizole[55]	1	94	MD (95% CI)	-0.43 (-1.30, 0.44)	NA
KQ2	**Additional pain medication use**					
	Lysine clonixinate vs. metamizole[55]	1	94	OR (95% CI)	3.00 (0.30, 29.94)	NA
	Mental status (e.g., delirium, confusion)					
	Lysine clonixinate vs. metamizole[55]	1	94	OR (95% CI)	0.96 (0.06, 15.77)	NA
KQ3	**Any adverse event**					
	Lysine clonixinate vs. metamizole[55]	1	94	OR (95% CI)	**3.50 (1.04, 11.81)***	NA
	Damage to surrounding structures					
	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine[42]	1	30		NE	
	Gastrointestinal disturbances					
	Lysine clonixinate vs. metamizole[55]	1	94	OR (95% CI)	**11.84 (1.45, 96.75)***	NA
	Headache					
	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine[42]	1	30		NE	
	Infection					
	Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine[42]	1	30		NE	
	Respiratory distress					
	Lysine clonixinate vs. metamizole[55]	1	94	OR (95% CI)	0.96 (0.06, 15.77)	NA

CI = confidence interval; IM = intramuscular; KQ = key question; MD = mean difference; NA = not applicable; NE = not estimable; OR = odds ratio; * = statistically significant difference

Anesthesia

Overview of Included Studies

Twenty-one RCTs[56-73,75,76,145] and one nRCT[77] evaluated the efficacy and/or harms of anesthesia including neuraxial (i.e., continuous or single administration spinal or epidural anesthesia) or neuraxial anesthesia versus general anesthesia in a total of 1,062 participants; study sample sizes ranged from 20 to 90. Additionally, eight cohort studies[78-85] provided data on spinal anesthesia versus general anesthesia or other modes of administration of spinal anesthesia in 3,086 participants; study sample sizes ranged from 25 to 1,333. The mean age of participants ranged from 69.8 to 86.0 years. Most were female (range = 38.9 to 100 percent). Acute pain was measured using different scales (numeric rating score [NRS] [1-5] and 10cm VAS). The average

baseline VAS pain score was 4.7. See Tables E-2 and F-2 (Appendices E and F) for details of the study characteristics and the interventions.

Four RCTs[56,60,64,68] and one nRCT[77] had a high risk of bias, while the other 17 RCTs[57-59,61-63,65-67,69-76] had an unclear risk of bias (Appendix G). The cohort studies were of moderate quality (median = 8) (Appendix I). Summary of the evidence from these trials is provided in Table 5.

Based on the primary interventions and comparison groups, the studies were grouped as follows:

1. Spinal anesthesia versus epidural or general anesthesia (n = 10);[56,59,60,64,65,78,81,82,84,85]
2. Neuraxial anesthesia: addition of clonidine, fentanyl, meperidine, morphine, or sufentanil (n = 14);[57,58,63,65-70,73,74,76,77,80]
3. Neuraxial anesthesia: different doses or modes of administration (n = 13)
   a. Spinal anesthesia (mode of administration: [e.g., continuous vs. single administration])[62,64,65,71,82,83]
   b. Spinal anesthesia (different doses)[61,63,72,74,75,79,80,82]

Table 5. Evidence addressing key questions: Anesthesia

Key Question	Outcome	Evidence availability	Summary of evidence
KQ 1	**Acute pain***	Yes	1 RCT reported a statistically significant effect difference in favor of spinal anesthesia vs. general anesthesia. The strength of the evidence was rated as insufficient. 3 RCTs and 1 nRCT reported no significant difference comparing the addition of fentanyl, morphine or sufentanil vs. standard spinal anesthesia. The strength of the evidence was rated as insufficient.
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	Yes	2 RCTs and 2 cohort studies comparing continuous vs. single spinal anesthesia reported no statistically significant difference except for the incidence of 30-day mortality following continous spinal anesthesia compared with general anesthesia. The strength of the evidence was rated as low.

Table 5. Evidence addressing key questions: Anesthesia (continued)

Key Question	Outcome	Evidence availability	Summary of Evidence
KQ2	**Mortality (30-day* and up to 1-year postfracture)**		3 RCTs and 1 cohort study comparing continuous vs. single spinal anesthesia reported no statistically significant difference. The strength of the evidence was rated as insufficient.
	Functional status	No	
	Pain medication use; change in type and quantity	Yes	6 RCTs comparing the addition of clonidine, fentanyl, morphine or sufentanil with standard spinal anesthesia were indeterminate. 2 RCTs comparing continuous vs. single spinal anesthesia were indeterminate. 1 RCT comparing different doses of spinal anesthesia found no statistically significant difference.
	Mental status* (e.g., delirium, confusion)	Yes	1 RCT comparing the use of spinal anesthesia vs. general anesthesia found no statistically significant difference. The strength of the evidence was rated as insufficient. 1 RCT comparing the addition of morphine with standard spinal anesthesia found no statistically significant difference. The strength of the evidence was rated as low. 2 RCTs comparing continuous vs. single spinal anesthesia found no statistically significant difference. The strength of the evidence was rated as low. 1 cohort study comparing 4 vs. 12mg bupivacaine found no statistically significant difference. The strength of the evidence was rated as insufficient.
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	Yes	2 RCTs comparing spinal vs. general anesthesia found LOS for acute hospitalization was significantly less in the general anesthesia group. 2 RCTs comparing continuous vs. single spinal anesthesia found no statistically significant difference.

Table 5. Evidence addressing key questions: Anesthesia (continued)

Key Question	Outcome	Evidence availability	Summary of Evidence
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	Yes	2 cohort studies comparing single dose spinal vs. general anesthesia, and 4mg vs. 12mg bupivacaine reported a statistically significant effect difference in hypotension in favor of spinal anesthesia and less bupivacine. Evidence for the other outcomes was indeterminate. 1 RCT comparing the addition of sufentanil vs. standard spinal anesthesia reported a significantly higher incidence of hypotension with standard spinal anethesia. Evidence for the other outcomes in 10 RCTs comparing the addition of clonidine, fentanyl, meperidine, morphine or sufentanil vs. standard spinal anesthesia was indeterminate. 1 RCT and 1 cohort study comparing different doses of spinal anesthesia reported the incidence of participants having hypotention was significantly greater with higher doses and higher concentrations of spinal anesthesia. Other adverse events were examined in single trials and the strength of the evidence for the probability of stroke, myocardial infarction, delirium or renal failure was rated as insufficient.
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

Spinal vs. General Anesthesia

One RCT[60] comparing spinal anesthesia (n = 15) vs. general anesthesia (n = 15) reported a statistically significant difference of additional pain relief in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42; p = 0.0001) (Table 6-B). This was not considered clinically significant. The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

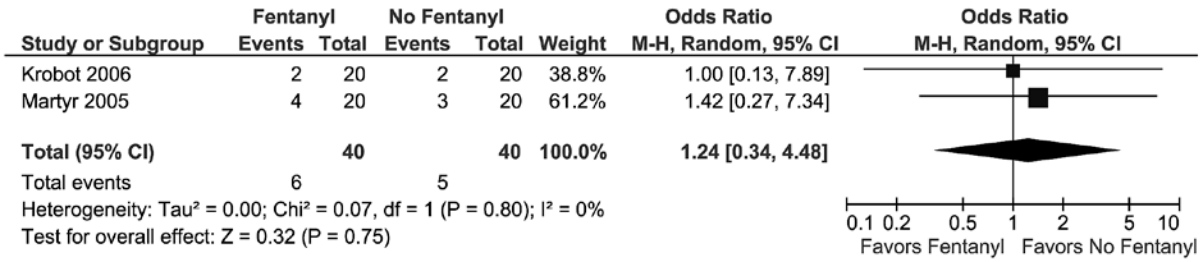
Neuraxial Anesthesia: Addition of Clonidine, Fentanyl, Meperidine, Morphine, or Sufentanil

Acute pain (post-treatment means) was reported in three RCTs[66,69,73] comparing additional fentanyl (n = 20) vs. standard spinal anesthesia (n = 20),[69] additional morphine (n = 20) versus standard spinal anesthesia (n = 20),[66] and additional sufentanil (n = 25) versus standard spinal anesthesia (n = 25).[73] In the studies comparing the addition of fentanyl or sufentanil, no patients reported feeling pain following the procedure. In the study comparing the addition of morphine, there was no significant difference in pain relief versus standard spinal anesthesia (MD = -0.36; 95% CI -1.11, 0.39; p = 0.35) (Table 6-G).

Acute pain on day 1 was reported in one RCT[69] and one nRCT[77] comparing additional fentanyl (n = 40) versus standard spinal anesthesia (n = 40). There was no significant difference

in pain on day 1 following the addition of fentanyl (OR 1.24; 95% CI 0.34, 4.48; p = 0.75) (Table 6-E and Figure 3). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Figure 3. Neuraxial anesthesia: Addition of fentanyl—acute pain (day 1)



Key Question 2. Other outcomes

Spinal vs. General Anesthesia or Spinal vs. Epidural Anesthesia

Mortality (30-day). Thirty-day mortality was reported in two RCTs[56,64] (n = 99 participants). There was no significant difference in mortality rates following spinal anesthesia versus general anesthesia (10/53 vs. 5/46; OR 1.73; 95% CI 0.53, 5.68; p = 0.36) (Table 6-B).

Additionally, 30-day mortality was reported in five cohort studies[78,81,82,84,85] (n = 2960 participants) (Table 7-A). There was no significant difference in mortality rates following spinal anesthesia vs. general anesthesia (78/1259 vs. 117/1701; OR 0.87; 95% CI 0.45, 1.67; p = 0.68. Subgroup analyses according to the mode of administration of spinal anesthesia revealed a statistically significant difference in the incidence of 30-day mortality for participants receiving continuous spinal anesthesia compared with general anesthesia (8/182 vs. 4/28; OR 0.28; 95% CI 0.08, 0.99; P = 0.05) favoring spinal anesthesia. There was no significant difference in mortality rates following single dose spinal versus general anesthesia (70/1077 vs. 113/1673; OR 1.08; 95% CI 0.58, 2.01; p = 0.80). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Mental status. Delirium measured with the Mini Mental State Examination (MMSE) was reported in one RCT[60] comparing spinal anesthesia (n = 15) vs. general anesthesia (n = 15) (Table 6-B). There was no significant difference between the two groups (8/15 vs. 9/15; OR 0.76; 95% CI 0.18, 3.24; p = 0.71). Additionally, delirium was reported in two cohort studies[78,84] There was no significant difference in the incidence of delirium comparing spinal versus general anesthesia (12/448 vs. 11/529; OR 0.79; 95% CI 0.04, 14.13; p = 0.87). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Health services utilization. Length of stay (LOS) for acute hospitalization was reported in two RCTs[56,64] comparing spinal anesthesia (n = 53) vs. general anesthesia (n = 46) (Table 6-B). The LOS was significantly less in the general anesthesia group (MD 1.69; 95% CI 0.38, 3.01; p = 0.01). The variance for one trial[64] was imputed from the reported p-value, while the variance for the second trial[56] was imputed from the first trial,[64] as no measure of variance was reported. LOS for acute hospitalization was also reported in one cohort study[85] comparing single spinal anesthesia (n = 383) to general anesthesia (n = 950) but the difference could not be estimated as no measure of variance was reported.

Neuraxial Anesthesia: Addition of Clonidine, Fentanyl, Meperidine, Morphine, or Sufentanil

Additional pain medication use. Additional pain medication use was reported in sixRCTs[58,65-67,73,76] (Table 6D to 6-H). Differences in effect estimates from one RCT[65] (n = 40 participants) comparing the addition of clonidine vs. standard spinal anesthesia was not estimable because all participants required additional pain medication. The pooled estimate from three trials[58,67,76] comparing the addition of fentanyl vs. standard spinal anesthesia (n = 102 participants) showed no statistically significant difference between groups (2/51 vs. 0/51; OR 5.51; 95% CI 0.25, 122.08; p = 0.28).

There was no significant difference in additional pain medication use in the RCT[66] (n = 40) that compared the addition of morphine to spinal anesthesia vs. standard spinal anesthesia (9/20 vs. 15/20; OR 0.27; 95% CI 0.07, 1.04; p = 0.06). Similarly, there was no difference in reported additional pain medication use between three RCTs[67,73,76] that compared the addition of sufentanil to spinal anesthesia with standard spinal anesthesia (1/66 vs. 0/ 66; Peto OR 7.39; 95% CI 0.15, 372.38; p = 0.32).

Mental status. Confusion was reported in one RCT[66] (n = 40) comparing the addition of morphine versus standard spinal anesthesia (Table 6-G). There was no significant difference in the incidence of postoperative confusion (1/20 vs. 0/20; OR 3.15; 95% CI 0.12, 82.16; p = 0.49). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Neuraxial Anesthesia: Different Doses and Modes of Administration

Spinal Anesthesia (Continuous vs. Single Administration)

Mortality (30-day). Three RCTs[62,64,71] (n = 163) reported 30-day mortality (Table 6-C). Two of the RCTs[62,71] did not record any events in either group. In the third RCT,[64] there was no significant difference between continuous vs. single administration spinal anesthesia (2/14 vs. 4/15; OR 0.46; 95% CI 0.07, 3.02; p = 0.42). Additionally, it should be noted that 30-day mortality was reported in one other cohort study[82] (n = 291) (Table 7-B). There was no significant difference between continuous vs. single administration of spinal anesthesia (8/182 vs. 5/109; OR 0.96; 95% CI 0.30, 3.00; p = 0.94). The strength of the evidence was rated as low to make any firm conclusions regarding these interventions.

Additional pain medication. Additional pain medication use was reported in two RCTs[62,71] (n = 134) (Table 6-C). The OR in additional pain medication use was not estimable as there were no events in either group.

Health services utilization. LOS for acute hospitalization was reported in two RCTs[62,64] (n = 89). There was no significant difference between groups (MD = -0.98; 95% CI -2.06, 0.10; p = 0.07; Table 6-C). The variance for one trial[64] was imputed from the reported p-value.

Mental status. Confusion was reported in two RCTs[62,71] (n = 134) (Table 6-C). There was no significant difference between groups in the occurrence of confusion (5/67 vs. 4/67; OR 1.27; 95% CI 0.32, 4.99; p = 0.73). The strength of the evidence was rated as low to make any firm conclusions regarding these interventions.

Spinal Anesthesia (Different Doses)

Delirium. One cohort study[80] (n = 60) reported that there was no significant difference in the incidence of delirium between the two groups (2/30 vs. 4/30; OR 0.46; 95% CI 0.08, 2.75; p = 0.40) (Table 7-D). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Mortality (30-day). One cohort study[82] (n = 182) reported that there was no significant difference in 30-day mortality rates between the two groups (4/121 vs. 4/61; OR 0.49; 95% CI 0.12, 2.02; p = 0.32) (Table 7-D). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Pain medication use. Additional pain medication use was reported in one RCT[63] (n = 60) (Table 6-I). There was no significant difference between groups following spinal anesthesia at different doses (4 vs. 5mg, 4 vs. 6mg, or 5 vs. 6mg).

Key Question 3. Adverse effects

Spinal vs. General Anesthesia or Spinal vs. Epidural Anesthesia

Two RCTs[60,64] (n = 73) and one cohort study[82] (n = 333) evaluated the nature and frequency of adverse effects associated with the administration of spinal anesthesia versus general anesthesia (Table 6-B, 7-A). There were no significant differences in the occurrence of hypotension in the RCTs[60,64] (21/44 vs. 21/29; OR 0.36; 95% CI 0.04, 2.92; p = 0.34). The pooled incidence of hypotension from the different arms of the cohort study[82] is not reported because of marked heterogeneity among the included cohorts. There was no significant difference in the incidence of hypotension in the continuous spinal anesthesia groups compared with general anesthesia (OR 0.35; 95% CI 0.10, 1.28; p = 0.11). There was a significantly lower incidence of hypotension with single dose spinal anesthesia compared with general anesthesia (OR 0.04; 95% CI 0.01, 0.13; p < 0.00001). The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences between the pain management interventions.

Neuraxial Anesthesia: Addition of Clonidine, Fentanyl, Meperidine, Morphine, or Sufentanil

A total of 11 RCTs[57,58,65-70,73,74,76] and one nRCT[77] (n = 490) evaluated the harms of the administration of clonidine, fentanyl, meperidine, morphine, or sufentanil during neuraxaial anesthesia (Table 6-D to 6-H).

Addition of Clonidine

The reported adverse effects were from a single RCT[65] and did not demonstrate any significant statistical differences (Table 6-D).

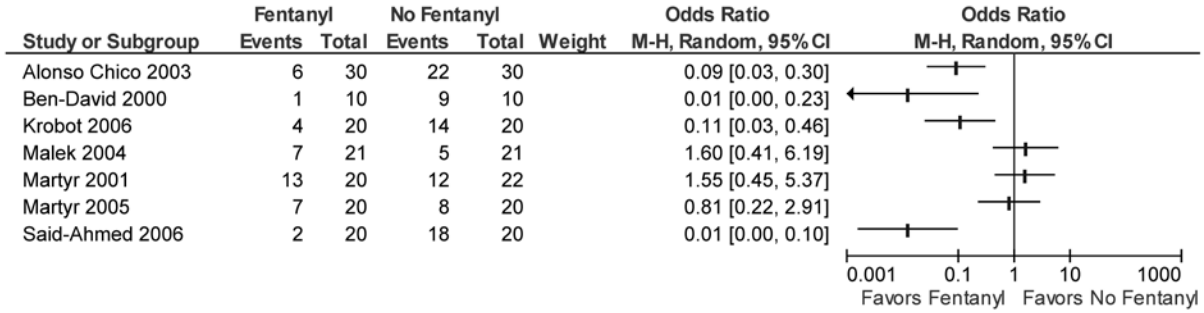
Addition of Fentanyl

Allergic reaction. There was no statistically significant difference in the number of participants reporting an allergic reaction in four trials[67-69,77] (14/81 vs. 5/83; OR 2.68; 95% CI 0.83, 9.80; p = 0.10) (Table 6-E).

Gastrointestinal (GI) symptoms. There were no reports of GI symptoms in three trials[69,74,77] (n = 140) (Table 6-E).

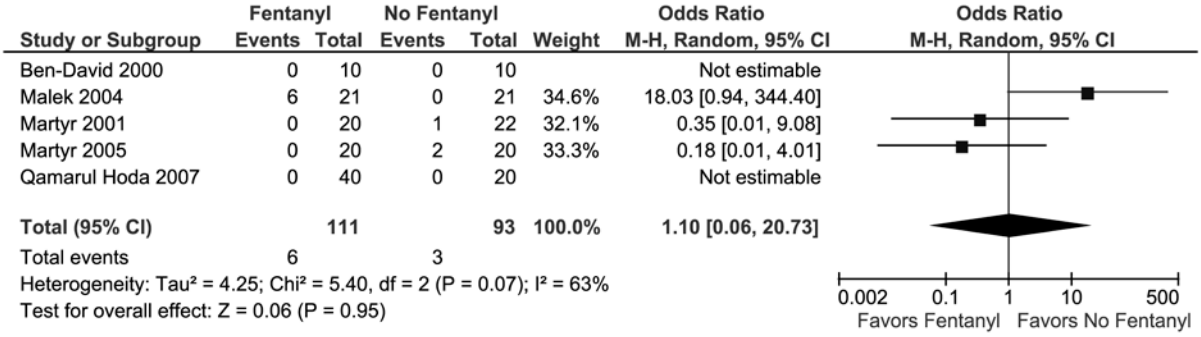
Hypotension. Seven trials[57,58,67-69,76,77] (n = 284) reported the frequency of hypotension (Figure 4). The pooled results are not reported due to high heterogeneity (I^2 = 83 percent) between the included studies, which was not explained by study design (i.e., removal of the nRCT[77]), risk of bias (i.e., removal of the trials[68,77] with a high risk of bias), or specific intervention details (i.e., type and quantity). No firm conclusion can be made regarding the impact of fentanyl on this outcome.

Figure 4. Neuraxial anesthesia: Addition of fentanyl—hypotension



Nausea/vomiting. In the five RCTs[58,67-69,74] (n = 204) that reported the frequency of nausea or vomiting there was no statistically significant difference between the groups (6/111 vs. 3/93; OR 1.10; 95% CI 0.06, 20.73; p = 0.95) (Figure 5).

Figure 5. Neuraxial anesthesia: Addition of fentanyl—nausea/vomiting



Respiratory distress. There were no reports of respiratory distress in three trials[67,68,77] (n = 124).

Other adverse effects. The remaining reported adverse effects were from single trials and did not demonstrate any statistically significant differences.

Addition of Meperidine

Adverse effects. The reported adverse effects were from a single trial and did not demonstrate any significant statistical differences.

Addition of Morphine

Adverse effects. The reported adverse effects were from a single trial and did not demonstrate any significant statistical differences.

Addition of Sufentanil

Hypotension. Three RCTs[67,73,76] (n = 132) reported a significantly lower incidence of hypotension in participants receiving sufentanil (8/66 in the group with sufentanil vs. 45/66 in the group with no sulfentantil; OR 0.05; 95% CI 0.01, 0.34; p = 0.002).

Other adverse effects. The remaining reported adverse effects were from single studies and did not demonstrate any significant statistical differences.

Neuraxial Anesthesia: Different Doses and Modes of Administration (i.e., Continuous vs. Single Administration)

Spinal Anesthesia (Continuous vs. Single Administration)

Hypotension. Hypotension was reported for two RCTs[64,71] (n = 103). There was a statistically significant difference between the groups (13/51 vs. 37/52; OR 0.12; 95% CI 0.03, 0.51; p = 0.004). Similarly, one cohort study[82] (n = 291) reported a statistically significant difference between groups (26/182 vs. 74/109; OR 0.08; 95% CI 0.04, 0.14; p < 0.00001).

Other adverse effects. The remaining reported adverse effects were from single trials and studies and did not demonstrate any significant statistical differences between the pain management interventions.

Spinal Anesthesia (Different Doses)

Bradycardia. Bradycardia was reported in two RCTs[61,63] (n = 180). There was no significant difference for different doses of spinal anesthesia (bupivacaine: 4 vs. 5mg: 0/30 vs. 0/30; 4 vs. 6mg: 0/30 vs. 0/30; 5 vs. 6 mg: 3/29 vs. 3/31; levobupivacaine: 3/29 vs. 3/31).

Hypotension. Hypotension was reported in four RCTs[61,63,72,75] (n = 210). There were statistically significant differences in hypotension following spinal anesthesia with 4mg versus 6mg of bupivacaine (0/30 vs. 10/30; OR 0.03; 95% CI 0.00, 0.58; p = 0.02). The remaining comparisons were not statistically significant.

Three cohort studies[79,80,82] reported hypotension in 267 participants. There was a statistically significant reduction in hypotension following spinal anesthesia with 2.5mg versus 5mg of bupivacaine (5/121 vs. 21/61; OR 0.08; 95% CI 0.03, 0.23; p <0.00001), 4mg versus 12mg of bupivacaine (3/30 vs. 23/30; OR 0.03; 95% CI 0.01, 0.15) and 0.125% vs. 0.5% of bupivacaine (4/12 vs. 10/13; OR 0.15; 95% CI 0.03, 0.87; p = 0.03).

Nausea/vomiting. There were no reports of nausea or vomiting in two RCTs[63,74] (n = 100).

Other adverse effects. The remaining reported adverse effects were from single RCTs and cohort studies and did not demonstrate any significant statistical differences between the pain management interventions.

Key Question 4. Efficacy, effectiveness, and safety in subpopulations

No data were reported on subpopulations.

Table 6. Evidence summary table (randomized and nonrandomized controlled trials): Anesthesia

Table 6-A. Epidural (continuous) versus spinal anesthesia (continuous): (RCT/nRCT)

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ3	**Damage to surrounding structures**[65]	1	40		NE	NA

KQ = key question; NA = not applicable; NE = not estimable; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-B. Spinal versus general anesthesia: (RCT/nRCT)

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**					
	Spinal anesthesia (single)[60]	1	30	MD (95% CI)	**-0.86 (-1.30, -0.42)***	NA
KQ2	**Mental status (e.g., delirium, confusion)**					
	Spinal anesthesia (single)[60]	1	30	OR (95% CI)	0.76 (0.18, 3.24)	NA
	LOS[56,64]	2	99	MD (95% CI)	**1.69 (0.38, 3.01)***	0%
	Spinal anesthesia (incremental)[64]	1	21	MD (95% CI)	2.00 (-0.16, 4.16)	NA
	Spinal anesthesia (single)[56,64]	2	78	MD (95% CI)	1.55 (-0.20, 3.31)	7%
KQ2	**Mortality 30-day**[56,64]	2	99	OR (95% CI)	1.73 (0.53, 5.68)	0%
	Spinal anesthesia (incremental)[64]	1	21	OR (95% CI)	1.00 (0.07, 13.37)	NA
	Spinal anesthesia (single)[56,64]	2	78	OR (95% CI)	2.01 (0.53, 7.61)	0%
KQ3	**Hypotension**	2	73	OR (95% CI)	0.36 (0.04, 2.92)	72%
	Spinal anesthesia (incremental)[64]	1	21	OR (95% CI)	**0.07 (0.01, 0.61)***	0%
	Spinal anesthesia (single)[60,64]	2	52	OR (95% CI)	0.76 (0.06, 9.90)	75%
	Myocardial infarction	1	43	OR (95% CI)	1.55 (0.06, 42.91)	NA
	Spinal anesthesia (incremental)[64]	1	21		NE	
	Spinal anesthesia (single)[64]	1	22	OR (95% CI)	1.55 (0.06, 42.91)	NA
	ST depression	1	43	OR (95% CI)	0.56 (0.11, 2.81)	27%
	Spinal anesthesia (incremental)[64]	1	21	OR (95% CI)	0.22 (0.03, 1.85)	NA
	Spinal anesthesia (single)[64]	1	22	OR (95% CI)	1.17 (0.19, 7.12)	NA

CI = confidence intervals; KQ = key question; LOS = length of stay; MD = mean difference; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials; * = statistically significant

Table 6-C. Spinal anesthesia (continuous vs. single administration): (RCT/nRCT)

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Additional pain medication use**[62,71]	2	134		NE	
	Mental status (e.g., delirium or confusion)[62,71]	2	134	OR (95% CI)	1.27 (0.32, 4.99)	0%
	LOS[62,64]	2	89	MD (95% CI)	-0.98 (-2.06, 0.10)	0%
	Mortality 30-day[62,64,71]	3	163	OR (95% CI)	0.46 (0.07, 3.02)	NA
KQ3	**Bradycardia**[71]	1	74		NE	
	GI symptoms[62]	1	60	OR (95% CI)	1.00 (0.06, 16.76)	NA
	Headache[62]	1	60		NE	
	Hypotension[64,71]	2	103	OR (95% CI)	**0.12 (0.03, 0.51)***	50%
	MI[64]	1	29	OR (95% CI)	0.33 (0.01, 8.88)	NA
	Myocardial ischemia[71]	1	74		NE	
	ST depression[64]	1	29	OR (95% CI)	0.19 (0.03, 1.16)	NA
	Stroke[71]	1	74		NE	

CI = confidence intervals; KQ = key question; LOS = length of stay; MD = mean difference; MI = myocardial infarction; NE = not estimable; OR = odds ratio; * = statistically significant; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-D. Neuraxial anesthesia (addition of clonidine): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Additional pain medication use**[65]	1	40		NE	
	Epidural anesthesia (continuous)[65]	1	20		NE	
	Spinal anesthesia (continuous)[65]	1	20		NE	
KQ3	**Damage to surrounding structures**[65]	1	40		NE	
	Epidural anesthesia (continuous)[65]	1	20		NE	
	Spinal anesthesia (continuous)[65]	1	20		NE	
	Headache[65]	1	40		NE	
	Epidural anesthesia (continuous)[65]	1	20		NE	
	Spinal anesthesia (continuous)[65]	1	20		NE	
	Infection[65]	1	40		NE	
	Epidural anesthesia (continuous)[65]	1	20		NE	
	Spinal anesthesia (continuous)[65]	1	20		NE	

KQ = key question; NE = not estimable; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-E. Spinal (single) anesthesia (addition of fentanyl): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**[69]	1	40		NE	
	Day 1 pain[69,77]	2	80	OR (95% CI)	1.24 (0.34, 4.48)	0%
KQ2	**Additional pain medication use**[58,67,76]	3	102	OR (95% CI)	5.51 (0.25, 122.08)	
KQ3	**Allergic reaction**[67-69,77]	4	164	OR (95% CI)	2.86 (0.83, 9.80)	16%
	Bradycardia[67]	1	42	OR (95% CI)	8.14 (0.39, 167.98)	NA
	GI symptoms[69,74,77]	3	140		NE	
	Headache[77]	1	40		NE	
	Hypotension[57,58,67-69,74,77]	7	284		NR	83%
	Nausea/ vomiting[58,67-69,74]	5	204	OR (95% CI)	1.10 (0.06, 20.73)	63%
	Neurological complications[77]	1	40		NE	
	Respiratory distress[67,68,77]	3	124		NE	

CI = confidence intervals; KQ = key question; NA = not applicable; NR = not reported; NE = not estimable OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-F. Spinal (continuous) anesthesia (addition of meperidine): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ3	**Headache**[70]	1	34		NE	

KQ = key question; NE = not estimable; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-G. Spinal (single) anesthesia (addition of morphine): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**[66]	1	40	MD (95% CI)	-0.36 (-1.11, 0.39)	NA
KQ2	**Additional pain medication use**[66]	1	40	OR (95% CI)	0.27 (0.07, 1.04)	NA
	Mental status (e.g., delirium, confusion)[66]	1	40	OR (95% CI)	3.15 (0.12, 82.16)	NA
KQ3	**Allergic reaction**[66]	1	40	OR (95% CI)	1.00 (0.06, 17.18)	NA
	Any adverse event[66]	1	40	OR (95% CI)	4.75 (0.48, 46.91)	NA
	GI symptoms[66]	1	40	OR (95% CI)	11.18 (0.56, 222.98)	NA
	Headache[66]	1	40		NE	
	Hypopnoea[66]	1	40		NE	
	Hypotension[66]	1	40		NE	
	Nausea/vomiting[66]	1	40	OR (95% CI)	11.18 (0.56, 222.98)	NA
	Respiratory distress[66]	1	40		NE	

CI = confidence intervals; KQ = key question; MD = mean difference; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-H. Spinal (single) anesthesia (addition of sufentanil): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**[73]	1	50		NE	
KQ2	**Additional pain medication use)**[67,73,76]	3	132	OR (95% CI)	7.39 (0.15, 372.38)	0%
KQ3	**Allergic reaction**[67]	1	42		NE	
	Bradycardia[67]	1	42	OR (95% CI)	11.06 (0.56, 219.68)	NA
	Hypotension[67,73,76]	3	132	OR (95% CI)	**0.05 (0.01, 0.34)***	71%
	Nausea/vomiting[67]	1	42		NE	
	Respiratory distress[67]	1	42		NE	

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; OR = odds ratio; * = statistically significant; RCT/nRCT = randomized and nonrandomized controlled trials

Table 6-I. Spinal anesthesia (Different doses): RCT/nRCT

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Additional pain medication use**					
	Bupivacaine: 4 vs. 5mg[63]	1	60	OR (95% CI)	2.36 (0.63, 8.92)	NA
	Bupivacaine: 4 vs. 6mg[63]	1	60	OR (95% CI)	3.27 (0.77, 13.83)	NA
	Bupivacaine: 5 vs. 6mg[63]	1	60	OR (95% CI)	1.38 (0.28, 6.80)	NA
KQ3	**Allergic reaction**					
	Bupivacaine: 4 vs. 5mg[63]	1	60	OR (95% CI)	0.62 (0.15, 2.45)	NA
	Bupivacaine: 4 vs. 6mg[63]	1	60	OR (95% CI)	0.62 (0.15, 2.45)	NA
	Bupivacaine: 5 vs. 6mg[63]	1	60	OR (95% CI)	1.00 (0.28, 3.54)	NA

Table 6-I. Spinal anesthesia (Different doses): RCT/nRCT (continued)

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ3	**Bradycardia**					
	Bupivacaine: 4 vs. 5mg[63]	1	60		NE	
	Bupivacaine: 4 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 5 vs. 6mg[63]	1	60		NE	
	Levobupivacaine: 0.5% vs. 0.75%[61]	1	60	OR (95% CI)	1.08 (0.20, 5.82)	NA
	GI symptoms					
	Bupivacaine: 6 vs. 8mg[74]	1	40		NE	
	Bupivacaine: 6 vs.10mg[74]	1	40		NE	
	Bupivacaine: 8 vs.10mg[74]	1	40		NE	
	Hypotension					
	Bupivacaine: 2.5 vs. 5mg[75]	1	40	OR (95% CI)	0.81 (0.22, 2.91)	NA
	Bupivacaine: 4 vs. 5mg[63]	1	60	OR (95% CI)	0.10 (0.00, 1.88)	NA
	Bupivacaine: 4 vs. 6mg[63]	1	60	OR (95% CI)	**0.03 (0.00, 0.58)***	NA
	Bupivacaine: 5 vs. 6mg[63]	1	60	OR (95% CI)	0.31 (0.08, 1.13)	NA
	Bupivacaine: 0.15 – 0.25% vs. 0.5%[72]	1	30	OR (95% CI)	0.22 (0.04, 1.11)	NA
	Levobupivacaine: 0.5% vs. 0.75%[61]	1	60	OR (95% CI)	1.71 (0.60, 4.88)	NA
	Nausea/vomiting					
	Bupivacaine: 4 vs. 5mg[63]	1	60		NE	
	Bupivacaine: 4 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 5 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 6 vs. 8mg[74]	1	40		NE	
	Bupivacaine: 6 vs.10mg[74]	1	40		NE	
	Bupivacaine: 8 vs.10mg[74]	1	40		NE	
	Residual sensory deficits/motor weakness					
	Levobupivacaine: 0.5% vs. 0.75%[61]	1	60		NE	
	Respiratory distress					
	Bupivacaine: 4 vs. 5mg[63]	1	60		NE	
	Bupivacaine: 4 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 5 vs. 6mg[63]	1	60		NE	

Table 6-I. Spinal anesthesia (Different doses): RCT/nRCT (continued)

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ3	**Sedation**					
	Bupivacaine: 4 vs. 5mg[63]	1	60		NE	
	Bupivacaine: 4 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 5 vs. 6mg[63]	1	60		NE	
	Urinary retention					
	Bupivacaine: 4 vs. 5mg[63]	1	60		NE	
	Bupivacaine: 4 vs. 6mg[63]	1	60		NE	
	Bupivacaine: 5 vs. 6mg[63]	1	60		NE	

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 7. Evidence summary table (cohort studies): Anesthesia

Table 7-A. Spinal versus general anesthesia: Cohort studies

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Mortality 30-day**[78,81,82,84,85]	5	2960	OR (95% CI)	0.87 (0.45, 1.67)	61%
	Spinal anesthesia (continuous)[82]	1	210	OR (95% CI)	**0.28 (0.08, 0.99)***	NA
	Spinal anesthesia (single)[78,81,82,84,85]	5	2750	OR (95% CI)	1.08(0.58, 2.01)	53%
KQ3	**Headache**[82]	1	333		NE	
	Spinal anesthesia (continuous)[82]	1	203		NE	
	Spinal anesthesia (single)[82]	1	130		NE	
	Hypotension[82]	1	333		NR	84%
	Spinal anesthesia (incremental)[82]	1	130	OR (95% CI)	0.35 (0.10, 1.28)	NA
	Spinal anesthesia (single)[82]	1	203	OR (95% CI)	**0.04 (0.01, 0.13)***	NA

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; NR = not reported; OR = odds ratio; * = statistically significant

Table 7-B. Spinal anesthesia (continuous vs. single administration): Cohort studies

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Mortality 30-day**[82]	1	291	OR (95% CI)	0.96 (0.30, 3.00)	NA
KQ3	**Any adverse event**[82]	1	291		NE	
	Headache[82]	1	291		NE	
	Hypotension[82]	1	291	OR (95% CI)	**0.08 (0.04, 0.14)***	NA

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; OR = odds ratio; * = statistically significant

Table 7-C. Spinal (single) anesthesia (lateral vs. supine position): Cohort studies

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ3	**Bradycardia**[83]	1	41	OR (95% CI)	0.55 (0.15, 1.98)	NA
	Hypotension[83]	1	41	OR (95% CI)	**0.22 (0.06, 0.86)***	NA

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; OR = odds ratio; * = statistically significant

Table 7-D. Spinal anesthesia (Different doses): Cohort studies

	Outcome or Subgroup	Studies (N)	Participants (N)	Statistical Method	Effect Estimate	I^2
KQ2	**Delirium**					
	Bupivacaine 4 vs. 12mg[80]	1	60	OR (95% CI)	0.46 (0.08, 2.75)	NA
	Mortality 30-day					
	Bupivacaine 2.5 vs.5mg[82]	1	182	OR (95% CI)	0.49 (0.12, 2.02)	NA
KQ3	**Any adverse event**					
	Bupivacaine 2.5 vs.5mg[82]	1	182		NE	
	Headache					
	Bupivacaine 2.5 vs.5mg[82]	1	182		NE	
	Hypotension					
	Bupivacaine: 2.5 vs.5mg[82]	1	182	OR (95% CI)	**0.08 (0.03, 0.23)***	NA
	Bupivacaine: 4 vs. 12mg[80]	1	60	OR (95% CI)	**0.03 (0.01, 0.15)***	NA
	Bupivacaine: 0.125% vs. 0.5%[79]	1	25	OR (95% CI)	**0.15 (0.03, 0.87)***	NA

CI = confidence intervals; KQ = key question; NA: not applicable; NE = not estimable; OR = odds ratio; * = statistically significant

Complementary and Alternative Medicine (CAM)

Overview of Included Studies

Two RCTs[43,54] evaluated the efficacy and/or harms of the administration of complementary and alternative medicine (CAM) interventions vs. no intervention or sham intervention (n = 98 participants); sample sizes ranged from 38 to 60. The mean age ranged from 76.8 to 86.3 years. Most were female (81.7 to 86.7 percent). One RCT[43] compared acupressure (n = 18 participants) to sham control (n = 20) delivered preoperatively. Acute pain was measured using the VAS and the baseline pain measure was 6.5cm. The second RCT[54] compared the Jacobson relaxation technique (n = 30 participants) with no intervention (n = 30). Acute pain was measured using the 10-point verbal "Sensation of Pain and Distress Scale." Baseline pain measure was not reported for this trial. See Tables E-3 and F-3 (Appendices E and F) for details of the study characteristics and interventions.

One RCT[43] had an unclear risk of bias, while the other[54] had a high risk of bias (Appendix G). Summary of the evidence from these trials is provided in Table 8.

Table 8. Evidence addressing key questions: Complementary and alternative medicine

Key Question	Outcome	Evidence availability	Summary of Evidence
KQ 1	Acute pain*	Yes	2 RCTs reported a statistically significant effect in favor of the CAM interventions. The strength of the evidence was rated as insufficient.
	Chronic pain*	No	
KQ2	Mortality (30-day* and up to 1-year postfracture)	No	
	Functional status	No	
	Pain medication use; change in type and quantity	Yes	1 RCT reported a statistically significant effect in favor of relaxation.
	Mental status* (e.g., delirium, confusion)	No	
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	No	
KQ3	Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)	No	
KQ4	Effectiveness and safety in differing subpopulations	No	

KQ = key question; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation); CAM = complementary and alternative medicine

Key Question 1. Acute and chronic pain management

Acute Pain (Post-Treatment Means)

Acupressure reduced pain compared with a sham intervention[43] (MD -3.01; 95% CI -4.53, -1.49; p <0.0001; Table 9). It should be noted that the variance was imputed from the reported p value presented in this study. Relaxation also showed a reduction in pain compared with no relaxation (Sensation of Pain Scale (0-10): MD -1.10; 95% CI -1.43, -0.77; p <0.00001) (Table 9). This was not considered clinically significant. The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Key Question 2. Other outcomes

In the RCT[54] that compared relaxation versus no intervention, patients in the relaxation group required less additional pain medication (e.g., meperidine (mg) or morphine (mg)) compared with the control group (MD -8.43; 95% CI -15.11, -1.75; p = 0.01; Table 9).

Key Question 3. Adverse effects

No data were reported on adverse effects.

Key Question 4. Efficacy, effectiveness and safety in subpopulations

No data were reported on subpopulations.

Table 9. Evidence summary table (randomized controlled trials): Complementary and alternative medicine

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**					
	Acupressure[43]	1	38	MD (95% CI)	**-3.01 (-4.53, -1.49)***	NA
	Relaxation[54]	1	60	MD (95% CI)	**-1.10 (-1.43, -0.77)***	NA
KQ2	**Additional pain medication**					
	Relaxation[54]	1	60	MD (95% CI)	**-8.43 (-15.11, -1.75)***	NA

KQ = key question; CI = confidence intervals; MD = mean difference; NA = not applicable; * = statistically significant

Multimodal Pain Management

Overview of Included Studies

Two prospective cohort studies[86,87] evaluated the effectiveness and/or harms of the administration of multimodal pain management versus standard care in 226 participants; sample size ranged from 106 to 120. The mean age was not reported for either study. Most were female (80.8 percent). One study[86] compared a formal postoperative protocol of IV and oral tramadol plus acetaminophen versus standard care. The second study[87] compared a formal preoperative protocol of skin traction, morphine and acetaminophen versus standard care. See Tables E-4 and F-4 (Appendixes E and F) for details of the study characteristics and interventions.

Based on the NOS, the study quality for both studies was moderate (5 to 7 stars) (Appendix I). Summary of the evidence from these studies is provided in Table 10.

Table 10. Evidence addressing key questions: Multimodal pain management

Key Question	Outcome	Evidence avaiability	Summary of evidence
KQ 1	**Acute pain***	No	
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	Yes	1 prospective cohort study comparing multimodal pain management with standard care reported no statistically significant difference. The strength of the evidence was rated as insufficient.
	Functional status	No	
	Pain medication use; change in type and quantity	No	
	Mental status* (e.g., delirium, confusion)	Yes	2 prospective cohort studies comparing multimodal pain management with standard care reported no statistically significant difference. The strength of the evidence was rated as insufficient.
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	No	
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	Yes	1 prospective cohort study comparing multimodal pain management with standad care reported no statistically significant difference. The strength of the evidence for the probability of stroke, myocardial infarction, delirium or renal failure was rated as insufficient.
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management.

There were no data on pain management.

Key Question 2. Other outcomes

Mortality (30-day and one year). Mortality was reported in one prospective cohort study[87] (n = 106) (Table 11). There was no significant difference between groups after 30 days (5/55 vs. 8/51; OR 0.54; 95% CI 0.16, 1.77; p = 0.31), or at 1 year (11/55 vs. 15/51; OR 0.60; 95% CI 0.25, 1.47; p = 0.26). The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Mental status. Delirium was reported in two prospective cohort studies[86,87] (n = 226) (Table 11). There was no significant difference between groups in the number of patients with delirium (12/60 vs. 14/60; OR 0.82; 95% CI 0.34, 1.96; p = 0.66);[86] (1/55 vs. 2/51; OR 0.45; 95% CI 0.04, 5.16; p = 0.52).[87] The strength of the evidence was rated as insufficient to make any firm conclusions regarding these interventions.

Key Question 3. Adverse effects

Data on adverse effects were reported in one prospective cohort study[87] and were not statistically significant (Table 11).

Key Question 4. Efficacy, effectiveness and safety in subpopulations

No data were reported on subpopulations.

Table 11. Evidence summary table (cohort studies): Multimodal pain management

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ2	**Mental status (e.g., delirium or confusion)**					
	Postoperative protocol[86]	1	120	OR (95% CI)	0.82 (0.34, 1.96)	NA
	Preoperative protocol[87]	1	106	OR (95% CI)	0.45 (0.04, 5.16)	NA
	Mortality 30-day					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.54 (0.16, 1.77)	NA
	Mortality 1 year					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.60 (0.25, 1.47)	NA
KQ3	**Angina**					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.13 (0.00, 6.32)	NA
	Deep venous thrombosis					
	Preoperative protocol[87]	1	106	OR (95% CI)	6.87 (0.14, 347.23)	NA
	Dehydration					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.93 (0.06, 15.20)	NA
	GI bleeding					
	Preoperative protocol[87]	1	106	OR (95% CI)	6.87 (0.14, 347.23)	NA
	Hyponatremia					
	Preoperative protocol[87]	1	106	OR (95% CI)	6.87 (0.14, 347.23)	NA
	Myocardial infarction					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.45 (0.04, 5.16)	NA
	Postoperative ileus					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.13 (0.00, 6.32)	NA
	Pulmonary edema					
	Preoperative protocol[87]	1	106	OR (95% CI)	6.87 (0.14, 347.23)	NA
	Pulmonary embolism					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.45 (0.04, 5.16)	NA
	Respiratory infection					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.13 (0.00, 6.32)	NA
	Sepsis					
	Preoperative protocol[87]	1	106	OR (95% CI)	6.87 (0.14, 347.23)	NA
	Stroke					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.13 (0.00, 6.32)	NA
	Urinary retention					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.10 (0.00, 1.81)	NA
	Urinary tract infection					
	Preoperative protocol[87]	1	106	OR (95% CI)	0.45 (0.04, 5.16)	NA

CI = confidence intervals; KQ = key question; NA = not applicable; OR = odds ratio

Nerve Blocks

Overview of Included Studies

Twenty-nine RCTs[88-116] (n = 1,757) evaluated the efficacy and/or harms of the administration of nerve blocks, including 3-in-1 (neurostimulation [NS]/ultrasound-guided [US]), combined lumbar/sacral plexus, fascia iliaca compartment, femoral, lumbar plexus ± sciatic nerve, posterior lumbar plexus, psoas compartment, obutarator and epidural nerve blocks. These were

compared with standard care ± placebo, or a different method of nerve blocks. Sample sizes ranged from 14 to 207 participants. Additionally, three retrospective cohort studies[117-119] (n = 696) evaluated 3-in-1, femoral, lumbar plexus plus sciatic nerve blocks versus systemic analgesia, or comparing different analgesic medications in femoral, lumbar plexus plus sciatic blocks. Sample sizes ranged from 62 to 535 participants. The mean age ranged from 59.2 to 85.9 years. Most were female (43.3 to 90.0 percent). Acute pain was measured using different scales (i.e., NRS (0-3, 1-5 and 1-10) and 10cm VAS). Eight studies using the 10cm VAS reported mean baseline pain scores ranging from 1.4cm to 7.3cm. See Tables E-5 and F-5 (Appendices E and F) for details of the study characteristics and interventions.

Two RCTs[95,96] had a low risk of bias, 16 RCTs[89,91,97,99-105,107-109,111,113,115] had an unclear risk of bias, while the remaining 11[88,90,92-94,98,106,110,112,114,116] had a high risk of bias (Appendix G). Summary of the evidence from these trials is provided in Table 12.

Based on the primary interventions and comparison groups, the studies were grouped as follows:

1. Nerve blocks versus standard care ± placebo
2. Nerve blocks versus neuraxial anesthesia
3. Nerve blocks: ropivacaine versus bupivacaine
4. Nerves blocks: addition of clonidine
5. Nerve blocks: US versus NS

Table 12. Evidence addressing key questions: Nerve blocks

Key Question	Outcome	Evidence availability	Summary of evidence
KQ 1	**Acute pain***	Yes	11 RCTs reported on acute pain following nerve blocks compared with standard care. There was marked heterogeneity between the studies and subgroup analyses revealed that the type and timing of the intervention affected the homogeneity of the results. Additionally removal of the outlying study also generated more homogenous results. In general, there was a statistically significant effect in favor of nerve blocks over standard care. Additional analyses of pain at rest and on movement were also not reported due to marked statistical heterogeneity. One RCT reported a statistically significant reduction in number of participants with pain on day 1. The strength of the evidence was rated as moderate. 3 RCTs reported no significant difference between the use of nerve blocks vs. neuraxial anesthesia on acute pain reduction. The strength of the evidence was rated as low.
	Chronic pain*	No	

Table 12. Evidence addressing key questions: Nerve blocks (continued)

Key Question	Outcome	Evidence availability	Summary of evidence
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	Yes	4 RCTs reported no statistically significant difference between nerve blocks and standard care regarding 30-day mortality. The strength of the evidence was rated as low. 2 RCTs and 1 retrospective cohort study reported no statistically significant difference between nerve blocks and standard care regarding 1-year mortality.
	Functional status	No	
	Pain medication use; change in type and quantity	Yes	7 RCTs and 1 retrospective cohort study reported statistically significantly fewer participants requiring additional pain medications when nerve blocks were administered compared with standard care. 1 RCT comparing nerve blocks with neuraxial anesthesia found no significant difference in the number of participants requiring additional pain medications. 1 Retrospective cohort study comparing ropivacaine with bupivacaine for nerve block found no significant difference in the number of participants requiring additional pain medications.
	Mental status* (e.g., delirium, confusion)	Yes	3 RCTs and 2 retrospective cohort studies reported a statistically significant difference in participants developing delirium in favor of the nerve blocks compared with standard care. The strength of the evidence was rated as moderate. 1 RCT comparing nerve blocks with neuraxial anesthesia found no significant difference in the number of participants experiencing delirium. 1 Retrospective cohort study comparing ropivacaine with bupivacaine for nerve block found no significant difference in the number of participants experiencing delirium.
	Health-related quality of life	No	
	Quality of sleep in the hospital	Yes	1 RCT reported no statistically significant difference between nerve blocks and standard care.
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	Yes	2 retrospective cohort studies reported conflicting results between nerve blocks and standard care with one demonstrating a statistically significant decrease in hospital LOS while the other showed no difference.

Table 12. Evidence addressing key questions: Nerve blocks (continued)

Key Question	Outcome	Evidence availability	Summary of Evidence
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	Yes	20 RCTs and 2 retrospective cohort studies reported on different adverse effects between nerve blocks and other modes of care with no statistically significant differences except between nerve blocks and standard care except for urinary tract and respiratory infections, drowsiness and dizziness which occurred less frequently in the nerve block groups. The strength of the evidence for the probability of stroke, myocardial infarction, or renal failure was rated as insufficient.
KQ4	**Effectiveness and safety in differing subpopulations**	Yes	Comparing nerve blocks and standard care, 1 RCT included only participants with heart disease and 1 RCT included only participants who were independent prior to the hip fracture.

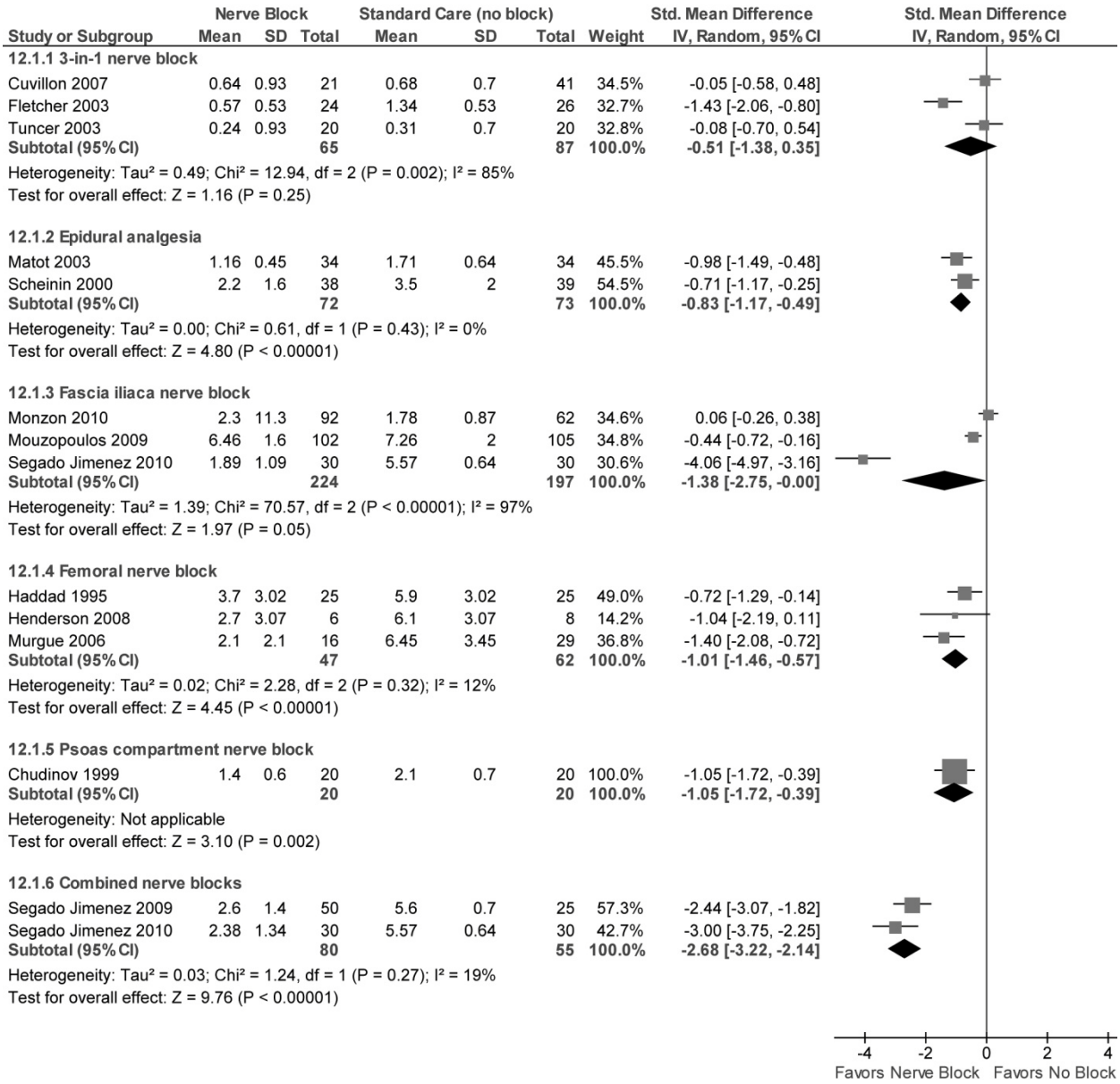
KQ = key question; LOS = length of stay; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

Nerve Blocks vs. No Block

Acute pain (post-treatment) was reported in 13 RCTs[89,91,94,99,100,106-112,114] (Figure 6 and Table 13-A). The pooled results are not reported due to high heterogeneity (I^2 = 92 percent) between the included studies, which was not explained by study design (i.e. all were RCTs) or risk of bias (i.e., removal of the trials with a high risk of bias). Specific intervention details (i.e., type and quantity) could partially explain the heterogeneity with removal of combined nerve blocks groups (e.g. 3-in-1 nerve block group) substantially decreasing the quantified heterogeneity (I^2 = 41%). Additionally, another source of identified heterogeneity is the timing of the intervention with postoperative administration of nerve blocks in three RCTs[91,111,114] showing marked heterogenous results (I^2 = 95%), while preoperative administration showed more homogenous results (I^2 = 53%) in eight RCTs.[89,94,99,100,106,108-110] Removal of one of the included RCTs[111] decreased the heterogeneity for both the overall results (I^2 = 64%) and the subgroup analysis (I^2 = 0%) of only postoperative administration of nerve blocks.

Figure 6. Nerve blocks versus no block—acute pain (post-treatment)



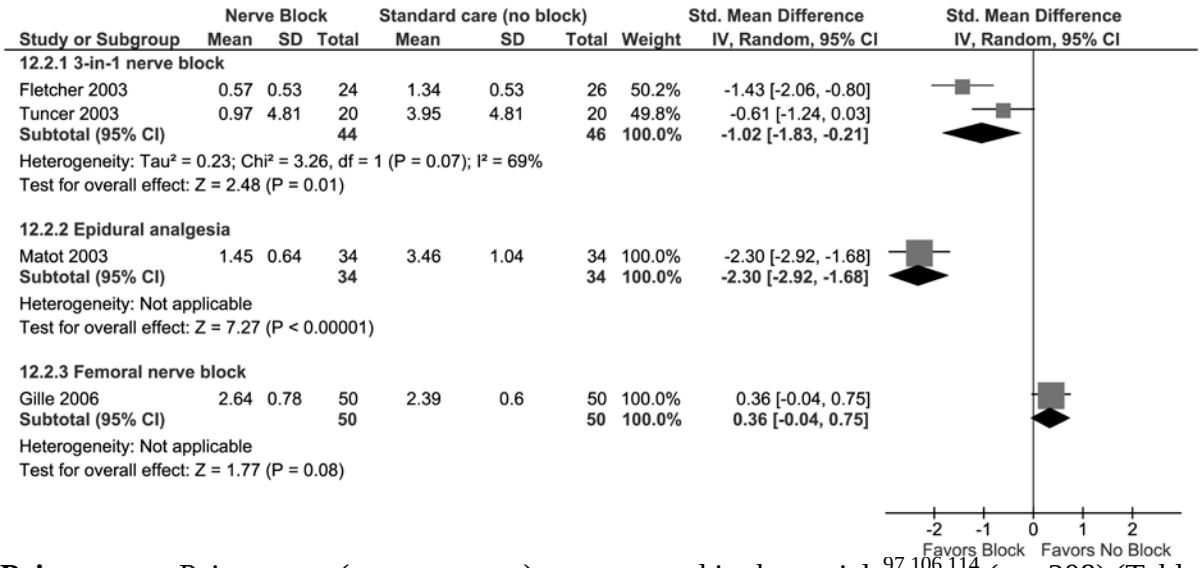
Day 1 pain. One trial[101] (n = 50) reported a statistically significant difference in the frequency of patients who reported postoperative pain on day 1 favoring nerve blocks (7/25 vs. 20/25; OR 0.10; 95% CI 0.03, 0.36; p = 0.0005) (Table 13-A).

Pain on movement. Pain on movement (post-treatment means) was reported in four trials[94,97,106,114] (n = 258) (Table 13-A). The pooled results were not reported due to significant heterogeneity (I^2 = 95 percent) between the studies (Figure 7). Meta-analysis restricted to two RCTs[94,114] using 3-in-1 nerve block vs. no block showed a significant reduction in pain on movement favoring nerve blocks (SMD -1.02; 95% CI -1.83, -0.21; p = 0.01). One RCT[94] investigated preoperative pain relief (numeric rating scale [0-3]) while the other RCT[114] investigated postoperative pain (10cm VAS) relief. Both trials had a high risk of bias.

The third RCT[106] examined preoperative epidural analgesia versus no block and showed a significant increase in pain relief (10cm VAS) on movement favoring nerve blocks (MD-2.30; 95% CI -2.92, -1.68; p <0.00001). The trial had a high risk of bias.

The last RCT[97] examined preoperative femoral nerve block versus no block and showed no significant difference in pain relief (5-point Verbal Rating Scale) on movement (MD 0.36; 95% CI -0.04, 0.75; p = 0.08).

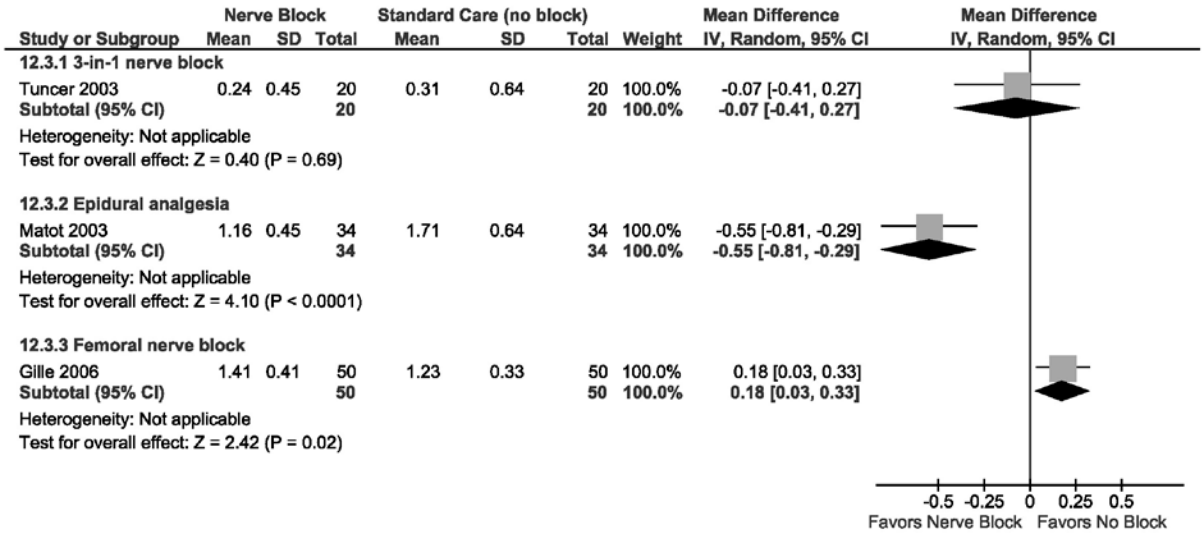
Figure 7. Nerve blocks versus no block—pain on movement (post-treatment)



Pain on rest. Pain on rest (posttreatment) was reported in three trials[97,106,114] (n = 208) (Table 13-A). The pooled results were not reported due to significant heterogeneity (I^2 = 91 percent) between the studies (Figure 8). One RCT[114] examined postoperative 3-in-1 nerve block versus standard care and found no significant difference in pain relief (10cm VAS) (MD -0.07; 95% CI -0.41, 0.27; p = 0.69). This study had a high risk of bias. The second RCT[106] examined preoperative epidural analgesia versus standard care and found a statistically difference in pain relief in favor of the nerve blocks (10cm VAS) (MD -0.55; 95% CI -0.81, -0.29; p < 0.0001). This study had a high risk of bias.The last RCT[97] examined preoperative femoral nerve block versus standard care and reported a statistically significant difference in pain relief in favor of standard care (5-point Verbal Rating Scale) (MD 0.18; 95% CI 0.03, 0.33; p = 0.02). This study had an unclear risk of bias.

The strength of the evidence was rated as moderate regarding these interventions.

Figure 8. Nerve blocks versus no block – pain on rest (posttreatment)



Nerve Blocks vs. Neuraxial Anesthesia

Acute pain (posttreatment) was reported in three RCTs[92,93,115] (n = 109) (Table 13-B). There was no statistically significant difference in pain between the two groups (MD -0.35; 95% CI -1.10, 0.39; p = 0.35).

Key Question 2. Other outcomes

Nerve Blocks vs. No Block

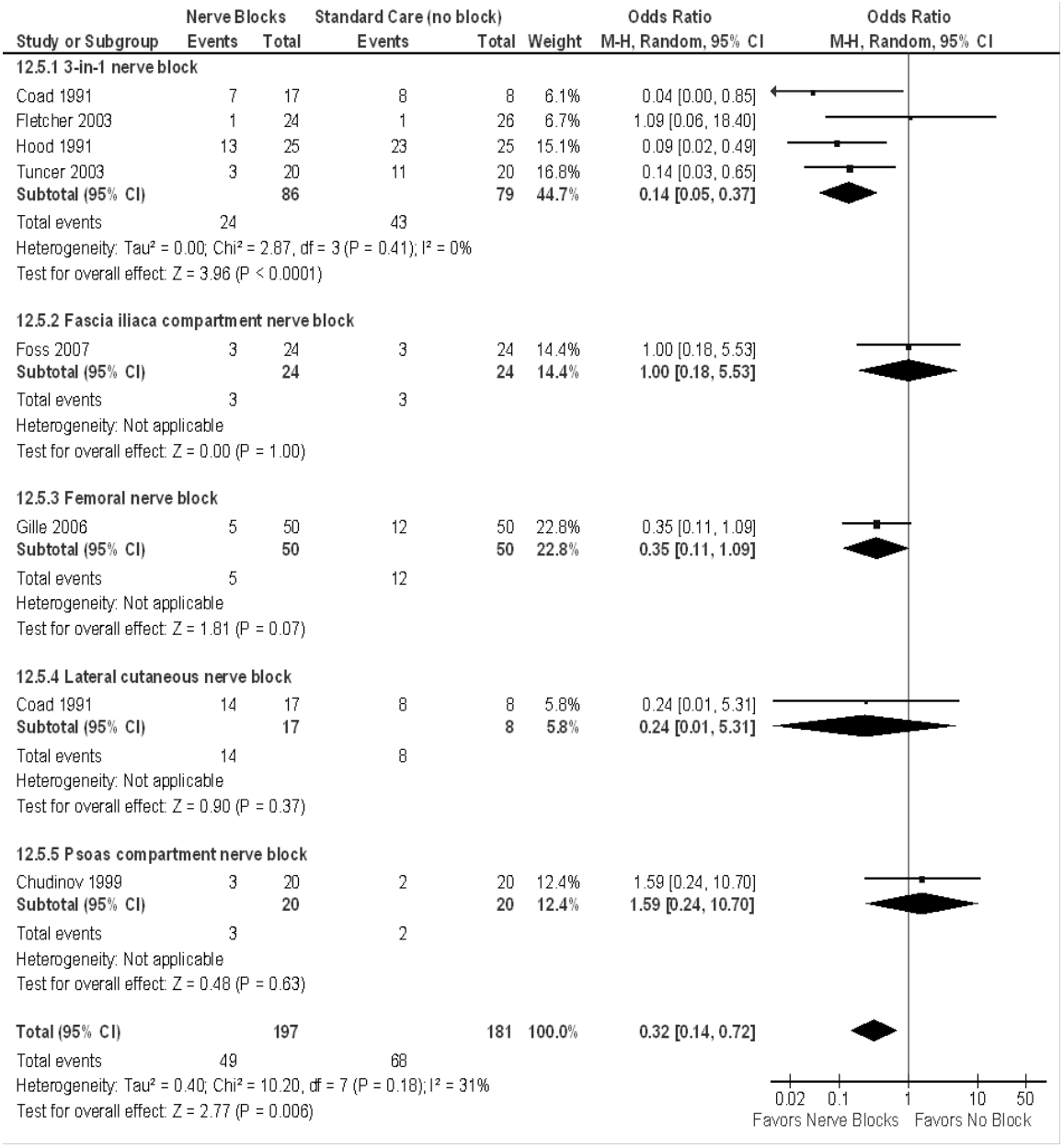
30-day mortality. A total of four RCTs[95,99,105,106] evaluated 30-day mortality in a total of 228 participants (Table 13-A). Meta-analysis did not provide evidence of a significant difference in 30-day mortality (2/114 vs. 10/114; OR 0.28; 95% CI 0.07, 1.12; p = 0.07). The strength of the evidence was rated as low to make any firm conclusions regarding these interventions.

1-year mortality. Two RCTs[91,94] evaluated 1-year mortality in a total of 112 participants (Table 13-A). Additionally, one retrospective cohort study[119] reported data for 535 participants (Table 14). There was no evidence of a significant difference in mortality in the RCTs (5/45 vs. 9/67; OR 0.82; 95% CI 0.25, 2.72; p = 0.74), or in the cohort study (41/178 vs. 104/357; OR 0.73; 95% CI 0.48, 1.10; p = 0.14).

Additional pain medication use. Seven RCTs[89,90,94,96,97,101,114] evaluated additional pain medication use in a total of 378 participants (Table 13-A). Additionally, one retrospective cohort study[117] compared femoral nerve block vs. no block, reporting data for 99 participants (Table 14). Meta-analysis of the seven trials[89,90,94,96,97,101,114] resulted in a significant difference in additional pain medication use, favoring nerve blocks (49/197 vs. 68/181; OR 0.32; 95% CI 0.14, 0.72; p = 0.006) (Figure 9). The retrospective cohort study[117] reported a statistically

significant effect difference favoring nerve blocks (0/49 vs. 14/50; OR 0.03; 95% CI 0.00, 0.44; p = 0.01).

Figure 9. Nerve blocks versus no block – participants requiring additional pain medication



Mental status. Four RCTs[95,98,107,108] (n = 461) and two cohort studies[117,119] (n = 634) reported the occurrence of delirium (Table 13-A, 14-A). Meta-analysis of the trials[95,98,107,108] showed a significant difference favoring nerve blocks (11/242 vs. 33/219; OR 0.33; 95% CI 0.16, 0.66; p = 0.002). The pooled results of the cohort studies[117,119] also showed a significant difference in favor

of nerve blocks (11/227 vs. 55/407; OR 0.24; 95% CI 0.08, 0.72; p = 0.01). The strength of the evidence was rated as moderate.

Length of stay for acute hospitalization. LOS for acute hospitalization (days) was reported in two retrospective cohort studies[117,119] (n = 634) (Table 14-A). There was significant heterogeneity between the studies and pooled results are not reported. The first study[117] was performed using a 3-in-1 nerve block while the second study[119] used a femoral nerve block. Both studies showed lower LOS for the nerve blocks with the magnitude larger for the 3-in-1 block.

Quality of sleep. Quality of sleep (10cm VAS) (post-treatment means) was reported in one RCT[110] (n = 77) (Table 13-A). There was no significant difference between groups (MD 0.30; 95% CI -0.46, 1.06; p = 0.44).

Nerve Blocks vs. Neuraxial Anesthesia

Additional pain medication use. Additional pain medication use was reported in one RCT[115] (n = 30) (Table 13-B). There was no significant difference between the two groups (5/15 vs. 3/15; OR 2.00; 95% CI 0.38, 10.51; p = 0.41).

Mental status. Delirium (MMSE) was reported in one RCT[92] (n = 29) (Table 13-B). There was no significant difference between the two groups (6/15 vs. 5/14; OR 1.20; 95% CI 0.27, 5.40; p = 0.81). The strength of the evidence was rated as insufficient to make any firm conclusions.

Nerve Blocks: Ropivacaine vs. Bupivacaine

Additional pain medication use. Additional pain medication use was reported in one cohort study[118] (n = 62) (Table 14-B). There was no significant difference between the two groups (10/32 vs. 8/30; OR 1.25; 95% CI 0.42, 3.76; p = 0.69).

Mental status. Delirium (user defined) was reported in one cohort study[118] (n = 62) (Table 14-B). There was no significant difference between the two groups (2/32 vs. 1/30; OR 1.93; 95% CI 0.17, 22.50; p = 0.60). The strength of the evidence was rated as insufficient to make any firm conclusions.

Key Question 3. Adverse effects

Nerve Blocks vs. No Block

Any adverse event. Any adverse effects were reported in five RCTs[88,97,98,100,107] (n =392) and there was significant heterogeneity (I^2=94%) (Table 13-A). Two retrospective cohort studies[117,119] (n = 634) found no significant effect difference between the two groups (62/227 vs. 76/407; OR 1.64; 95% CI 0.79, 3.42; p = 0.18) (Table 14-A).

Cardiac complications. Cardiac complications were reported in two RCTs[95,106] (n = 128). There was no significant difference between the two groups (3/64 vs. 8/64; OR 0.35; 95% CI 0.08, 1.44; p = 0.15) (Table 13-A). One retrospective cohort study[117] (n = 99) found no significant difference between the two groups (0/49 vs. 1/50; OR 0.33; 95% CI 0.01, 8.38; p = 0.50) (Table 14-A).

Damage to surrounding structures. Damage to surrounding structures was reported in three RCTs[88,97,116] (n = 224) and found no significant difference between the two groups (3/119 vs. 0/105; OR = 7.44; 95% CI 0.37, 147.92; p = 0.19) (Table 13-A).

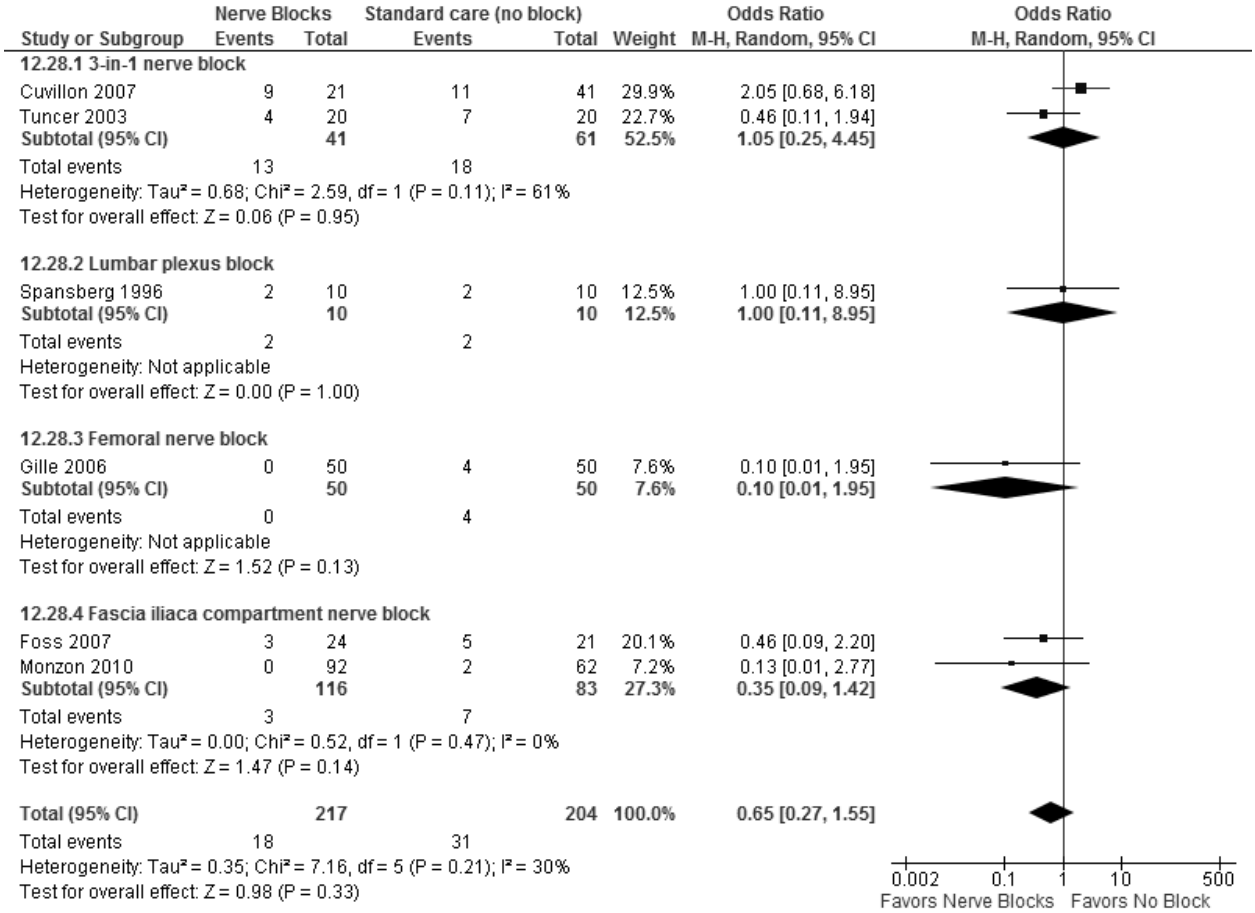
Deep venous thrombosis. Deep venous thrombosis was reported in two RCTs[94,99] (n = 100). There was no significant difference between the two groups (4/49 vs. 3/51; OR 1.40; 95% CI 0.29, 6.72; p = 0.67) (Table 13-A).

Infection. There were no reports of infection in two RCTs[88,97] (n = 184) (Table 13-A).

Myocardial infarction. Myocardial infarction was reported in two RCTs[106,110] (n = 145). There was no significant difference between the two groups (1/72 vs. 1/73; OR 1.00; 95% CI 0.06, 16.67; p = 1.00) (Table 13-A). One retrospective cohort study[119] (n = 535) found no significant difference between the two groups (1/178 vs. 3/357; Peto OR 0.69; 95% CI 0.09, 5.53; p = 0.72) (Table 14-A).

Nausea/vomiting. Nausea/vomiting was reported in six RCTs[91,96,97,107,113,114] (n = 421) and found no evidence of a significant difference between the two groups (18/217 vs. 31/204; OR 0.65; 95% CI 0.27, 1.55; p = 0.33) (Table 13-A and Figure 10).

Figure 10. Nerve blocks versus no block—nausea/vomiting



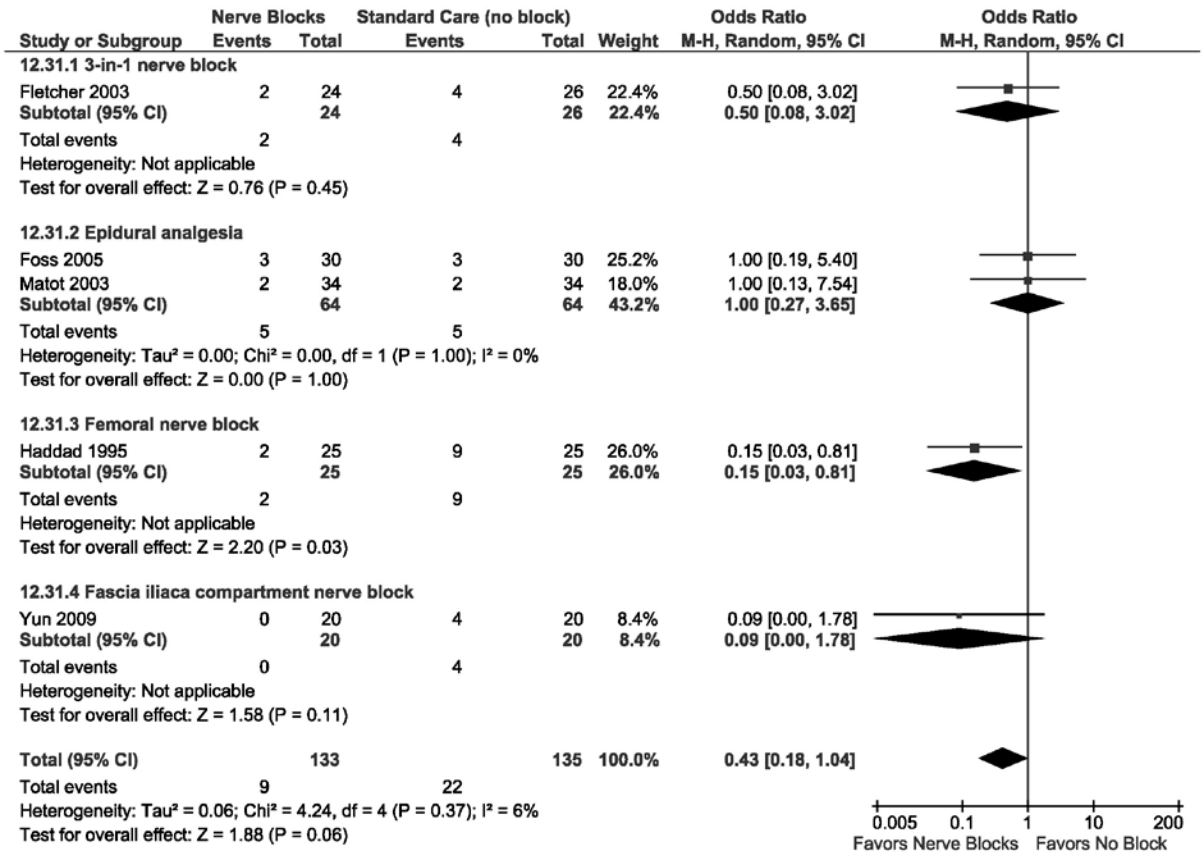
Pulmonary embolism. Pulmonary embolism was reported in two RCTs[95,106] (n = 128) and found no significant difference between the two groups (2/64 vs. 1/64; OR 1.63; 95% CI 0.19, 13.61; p = 0.65) (Table 13-A).

Respiratory infection. Respiratory infection was reported in five RCTs[94,95,99,106,116] (n = 268) and found no significant difference between the two groups (9/133 vs. 22/135; OR 0.43; 95% CI 0.18, 1.04; p = 0.06) (Table 13-A and Figure 11). One retrospective cohort study[119] (n = 535) found a statistically significant difference favoring nerve blocks (9/178 vs. 39/357; OR 0.43; 95% CI 0.21, 0.92; p = 0.03) (Table 14-A).

Stroke. Stroke was reported in one RCT[99] (n = 50) and found no significant effect between the two groups (1/25 vs. 0/25; OR 3.12; 95% CI 0.12, 80.39; p = 0.49) (Table 13-A). Stroke was also reported in one retrospective cohort study[119] (n = 535) and found no significant difference between the two groups (1/178 vs. 8/357; OR 0.25; 95% CI 0.03, 1.99; p = 0.19) (Table 14-A).

Surgical wound infection. Surgical wound infection was reported in two RCTs[95,99] (n = 110) and found no significant difference between the two groups (3/55 vs. 4/55; OR 0.77; 95% CI 0.11, 5.63; p = 0.80) (Table 13-A).

Figure 11. Nerve blocks versus no block—respiratory infection



Urinary retention. Urinary retention was reported in two RCTs[91,113] (n = 62) and found no significant difference between the two groups (3/31 vs. 1/31; OR 2.23; 95% CI 0.27, 18.71; p = 0.46) (Table 13-A). One retrospective cohort study[119] (n = 535) and found no significant difference between the two groups (4/178 vs. 17/357; OR 0.46; 95% CI 0.15, 1.39; p = 0.17) (Table 14-A).

Urinary tract infection. Urinary tract infection was reported in one RCT[99] (n = 50) and found no significant difference between the two groups (4/25 vs. 6/25; OR 0.60; 95% CI 0.15, 2.47; p = 0.48) (Table 13-A). One retrospective cohort study[119] (n = 535) found a statistically significant difference favoring nerve blocks (12/178 vs. 63/357; OR 0.34; 95% CI 0.18, 0.64; p = 0.001) (Table 14-A).

Other adverse effects. The remaining reported adverse effects were from single RCTs and cohort studies and did not demonstrate any significant statistical differences between the pain management interventions (Tables 13-A and 14-A).

Nerve Blocks vs. Neuraxial Anesthesia

Adverse effects. The reported adverse effects were from single RCTs and did not demonstrate any significant statistical differences between the pain management interventions (Table 13-B).

Nerve Blocks: Ropivacaine vs. Bupivacaine

Adverse effects. The reported adverse effects were from single RCTs and cohort studies and did not demonstrate any significant statistical differences between the pain management interventions (Tables 13-C, 14-B).

Nerve Blocks: Addition of Clonidine

Adverse effects. The reported adverse effects were from single RCTs and did not demonstrate any significant statistical differences between the pain management interventions (Table 13-D).

Nerve Blocks: US vs. NS

Damage to surrounding structures. Damage to surrounding structures was reported in two RCTs[103,104] (n = 100) (Table 13-E). There was no statistically significant difference between the two groups (0/40 vs. 7/60; OR 0.16; 95% CI 0.02, 1.30; p = 0.09).

Other adverse effects. The remaining reported adverse effects were from a single RCT[103] and did not demonstrate any significant statistical differences between the pain management interventions.

Key Question 4. Efficacy, effectiveness and safety in subpopulations

One RCT[106] only recruited patients with pre-existing heart disease. There was a significant reduction in acute pain (MD -0.98; 95% CI -1.49, -0.48; p <0.0001) favoring nerve blocks. There was no significant difference in 30-day mortality (0/34 vs. 4/34; OR 0.10; 95 % CI 0.01, 1.90; p = 0.12) or adverse effects: participants with any cardiac complications (2/34 vs. 7/34; OR 0.24; 95% CI 0.05, 1.26; p = 0.09); congestive heart failure (1/34 vs. 2/34; OR 0.48; 95% CI 0.04, 5.61; p = 0.56); myocardial infarction (1/34 vs. 1/34; OR 1.00; 95 % CI 0.06, 16.67; p = 1.00); respiratory infection (2/34 vs. 2/34; OR 1.00; 95% CI 0.13, 7.54; p = 1.00); or pulmonary embolism (1/34 vs. 1/34; OR 1.00; 95% CI 0.06, 16.67; p = 1.00).

One RCT[95] only recruited participants that were independent prior to their hip fracture. There was no significant difference between nerve blocks versus standard care for 30-day mortality (1/30 vs. 1/30; OR 1.00; 95 % CI 0.06, 16.76; p = 1.00).

Table 13. Evidence summary table (randomized controlled trials): Nerve blocks

Table 13-A. Nerve blocks versus no block: RCT/nRCT

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**[89,91,94,99,100,106-112,114]	13	1002		NR	92%
	3-in-1 NB[91,94,114]	3	152		NR	85%
	Epidural analgesia[106,110]	2	145	SMD (95% CI)	**-0.83 (-1.17, -0.49)***	0%
	Fascia iliaca NB[107,108,112]	3	421	MD (95% CI)	NR	97%
	Femoral NB[99,100,109]	3	109	SMD (95% CI)	**-1.01 (-1.46, -0.57)***	12%
	Psoas compartment NB[89]	1	40	MD (95% CI)	**-0.70 (-1.10, -0.30)***	NA
	Combined NB[111,112]	2	135	MD (95% CI)	**-3.08 (-3.44, -2.73)***	19%
	Day 1 pain					
	3-in-1 NB[101]	1	50	OR (95% CI)	**0.10 (0.03, 0.36)***	NA
	Pain on movement (post-treatment)[94,97,106,114]	4	258		NR	95%
	3-in-1 NB[94,114]	2	90	SMD (95% CI)	**-1.02 (-1.83, -0.21)***	69%
	Epidural analgesia[106]	1	68	MD (95% CI)	**-2.30 (-2.92, -1.68)**	NA
	Femoral NB[97]	1	100	MD (95% CI)	0.36 (-0.04, 0.75)	NA
	Pain on rest (post-treatment)[97,106,114]	3	208		NR	91%
	3-in-1 NB[114]	1	40	MD (95% CI)	-0.07 (-0.41, 0.27)	NA
	Epidural analgesia[106]	1	68	MD (95% CI)	**-0.55 (-0.81, -0.29)***	NA
	Femoral NB[97]	1	100	MD (95% CI)	**0.18 (0.03, 0.33)***	NA
KQ2	**Additional pain medication use**[89,90,94,96,97,101,114]	7	378	OR (95% CI)	**0.32 (0.14, 0.72)***	31%
	3-in-1 NB[90,94,101,114]	4	165	OR (95% CI)	**0.14 (0.05, 0.37)***	0%
	Fascia iliaca NB[96]	1	48	OR (95% CI)	1.00 (0.18, 5.53)	NA
	Femoral NB[97]	1	100	OR (95% CI)	0.35 (0.11, 1.09)	NA
	Lateral cutaneous NB[90]	1	25	OR (95% CI)	0.24 (0.01, 5.31)	NA
	Psoas compartment NB[89]	1	40	OR (95% CI)	1.59 (0.24, 10.70)	NA
	Mental status (e.g., delirium, confusion)[95,98,107,108]	4	461	OR (95% CI)	**0.33 (0.16, 0.66)***	0%
	3-in-1 NB[98]	1	40	OR (95% CI)	0.22 (0.01, 4.92)	NA
	Epidural analgesia[95]	1	60	OR (95% CI)	0.19 (0.01, 4.06)	NA
	Fascia iliaca NB[107,108]	2	361	OR (95% CI)	**0.30(0.09, 1.00)**	19%
	Mortality 30-day[95,99,101,106]	4	228	OR (95% CI)	0.28 (0.07, 1.12)	0%
	3-in-1 NB[101]	1	50	OR (95% CI)	0.32 (0.01, 8.25)	NA
	Epidural analgesia[95,106]	2	128	OR (95% CI)	0.33 (0.03, 3.34)	23%
	Femoral NB[99]	1	50	OR (95% CI)	0.22 (0.02, 2.11)	NA
	Mortality 1 year					
	3-in-1 NB[91,94]	2	112	OR (95% CI)	0.82 (0.25, 2.72)	0%
	Quality of sleep					
	Epidural analgesia[110]	1	77	MD (95% CI)	0.30 (-0.46, 1.06)	NA
KQ3	**Allergic reaction**					
	3-in-1 NB[114]	1	40	OR (95% CI)	0.07 (0.00, 1.34)	NA

Table 13-A. Nerve blocks versus no block: RCT/nRCT (continued)

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ3	**Any adverse event**[88,97,98,100,107]	5	392	OR (95% CI)	NE	94%
	3-in-1 NB[98]	1	40		NE	
	Femoral NB[88,97,100]	3	198	OR (95% CI)	4.49 (1.61, 12.55)*	NA
	Cardiac complications					
	Epidural analgesia[95,106]	2	128	OR (95% CI)	0.35 (0.08, 1.44)	0%
	Cardiovascular complications					
	Femoral NB[99]	1	50	OR (95% CI)	1.00 (0.13, 7.72)	NA
	Cardiovascular or neurological toxicity					
	Femoral NB[88]	1	84		NE	
	Congestive heart failure					
	Epidural analgesia[106]	1	68	OR (95% CI)	0.48 (0.04, 5.61)	NA
	Constipation					
	3-in-1 NB[91]	1	42	OR (95% CI)	3.86 (0.97, 15.44)	NA
	Damage to surrounding structures[88,97,116]	3	224	OR (95% CI)	7.44 (0.37, 147.92)	NA
	Fascia iliaca compartment NB[116]	1	40		NE	
	Femoral NB[88,97]	2	184	OR (95% CI)	7.44 (0.37, 147.92)	0%
	Deep venous thrombosis[94,99]	2	100	OR (95% CI)	1.40 (0.29, 6.72)	0%
	3-in-1 NB[94]	1	50	OR (95% CI)	1.09 (0.06, 18.40)	NA
	Femoral NB[99]	1	50	OR (95% CI)	1.57 (0.24, 10.30)	NA
	Direct skin damage					
	Femoral NB[99]	1	50	OR (95% CI)	0.17 (0.02, 1.55)	NA
	Dizziness					
	Fascia iliaca compartment NB[116]	1	40	OR (95% CI)	**0.00 (0.00, 0.03)***	NA
	Drowsiness					
	Fascia iliaca compartment NB[116]	1	40	OR (95% CI)	**0.02 (0.00, 0.31)***	NA
	Hematoma					
	Lumbar plexus block[113]	1	20		NE	
	Hypotension					
	3-in-1 NB[101]	1	50	OR (95% CI)	0.52 (0.17, 1.61)	NA
	Infection					
	Femoral NB[88,97]	2	184		NE	
	Major medical complications					
	Epidural analgesia[95]	1	60	OR (95% CI)	0.69 (0.21, 2.30)	NA
	Myocardial infarction					
	Epidural analgesia[106,110]	2	145	OR (95% CI)	1.00 (0.06, 16.67)	0%
	Myocardial ischemia					
	Epidural analgesia[110]	1	77	OR (95% CI)	0.92 (0.36, 2.40)	NA
	Nausea/ vomiting[91,96,97,113,114]	6	421	OR (95% CI)	0.65 (0.27, 1.55)	30%
	3-in-1 NB[91,114]	2	102	OR (95% CI)	1.05 (0.25, 4.45)	61%
	Lumbar plexus block[113]	1	20	OR (95% CI)	1.00 (0.11, 8.95)	NA
	Femoral NB[97]	1	100	OR (95% CI)	0.10 (0.01, 1.95)	NA
	Fascia iliaca NB[96,107]	2	199	OR (95% CI)	0.35 (0.09, 1.42)	0%
	Paresthesia[97,116]	2	140	OR (95% CI)	5.21 (0.24, 111.24)	NA
	Femoral NB[97]	1	100	OR (95% CI)	5.21 (0.24, 111.24)	NA
	Fascia iliaca compartment NB[116]	1	40		NE	

Table 13-A. Nerve blocks versus no block: RCT/nRCT (continued)

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
	Pulmonary embolism					
	Epidural analgesia[95,106]	2	128	OR (95% CI)	1.63 (0.19, 13.61)	0%
KQ3	**Respiratory infection**[94,95,99,106,116]	5	268	OR (95% CI)	0.43 (0.18, 1.04)	6%
	3-in-1 NB[94]	1	50	OR (95% CI)	0.50 (0.08, 3.02)	NA
	Epidural analgesia[95106]	2	128	OR (95% CI)	1.00 (0.27, 3.65)	0%
	Femoral NB[99]	1	50	OR (95% CI)	**0.15 (0.03, 0.81)***	NA
	Fascia iliaca compartment NB[116]	1	40	OR (95% CI)	0.09 (0.00, 1.78)	NA
	Stroke					
	Femoral NB[99]	1	50	OR (95% CI)	3.12 (0.12, 80.39)	NA
	Surgical wound infection[95,99]	2	110	OR (95% CI)	0.77 (0.11, 5.63)	0%
	Epidural analgesia[95]	1	60	OR (95% CI)	0.19 (0.01, 4.06)	NA
	Femoral NB[99]	1	50	OR (95% CI)	1.57 (0.24, 10.30)	NA
	Urinary retention[91,113]	2	62	OR (95% CI)	2.23 (0.27, 18.71)	0%
	Lumbar plexus block[113]	1	20	OR (95% CI)	1.00 (0.05, 18.57)	NA
	3-in-1 NB[91]	1	42	OR (95% CI)	5.51 (0.25, 122.08)	NA
	Urinary tract infection					
	Femoral NB[99]	1	50	OR (95% CI)	0.60 (0.15, 2.47)	NA

KQ: key question; CI = confidence intervals; MD = mean difference; NA = not applicable; NB = nerve block; NR = not reported; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials; SMD = standardized mean difference; * = statistically significant

Table 13-B. Nerve blocks versus neuraxial anesthesia: RCT/nRCT

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (posttreatment means)**[92,93,115]	3	109	MD (95% CI)	-0.35 (-1.10, 0.39)	0%
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	MD (95% CI)	0.34 (-1.22, 1.90)	NA
	Posterior lumbar plexus NB vs. spinal anesthesia (single)[93]	1	50	MD (95% CI)	-0.60 (-1.73, 0.53)	NA
	Combined lumbar + sacral plexus NB vs. spinal anesthesia (single)[92]	1	29	MD (95% CI)	-0.50 (-1.78, 0.78)	NA
KQ2	**Additional pain medication use**					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	OR (95% CI)	2.00 (0.38, 10.51)	NA
	Mental staus (e.g, delirium, confusion)					
	Combined lumbar + sacral plexus NB vs. spinal anesthesia (single)[92]	1	29	OR (95% CI)	1.20 (0.27, 5.40)	NA
KQ3	**Allergic reaction**					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	OR (95% CI)	0.23 (0.04, 1.41)	NA
	Cardiac arrest					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30		NE	
	Damage to surrounding structures					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30		NE	
	Deep venous thrombosis					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30		NE	
	GI symptoms					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	OR (95% CI)	**0.06 (0.00, 1.24)***	NA
KQ3	**Hematoma**					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30		NE	
	Hypotension					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	OR (95% CI)	0.11 (0.01, 1.04)	NA
	Infection					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30		NE	
	Urinary retention					
	Psoas compartment NB vs. epidural anesthesia (single)[115]	1	30	OR (95% CI)	0.04 (0.00, 0.72)*	NA

KQ: key question; CI = confidence intervals; MD = mean difference; NB = nerve block; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials; * = statistically significant

Table 13-C. Nerve blocks (Ropivacaine versus bupivacaine): RCT/nRCT

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ3	**Infection**					
	3-in-1 NB[105]	1	50		NE	

KQ: key question; CI = confidence intervals; NB = nerve block; NE = not estimable; RCT/nRCT = randomized and nonrandomized controlled trials

Table 13-D. Nerve block (addition of clonidine): RCT/nRCT

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ3	**Bradycardia**					
	Psoas compartment NB: clonidine IV vs. no clonidine[102]	1	24	OR (95% CI)	1.40 (0.28, 7.02)	NA
	Psoas compartment NB: clonidine intra-catheter vs. no clonidine[102]	1	24	OR (95% CI)	1.40 (0.28, 7.02)	NA
	Psoas compartment NB: clonidine IV vs. clonidine intra-catheter[102]	1	24	OR (95% CI)	1.00 (0.20, 4.95)	NA
	Hypotension					
	Psoas compartment NB: clonidine IV vs. no clonidine[102]	1	24	OR (95% CI)	1.00 (0.12, 8.56)	NA
	Psoas compartment NB: clonidine intra-catheter vs. no clonidine[102]	1	24	OR (95% CI)	1.00 (0.12, 8.56)	NA
	Psoas compartment NB: clonidine IV vs. clonidine intra-catheter[102]	1	24	OR (95% CI)	1.00 (0.12, 8.56)	NA
	Nausea/vomiting					
	Psoas compartment NB: clonidine IV vs. no clonidine[102]	1	24	OR (95% CI)	1.50 (0.25, 8.84)	NA
	Psoas compartment NB: clonidine intra-catheter vs. no clonidine[102]	1	24	OR (95% CI)	0.27 (0.02, 3.09)	NA
	Psoas compartment NB: clonidine IV vs. clonidine intra-catheter[102]	1	24	OR (95% CI)	5.50 (0.51, 59.01)	NA

KQ: key question; CI = confidence intervals; NA = not applicable; NB = nerve block; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 13-E. Nerve blocks (US vs. NS): RCT/nRCT

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ3	**Damage to surrounding structures**[103,104]	2	100	OR (95% CI)	0.16 (0.02, 1.30)	NA
	Infection[103]	1	40		NE	

KQ = key question; CI = confidence intervals; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 14. Evidence summary table (cohort studies): Nerve blocks

Table 14-A. Nerve blocks versus no block: Cohort studies

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ2	**Additional pain medication use**					
	Femoral NB[117]	1	99	OR (95% CI)	**0.03 (0.00, 0.44)***	NA
	Mental status (e.g, delirium, confusion)[117,119]	2	634	OR (95% CI)	**0.24 (0.08, 0.72)***	60%
	3-in-1 NB[119]	1	535	OR (95% CI)	**0.39 (0.17, 0.90)***	NA
	Femoral NB[117]	1	99	OR (95% CI)	**0.12 (0.04, 0.39)***	NA
	LOS[117,119]	2	634		NR	93%
	3-in-1 NB[119]	1	535	MD (95% CI)	**-6.10 (-8.40, -3.80)***	NA
	Femoral NB[117]	1	99	MD (95% CI)	-0.90 (-2.18, 0.38)	NA
	Mortality 1 year					
	3-in-1 NB[119]	1	535	OR (95% CI)	0.73 (0.48, 1.10)	NA
KQ3	**Acute heart failure**					
	3-in-1 NB[119]	1	535	OR (95% CI)	0.70 (0.33, 1.47)	NA
	Any adverse event	2	634	OR (95% CI)	1.64 (0.79, 3.42)	28%
	3-in-1 NB[119]	1	535	OR (95% CI)	**1.96 (1.31, 2.94)***	NA
	Femoral NB[117]	1	99	OR (95% CI)	0.75 (0.16, 3.54)	NA
	Cardiac complications					
	Femoral NB[117]	1	99	OR (95% CI)	0.33 (0.01, 8.38)	NA
	GI bleeding					
	3-in-1 NB[119]	1	535	OR (95% CI)	1.00 (0.18, 5.53)	NA
	Myocardial Infarction					
	3-in-1 NB[119]	1	535	OR (95% CI)	0.69 (0.09, 5.53)	NA
	Renal disease					
	Femoral NB[117]	1	99	OR (95% CI)	2.09 (0.18, 23.77)	NA
	Respiratory distress					
	Femoral NB[117]	1	99	OR (95% CI)	0.50 (0.04, 5.70)	NA
	Respiratory infection					
	3-in-1 NB[119]	1	535	OR (95% CI)	**0.43 (0.21, 0.92)***	NA
	Stroke					
	3-in-1 NB[119]	1	535	OR (95% CI)	0.25 (0.03, 1.99)	NA
	Urinary retention					
	3-in-1 NB[119]	1	535	OR (95% CI)	0.46 (0.15, 1.39)	NA
	Urinary tract infection					
	3-in-1 NB[119]	1	535	OR (95% CI)	**0.34 (0.18, 0.64)***	NA

CI = confidence intervals; KQ = key question; LOS: length of stay; MD = mean difference; NA = not applicable; NB: nerve block; NR = not reported; OR = odds ratio

Table 14-B. Nerve blocks (Ropivacaine vs. bupivacaine): Cohort studies

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ2	**Additional pain medication use**					
	Lumbar/sacral plexus NB[118]	1	62	OR (95% CI)	1.25 (0.42, 3.76)	NA
	Deleirium					
	Lumbar/sacral plexus NB[118]	1	62	OR (95% CI)	1.93 (0.17, 22.50)	NA
KQ3	**Any adverse event**					
	Lumbar/sacral plexus NB[118]	1	62		NE	

CI = confidence intervals; KQ = key question; NA = not applicable; NB: nerve block; NE = not estimable; OR = odds ratio

Neurostimulation

Overview of Included Studies

Two RCTs[120,121] evaluated the efficacy and/or harms of the administration of transcutaneous electrical neurostimulation (TENS) versus sham control in 123 participants; sample sizes ranged from 60 to 63. One trial administered the TENS preoperatively,[121] and the other post-operatively.[120] The mean age ranged from 71.2 to 80.5 years. Most were female (66.7 to 92.1 percent). Acute pain was measured using the VAS and the average baseline pain measure 8.8 to 8.9. See Tables E-6 and F-6 (Appendices E and F) for details of the study characteristics and interventions.

Both RCTs had a high risk of bias (Appendix G). Summary of the evidence from these trials is provided in Table 15.

Table 15. Evidence addressing key questions: Neurostimulation

Key Question	Outcome	Evidence avaiability	Summary of Evidence
KQ 1	**Acute pain***	Yes	2 RCTs reported a statistically significant effect in favor of neurostimulation compared with sham control. The strength of the evidence was rated as insufficient.
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	No	
	Functional status	No	
	Pain medication use; change in type and quantity	No	
	Mental status* (e.g., delirium, confusion)	No	
	Health-related quality of life	Yes	1 RCT reported a statistically significant difference in favor of neurostimulation.
	Quality of sleep in the hospital	Yes	1 RCT reported a statistically significant difference in favor of neurostimulation.
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	No	

Table 15. Evidence addressing key questions: Neurostimulation (continued)

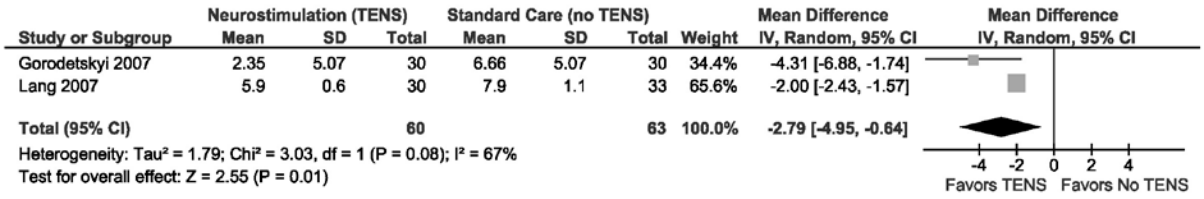
Key Question	Outcome	Evidence avaiability	Summary of Evidence
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	No	
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

Acute pain (post-treatment) was reported in both RCTs[120,121] (n = 123) (Table 16). It should be noted that the variance was imputed from the reported p value presented in one of the trials.[120] The pooled results showed a significant difference in additional pain relief in favor of TENS (MD -2.79; 95% CI -4.95, -0.64; p = 0.01) (Figure 12). This was not considered clinically significant.

Figure 12. Neurostimulation acute pain (post-treatment)



Pain on movement. Pain on movement (post-treatment means) was reported in one trial[120] (n = 60) (Table 16). Neurostimulation provided significantly more pain relief versus sham control (MD -3.90; 95% CI -6.22, -1.58; p = 0.001). The variance was imputed from the reported p value presented in the trial.[120]

Key Question 2. Other outcomes

One RCT[120] comparing TENS (n = 30) versus sham control (n = 30) provided data on health-related quality of lilfe (HRQOL) (10cm VAS) and quality of sleep (10cm VAS) (Table 16). Neurostimulation provided significant improvement in HRQOL versus sham control (MD -4.30; 95% CI -6.86, -1.74; p = 0.001). Similarly neurostimulation provided significant improvement in quality of sleep (MD -3.60; 95% CI -575, -1.45; p = 0.001). The variance was imputed from the reported p value in the trial for both outcomes.[120]

Key Question 3: Adverse effects

No data were reported on adverse effects.

Key Question 4. Efficiacy, effectiveness, and safety in subpopulations

No data were reported on subpopulations.

Table 16. Evidence summary table (randomized controlled trials): Neurostimulation

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment)**[120,121]	2	123	MD (95% CI)	**-2.79 (-4.95, -0.64)***	67%
	Pain on movement (post-treatment)[120]	1	60	MD (95% CI)	**-3.90 (-6.22, -1.58)***	NA
KQ2	**HRQOL**[120]	1	60	MD (95% CI)	**-4.30 (-6.86, -1.74)***	NA
	Quality of sleep[120]	1	60	MD (95% CI)	**-3.60 (-5.75, -1.45)***	NA

KQ = key question; CI = confidence intervals; MD = mean difference; NA = not applicable; * = statistically significant

Rehabilitation

Overview of Included Studies

One RCT[122] evaluated the efficacy and/or harms of the administration of physical therapy (stretching and strengthening of spinal and psoas muscles (n = 18) vs. standard care (n = 19)). The mean age was 67.1 years and all participants were female. Acute pain was measured using the 10cm VAS and the mean baseline pain measure was 7.9cm. See Tables E-7 and F-7 (Appendices E and F) for details of the study characteristics and interventions.

The trial had a high risk of bias (Appendix G). Summary of the evidence from this trial is provided in Table 17.

Table 17. Evidence addressing key questions: Rehabilitation

Key Question	Outcome	Evidence avaiability	Summary of Evidence
KQ 1	**Acute pain***	Yes	1 RCT reported a statistically significant effect in favor of physical therapy vs. standard care. The strength of the evidence was rated as insufficient.
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	No	
	Functional status	No	
	Pain medication use; change in type and quantity	No	
	Mental status (e.g., delirium, confusion)	No	
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	No	
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	No	
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; RCT = randomized controlled trial; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

Acute Pain (Post-Treatment Means)

There was a statistically significant difference in additional pain relief following stretching-strengthening of spinal and psoas muscles vs. standard care (MD -1.39; 95% CI -2.27, -0.51; p = 0.002) (Table 18). This was not considered clinically significant.

Key Question 2. Other outcomes

No other outcomes were reported.

Key Question 3. Adverse effects

No data were reported for adverse effects.

Key Question 4. Efficacy, effectiveness and safety in subpopulations

All participants in this trial were female.

Table 18. Evidence summary table (randomized controlled trials): Rehabilitation

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**[122]	1	37	MD (95% CI)	**-1.39 (-2.27, -0.51)***	NA

CI = confidence intervals; KQ = key question; MD = mean difference; NA = not applicable; * statistically significant

Traction

Overview of Included Studies

Six RCTs[26,123-127] and four nRCTs[128-131] (n = 1,310) evaluated the efficacy and/or harms of the administration of traction vs. no intervention or other interventions; sample sizes ranged from 64 to 311 participants. Additionally, one prospective cohort study[132] (n = 134) provided data. The mean age ranged from 74.0 to 81.0 years. Most were female (66.2 to 84.7 percent). Acute pain was measured using the VAS and the mean baseline pain measure ranged from 0.3 to 6.9. See Tables E-8 and F-8 (Appendices E and F) for details of the study characteristics and interventions.

All the RCTs and nRCTs had a high risk of bias; the cohort study had a moderate score (n = 6 stars) on the NOS (Appendices G, I). Summary of the evidence from these trials is provided in Table 19.

Table 19. Evidence addressing key questions: Traction

Key Question	Outcome	Evidence avaiability	Summary of Evidence
KQ 1	**Acute pain***	Yes	9 trials reported no statistically significant difference between skin, skeletal, and no traction. The strength of the evidence was rated as low. 1 trial reported no statistically significant difference between skin and skeletal traction. The strength of the evidence was rated as insufficient.
	Chronic pain*	No	
KQ2	**Mortality (30-day* and up to 1-year postfracture)**	Yes	1 trial reported no statistically significant difference between skin, skeletal, and no traction. The strength of the evidence was rated as insufficient.
	Functional status	No	
	Pain medication use; change in type and quantity	Yes	2 trials reported no statistically significant difference between skin traction and no traction.
	Mental status* (e.g., delirium, confusion)	No	
	Health-related quality of life	No	
	Quality of sleep in the hospital	No	
	Ability to participate in rehabilitation	No	
	Return to prefracture living arrangements	No	
	Health services utilization	Yes	2 trials reported no statistically significant difference between skin traction and no traction.
KQ3	**Frequency of adverse effects (e.g. stroke*, myocardial infarction*, renal failure*)**	Yes	7 trials and 1 cohort study demonstrated no statistically significant difference in any adverse event, peroneal palsy, damage to surrounding structures, difficult reduction, pressure sores, direct skin damage, deep venous thrombosis, or failure to heal.
KQ4	**Effectiveness and safety in differing subpopulations**	No	

KQ = key question; * = body of evidence rated using the AHRQ GRADE approach (Grading of Recommendation Assessment, Development and Evaluation)

Key Question 1. Acute and chronic pain management

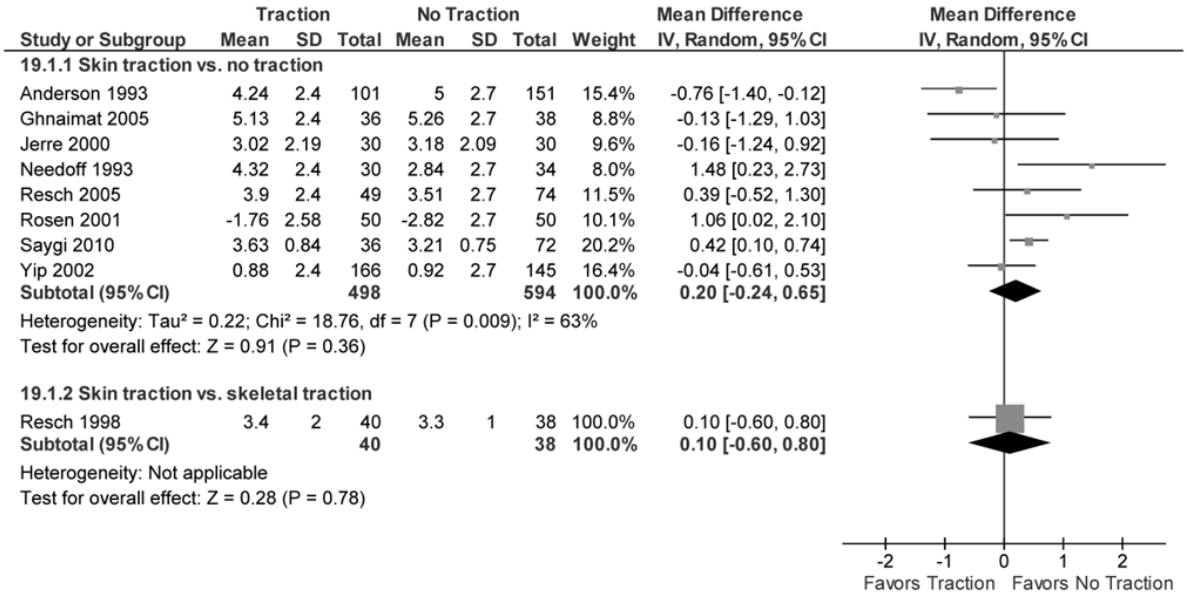
Acute Pain (Post-Treatment Means)

Eight trials[26,124,125,127-131] compared skin traction (n = 498) versus no traction (n = 594) (Table 20). There was no significant difference in pain relief between the groups (MD 0.20; 95% CI -0.24, 0.65; p = 0.36) (Figure 13). The variance was imputed for one of the trials[127] using the reported p value in the original publication and from the other included trials for four trials.[125,128,129,131] The strength of the evidence was rated as insufficient to make any firm conclusions.

In the trial[126] that compared skin traction (n = 40) vs. skeletal traction (n = 38), there was no significant difference between the two groups (MD 0.10; 95% CI -0.60, 0.80; p = 0.78).

The strength of the evidence was rated as insufficient to make any firm conclusions.

Figure 13. Traction—acute pain (post-treatment means)



Key Question 2. Other outcomes

Health services utilization. LOS for acute hospitalization was reported in two trials[128,129] comparing skin traction (n = 137) vs. no traction (n = 189) (Table 20). In one trial[128] there was no significant difference between the groups (MD 1.20; 95% CI -0.93, 3.33; p = 0.27). The MD was not estimable in the other study[129] as no measure of variance was reported; however, the authors reported that the difference was not statistically significant. In order to allow pooling of the two trials, the variance was imputed from the available study variance.[128] There was no significant difference in LOS between the two groups (MD 1.08; 95% CI -0.78, 2.95; p = 0.26).

Mortality (30-day). Thirty-day mortality was reported in one trial[123] (n = 80) (Table 20). There was no difference in mortality between skin or skeletal traction vs. no traction (0/55 vs. 2/25; OR 0.14; 95% CI 0.01, 1.44; p = 0.10). There were no reports of mortality when comparing skin vs. skeletal traction.

Pain medication use. Additional pain medication use was reported in two trials[127,128] (n = 352) (Table 20). There was no significant difference in pain medication use following skin traction vs. no traction (99/151 vs. 111/201; OR 1.47; 95% CI 0.83, 2.61; p = 0.18).

Key Question 3. Adverse effects

Seven trials[124,126-131] (n = 1,043) evaluated the nature and frequency of adverse effects associated with the administration of skin or skeletal traction vs. no traction (Table 20). Additionally, one cohort study[132] (n = 134) compared skeletal traction vs. pillow (Table 21). In two trials[126,131] (n = 389) no adverse effects were reported in either the intervention or control groups. For the following specific adverse effects, there were no significant differences between the study groups: damage to surrounding structures,[127] deep venous thrombosis,[124] difficult reduction,[128,129] direct skin damage,[129,130] failure to heal,[124] peroneal palsy,[127,130] and pressure sores.[124]

Key Question 4. Efficacy, effectiveness and safety in subpopulations

One trial[131] was conducted in Asian participants comparing skin traction (n = 166) versus no traction (n = 145). Acute pain reduction was not significantly different between the two groups (MD -0.04; 95% CI -0.61, 0.53; p = 0.89). No adverse effects were recorded (0/166 vs. 0/145).

Table 20. Evidence summary table (RCT/nRCT): Traction

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ1	**Acute pain (post-treatment means)**					
	Skin traction vs. no traction[26,124,125,127-129,131]	8	1092	MD (95% CI)	0.20 (-0.24, 0.65)	63%
	Skin traction vs. skeletal traction[26]	1	78	MD (95% CI)	0.10 (-0.60, 0.80)	NA
KQ2	**Additional pain medication use**					
	Skin traction vs. no traction[127,128]	2	352	OR (95% CI)	1.47 (0.83, 2.61)	17%
	Length of stay for acute hospitalization					
	Skin traction vs. no traction[128,129]	2	326	MD (95% CI)	1.08 (-0.78, 2.95)	0%
	Mortality 30-day					
	Traction vs. no traction[123]	1	80	OR (95% CI)	0.14 (0.01, 1.44)	NA
	Skin traction vs. no traction[123]	1	51	OR (95% CI)	0.18 (0.01, 3.89)	NA
	Skeletal traction vs. no traction[123]	1	54	OR (95% CI)	0.07 (0.00, 3.48)	NA
	Skin traction vs. skeletal traction[123]	1	55		NE	
KQ3	**Any adverse event**					
	Skin traction vs. no traction[131]	1	311		NE	
	Skin traction vs. skeletal traction[126]	1	78		NE	
	Damage to surrounding structures					
	Skin traction vs. no traction[127]	1	100	OR (95% CI)	5.21 (0.24, 111.24)	NA
	Deep venous thrombosis					
	Skin traction vs. no traction[124]	1	120		NE	
	Difficult reduction					
	Skin traction vs. no traction[128,129]	2	326	OR (95% CI)	0.90 (0.43, 1.98)	0%
	Direct skin damage					
	Skin traction vs. no traction[129,130]	2	182	OR (95% CI)	10.51 (0.49, 224.84)	0%
	Failure to heal					
	Skin traction vs. no traction[124]	1	120	OR (95% CI)	1.72 (0.68, 4.36)	NA
	Peroneal palsy					
	Skin traction vs. no traction[127,130]	2	208	OR (95% CI)	4.33 (0.44, 42.35)	0%
	Pressure sores					
	Skin traction vs. no traction[124]	1	120	OR (95% CI)	11.99 (0.65, 221.86)	NA
	Peroneal palsy					
	Skeletal traction vs. no traction[132]	1	134	OR (95% CI)	0.09 (0.00, 1.60)	NA

CI = confidence intervals; KQ = key question; NA = not applicable; NE = not estimable; OR = odds ratio; RCT/nRCT = randomized and nonrandomized controlled trials

Table 21. Evidence summary table (cohort studies): Traction

	Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
KQ3	**Peroneal palsy**					
	Skeletal traction vs. no traction[123]	1	134	OR (95% CI)	0.09 (0.00, 1.60)	NA

CI = confidence intervals; KQ = key question; NA = not applicable; OR = odds ratio

Discussion

Overview

Hip fracture due to low-energy trauma (e.g., slip and fall) is a common condition in the geriatric population. Today, nearly all hip fractures in the developed world are surgically treated and represent one of the most common emergency orthopedic procedures. Even so, the associated morbidity and mortality of hip fracture are significant. One year mortality for hip fracture is estimated to be up to 37 percent, and a large proportion of those patients who do survive will never recover to their prefracture level of function.[5]

Hip fractures are frequently characterized by acute pre-, peri- and postoperative pain; with pain manifesting on a number of fronts. Preoperative pain arises from injury to the muscles and joint capsule from the serrated edges of broken bone and the associated release of local inflammatory factors. Immediate postoperative pain is attributed to the procedures required for the surgical fixation of the femur (e.g., skin incision, femur stabilization). Patients with greater postoperative pain are slower to mobilize and have longer hospital stays.[147] Additionally, pain at all stages is aggravated by psychological stress and anxiety.

Pain that is not properly managed in geriatric patients can have deleterious effects in terms of increased risk of cardiovascular adverse effects and postoperative delirium. While little is known about the impact of postoperative pain in older adults, physicians are hesitant to prescribe opioid analgesics for fear of adverse effects such as delirium, nausea, respiratory depression, drowsiness, hypotension, and constipation as these events have been demonstrated to occur more frequently in the geriatric population.[147,148] Others have reported that postoperative pain management in older adults is more commonly undertreated and untreated than in younger patients.[149] This may reflect a belief among patients and health professionals that pain in the elderly is a natural phenomenon that is self-limiting and should be left to take its course without any intervention.[19]

This comparative effectiveness review (CER) identified, summarized, critically appraised, and compared the evidence on pain management interventions following hip fracture. We conducted a comprehensive search of over 25 electronic databases for published studies and ongoing trials. In addition, we hand searched major conference proceedings in order to identify additional relevant studies. Finally, we did not exclude studies on the basis of their published language. All these safeguards were implemented to help identify the evidence and limit the possibility of publication bias. To reduce the possibility of selection bias, we performed duplicate, independent study selection, and all data were independently extracted by two reviewers.

Summary of Findings

Table 22 summarizes the findings for key outcomes for each intervention. Many studies within this review included small numbers of participants and reported only a small number of outcome measures. Several studies had a poor level of methodological rigor, in particular regarding their inherent risk of bias. Of the 65 included trials, the majority were assessed with an unclear risk for bias. Twenty-eight trials were considered to be at high risk of bias while only two were considered to be of low risk of bias. The strength of the evidence for most outcomes was considered insufficient or low. This is a reflection of the general poor methodological

quality, lack of study power, and number of studies investigating each intervention in this population.

The majority of studies included in this review fell into the categories of nerve blocks (n = 30),[88-106,108-111,113-119] and anesthesia (n = 26),[56-58,60-73,75-777,79-83,145] while fewer studies dealt with traction (n = 11),[26,123-132] systemic analgesia (n = 3),[41,42,55] complementary and alternative medicine (n = 2),[43,54] multimodal pain management (n = 2),[86,87] neurostimulation (n = 2),[120,121] and rehabilitation (n = 1).[122] Although we restricted the publication of studies from 1990, there appears to be a trend for more recent studies to examine pain management following hip fracture (median publication date = 2003; IQR: 1998 to 2007). Most studies included in this review were RCTs conducted in single university settings in Europe with few studies included from North American sites.

Most studies examined the pharmaceutical management of peri- and postoperative pain in this patient population. Short-term (in hospital) postoperative pain was the most frequent pain examined. None of the studies examined the longer-term pain associated with hip fracture; that is pain extending beyond the initial 30 days of hip fracture. Management of pain was often evaluated from few perspectives such as reported pain, mortality and adverse effects. The ramifications of pain were infrequently examined in terms of functional recovery, HRQOL, and health services utilization.

Although the majority of hip fracture patients are elderly women, this patient population consists of subgroups that warrant further investigation. For instance, almost half of the studies (n = 31) reported excluding patients with any cognitive impairment, or inability to cooperate. Researchers have reported that approximately 35 percent of the elderly hip fracture population includes patients with some degree of cognitive impairment, be it, dementia, delirium, or acute confusion.[150] None of the included studies in this CER exclusively examined participants from institutional settings or with cognitive impairment, which reduces the external validity or generalizability of our findings to the overall hip fracture patient population.

Regardless of these limitations, some general consensus can be made from this review.

Key Questions 1 and 2: Pain management and other outcomes. The available evidence suggests that, in general, the **nerve blockade** is effective for the relief of the acute pain of hip fracture compared with standard care alone. Nerve blockade also reduces the need for supplemental systemic analgesia and may reduce the risk of delirium, a common and dangerous complication of hip fracture. However, most studies were limited to either assessing acute pain or examining use of additional analgesia and did not report on how nerve blockades may affect rehabilitation such as ambulation or mobility if the blockade has both sensory and motor effects. Furthermore, our decision to extract followup data demonstrating the greatest improvement for the intervention arm may have introduced a bias favoring the intervention. However, we do not expect this to have had a major impact because most studies presented data for only one time point. Nerve blockade of the types described in this CER are within the repertoire of most practicing anesthesiologists, but many institutions are deterred from providing them due to the additional time, effort, and supervision they require if they are to work well.

This review also calls into question some commonly held beliefs about the care of those with hip fracture. **Preoperative traction**, for instance, does not appear to reduce pain or complications in any demonstrable way compared with no traction. These results are consistent with those of the previously published Cochrane review on this topic.25 While the strength of evidence is insufficient to make firm conclusions, spinal **anesthesia** used during the operation to

fix the fracture, while effective and safe, does not demonstrably differ in rates of mortality, delirium, or other medical complications of the fracture as compared with general anesthesia. Adding other agents to plain local anesthetic for spinal anesthesia does not seem to make any difference to outcomes outside the operating room. Furthermore, bigger doses of spinal anesthetic may cause more hypotension issues without improving pain control or outcome.[151]

The evidence guiding the selection of **systemic drugs** for hip fracture analgesia is very scant and warrants further study.

This review also finds that **acupressure, relaxation therapy,** and **transcutaneous electrical neurostimulation** are safe interventions that may be associated with potentially clinically meaningful reductions in pain after hip fracture, but further evidence is warranted before any firm conclusions are reached. The obvious drawback of these is the amount of skilled health provider time that must be used to apply and/or teach these modalities correctly. **Physical therapy regimens** may potentially improve pain control in the postoperative period, but there is insufficient evidence to draw firm conclusions.

No evidence could be found that any analgesic intervention attenuated the progression of acute to chronic pain. Furthermore, there was insufficient evidence to show that **multimodal analgesia** (combinations of analgesic interventions) yields improvements over single modalities. Further research in this area might profitably focus on combinations of interventions that are known to be effective in isolation.

Key Question 3: Adverse effects. Although most studies reported on adverse effects associated with the specific interventions being evaluated, the included studies were small; thus most studies reported few, if any, adverse effects. Moreover, the horizon for adverse effects was over a short period of time, usually within the acute care setting, and did not examine the development of adverse effects outside of the acute care setting.

Key Question 4: Effectiveness and safety of pain management in differing subpopulations. This question was addressed by limited data from two RCTs of nerve blocks—one was restricted participants with heart disease and to participants who were independent prior to the hip fracture. The only significant difference reported was a reduction in acute pain in participants with heart disease who received a nerve block.

Applicability

The study populations in this body of evidence were relatively homogeneous. Studies included patients with all types of hip fractures due to low energy trauma. All participants were over 50 years of age; the mean age in most studies clustered between 77 and 82 years. Most patients were female. Studies generally included a mixture of hip fracture types and minimal data for specific fracture types were available. A majority of studies excluded patients on the basis of mental status (i.e., patients with dementia or other cognitive disorders). Studies did not generally provide information of the pre-fracture dwelling (i.e., community vs. institution) or social status/support of participants (e.g., married, living with relatives). Interventions were provided across the spectrum of the care pathway from preoperative to postoperative; however, no studies provided data on long-term followup for this patient population.

The other issue regarding applicability for this body of evidence relates to the practitioners administering the interventions (e.g., anesthetists, surgeons, physical therapists, or other health care providers). Outcome effects may differ between the trials and real life practice based on

practitioners' skills and experience, volume of surgery, and variations or rigor surrounding cointerventions or procedural protocols.

Limitations of Existing Evidence

To our knowledge, no specific evidence-based guidelines for pain management in hip fracture are available; however, this may be indirectly related to the fact that to the best of our knowledge there currently are no committees or task force groups for pain management in hip fracture. Further, there are no recommended standardized outcomes for assessing pain specific to this patient population. This patient population is different from other surgical patients in that they are older and predominantly women with a significant number of coexisting conditions, commonly including altered cognition.

Evaluations of common subpopulations found within the overall hip fracture patient populations were infrequent. A large proportion of the included studies excluded patients with altered cognition due to delirium or dementia, despite the high prevalence of dementia in the hip fracture population. Further, most studies performed limited assessment of either delirium or dementia in their participants using broad cognitive assessment tools (e.g., Mini-Mental State Examination) that were unable to distinguish between onset of dementia or acute delirium. In addition, although multiple comorbidities are common in patients who experience a hip fracture, risk adjustments for illness/health severity were not reported, nor were most of the subpopulations that we intended to investigate (e.g., prefracture functional status). These are all factors that could potentially affect reported pain levels.

Included studies were primarily pharmacologic interventions and represented evaluation by a single discipline (e.g., anesthesiology) despite evidence in other clinical areas that optimal chronic pain management is multidisciplinary.[19,152] In addition studies were primarily conducted in single centers in Europe or Asia with small samples sizes; minimal evidence was available from centers in North America. Study quality was low and thus, clear evidence to support clinical decision making for interventions is limited. Also the choice to limit the search to 1990 might have led to missing some earlier studies on pain management in this population, but its effect is not expected to change the conclusions of this report.

In addition, lack of standardized outcome reporting or use of standardized measures limits the interpretation and applicability of the results. Although pain and function are correlated,[147] most outcomes focused on pain relief and did not evaluate if the intervention had any positive or negative effects on the patients' ability to mobilize postoperatively, a factor that is linked to recovery levels following hip fracture.[153] There was no evidence about managing pain after hospital discharge or examining the long-term effects of early postoperative pain management on subsequent recovery.

Finally, because of the low incidence of complications following surgery, no individual included study had adequate numbers to detect associated adverse effects with the interventions. For example, the rationale for using a nerve block for pain management following a hip fracture is primarily to enable pain to be controlled with lower doses of systemic analgesia. Although the studies demonstrated a reduced requirement for systemic analgesics, this is only clinically useful if it associated with a reduction in the adverse effects of such analgesic use.

Recommendations for Future Research

Multicenter research studies. Adequately powered multi-center research studies are needed to provide a comprehensive assessment of safe, effective, and appropriate pain management

following a hip fracture. Studies need to be large enough to allow subgroup analyses by age, gender, comorbidities, functional groups (e.g., independent vs. dependent in ambulation), or multiple complex interventions (e.g. 3-in-1 vs. femoral block only). In addition, researchers need to consider inclusion of common subpopulations of hip fracture patients. In particular, those with altered cognition who make up a substantial proportion of the overall hip fracture patient population should be included in future studies of pain management following hip fracture.

Outcomes. Standardization of outcomes and outcome measures will allow easier and meaningful comparisons across different interventions and among studies. The types of outcomes reported do not reflect the multidimensional nature of pain. Relevant outcomes should include validated pain scores, prescription of opiates and other agents, adverse effects or complications attributable or related to the intervention. There should also be consideration for use of nonverbal pain assessment scales to allow assessment of pain in patients with communication issues such as delirium and/or dementia. Associated outcomes of pain such as function, quality of life, and time to recovery should also be evaluated.

The evaluation of pain should include preoperative assessment, daily assessments while in hospital, as well as regular and longer term followup of pain beyond the acute hospital setting. Researchers should consider pain outcomes up to 6 months post-hip fracture to determine the pattern of pain recovery and whether early effective pain management techniques affects ultimate recovery levels.

Methods. Investigators should consider including patients with cognitive impairment in future studies as this group represents a substantial proportion of the hip fracture patient population. Better cognitive screening and assessment tools are needed to determine the presence of delirium and to be able to distinguish between acute delirium and chronic underlying or new onset dementia. Future research should seek to minimize bias by blinding outcome assessors, use of validated and standardized outcome assessment instruments, adequate allocation concealment (where applicable), and appropriate handling and reporting of missing data.

Conclusions

For the majority of interventions, there are only sparse data available, which precludes firm conclusions for any single approach or for the optimal overall pain management following nonpathological hip fracture due to low energy trauma. The paucity of evidence related to long-term outcomes and the fact that the majority of the data is derived from studies of low methodological quality or from study designs associated with higher risk of bias (i.e., cohort studies). Overall, the evidence shows that most interventions result in improvements in short-term pain scores; however, few differences of long-term clinical importance are evident when comparisons between interventions are available. The rates of complications were generally low and the majority of complications were not significantly different among the interventions. Well-designed and -powered, long-term trials are needed in order to determine the relative effectiveness of pain interventions for hip fracture patients. Until then, pain management in this population will rely heavily on availability of the interventions, staff skills and training and pre-existing patient comorbidities.

Table 22. Summary of evidence for key outcomes for pain management following hip fracture

Outcome	Comparison (# studies)	Strength of evidence	Summary
Systemic analgesia			
Acute pain	Parecoxib IV vs. diclofenac ± meperidine IM (1 RCT) Intrathecal isotonic clonidine vs. intrathecal hypertonic clonidine (1 RCT) Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	Significant effect in favor of parecoxib IV (MD = -0.70; 95% CI -1.04, -0.36) Significant effect in favor of intrathecal isotonic clonidine (MD = -1.69; 95% CI -2.01, -1.37) No significant difference
Acute pain at rest	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Lysine clonixinate vs. metamizole (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal vs. general anesthesia			
Acute pain	Spinal vs. general anesthesia (1 RCT)	Insufficient	Significant effect in favor of spinal anesthesia (MD = -0.86; 95% CI -1.30, -0.42)
Chronic pain	None	Insufficient	No data
30-day mortality	Spinal vs. general anesthesia (2 RCTs, 2 cohort studies)	Low	No significant difference
Delirium	Spinal vs. general anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	Spinal vs. general anesthesia (2 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – continuous vs. single administration			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	Continuous vs. single administration (3 RCTs, 1 cohort study)	Low	No significant difference
Delirium	Continuous vs. single administration (2 RCTs)	Low	No significant difference
Myocardial infarction	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Stroke	Continuous vs. single administration (1 RCT)	Insufficient	No significant difference

Table 22. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of evidence	Summary
Anesthesia: spinal – addition of other medications			
Acute pain	Addition of fentanyl vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
	Addition of sufentanil vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Addition of morphine vs. standard spinal anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Anesthesia: spinal – different doses			
Acute pain	Bupivacaine 2.5mg vs. 5mg (1 cohort study)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Bupivacaine 4mg vs. 12mg (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Complementary and alternative medicine			
Acute pain	Acupressure vs. standard care (1 RCT)	Insufficient	No significant difference
	Relaxation vs. standard care (1 RCT)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Multimodal pain management			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Delirium	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data

Table 22. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of evidence	Summary
Stroke	Multimodal pain management vs. standard care (1 cohort study)	Insufficient	No significant difference
Nerve blockade			
Acute pain	Nerve block vs. no nerve block (11 RCTs)	Moderate	Significant effect in favor of nerve block in subgroup analyses
Pain on movement	Nerve block vs. no nerve block (4 RCTs)	Low	Significant effect in favor of nerve block in subgroup analyses
Pain at rest	Nerve block vs. no nerve block (3 RCTs)	Low	Data inconsistent for conclusions to be made
Day 1 pain	Nerve block vs. no nerve block (1 RCTs)	Insufficient	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	Nerve block vs. no nerve block (4 RCTs)	Low	No significant difference
Delirium	Nerve block vs. no nerve block (3 RCTs, 2 cohort studies)	Moderate	Significant effect in favor of nerve block (OR_{RCT} = 0.36; 95% CI 0.17, 0.74) (OR_{Cohort} = 0.24; 95% CI 0.08, 0.72)
Myocardial infarction	Nerve block vs. no nerve block (2 RCTs, 1 cohort study)	Insufficient	No significant difference
Stroke	Nerve block vs. no nerve block (1 RCT, 1 cohort study)	Insufficient	No significant difference
Renal failure	None	Insufficient	No data
Nerve blockade vs. regional anesthesia			
Acute pain	Nerve block vs. regional anesthesia (3 RCTs)	Low	No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Nerve block vs. regional anesthesia (1 RCT)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Nerve Blocks: ropivacaine vs. bupivacaine			
Acute pain	None	Insufficient	No data
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	Ropivacaine vs. bupivacaine (1 cohort study)	Insufficient	No significant difference
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Neurostimulation			
Acute pain	Neurostimulation vs. standard care (2 RCTs)	Insufficient	Significant effect in favor of neurostimulation (MD = -2.79; 95% CI -4.95, -0.64)
Pain on movement	Neurostimulation vs. standard care (1 RCT)	Insufficient	Significant effect in favor of neurostimulation (MD = -3.90; 95% CI -6.22, -1.58)
Chronic pain	None	Insufficient	No data

Table 22. Summary of evidence for key outcomes for pain management following hip fracture (continued)

Outcome	Comparison (# studies)	Strength of evidence	Summary
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Rehabilitation			
Acute pain	Physical therapy vs. standard care (1 RCT)	Insufficient	Significant effect in favor of physical therapy (MD = -1.39; 95% CI -2.27, -0.51)
Chronic pain	None	Insufficient	No data
30-day mortality	None	Insufficient	No data
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data
Traction			
Acute pain	Skin traction vs. no traction (7 RCTs) Skin traction vs. skeletal traction (1 RCT)	Low Insufficient	No significant difference No significant difference
Chronic pain	None	Insufficient	No data
30-day mortality	Skin traction vs. no traction (1 RCT) Skeletal traction vs. no traction (1 RCT)	Insufficient Insufficient	No significant difference No significant difference
Delirium	None	Insufficient	No data
Myocardial infarction	None	Insufficient	No data
Renal failure	None	Insufficient	No data
Stroke	None	Insufficient	No data

CI = confidence interval; IM = intramuscular; IV = intravenous; MD = mean difference; OR = odds ratio; RCT = randomized controlled trial; SMD = standardized mean difference

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Acronyms and Abbreviations

AE	adverse effect
AHRQ	Agency for Healthcare Research and Quality
CER	Comparative Effectiveness Review
CAM	complementary and alternative medicine
CI	confidence intervals
COX-2	Cyclooxygenase-2
EPC	Evidence-based Practice Center
GI	gastrointestinal
GRADE	Grading of Recommendation Assessment, Development and Evaluation
HRQOL	health-related quality of life
IM	intramuscular
IQR	interquartile range
IV	intravenous
KQ	Key Question
LOS	length of stay
MD	mean difference
mg	milligrams
MMSE	mini-mental state examination
MI	myocardial infarction
NB	nerve block
NS	neurostimulation
NOS	Newcastle-Ottawa Scale
NSAIDS	nonsteroidal anti-inflammatory drugs
nRCT	nonrandomized controlled trial
NA	not applicable
NE	not estimable
NR	not reported
NRS	numeric rating score
PICOTS	Population, Intervention, Comparison, Outcome, Timing, and Setting
RCT	randomized controlled trial
RoB	risk of bias
SRC	Scientific Resource Center
SD	standard deviation
SMD	standardized mean difference
TENS	transcutaneous electrical neurostimulation
US	ultrasound
UAEPC	University of Alberta Evidence-based Practice Center
VAS	visual analog scale

Appendix A. Technical Expert Panel and Peer Reviewers

Technical Expert Panel

In designing the study questions and methodology, the UAEPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Due to these differences in opinion, the study questions, design, and/or methodologic approaches do not necessarily represent the views of individual technical and content experts.

Technical Expert	Affiliations/Location
Paul M. Arnstein, R.N., Ph.D, A.P.R.N.-B.C.	Massacheusetts General Hospital Boston, MA
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Peer Reviewers

Peer reviewer comments on a preliminary draft of this report were considered by the University of Alberta Evidence-based Practice Center in preparation of the final report. The synthesis presented in this report does not necessarily represent the views of individual reviewers.

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Paul M. Arnstein, R.N., Ph.D, A.P.R.N.-B.C.	Massacheusetts General Hospital Boston, MA
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Roger Chou, M.D.	Oregon Health & Science University Portland, OR
Richard Rosenquist, M.D.	Anesthesia Pain Clinic Iowa City, IA

Appendix B. Exact Search Strings

Table B-1. MEDLINE—Ovid Version

Table B-2. AMED (Allied and Complementary Medicine), Global Health and International Pharmaceutical Abstracts (IPAB)—Ovid Version

Table B-3. BIOSIS Previews—Institute for Scientific Information–Thomson Reuters

Table B-4. CINAHL (Cumulative Index to Nursing & Allied Health Literature), Academic Search Elite and Health Source: Nursing and Academic Edition—Ebsco Version

Table B-5. Cochrane Complementary Medicine Trials Register and CAMPAIN (Complementary and Alternative Medicine and Pain Database) Grant Number R24-AT001293 from the National Center for Complementary and Alternative Medicine (NCCAM)

Table B-6. Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects—Wiley Version

Table B-7. EBM Reviews—Cochrane Central Register of Controlled Trials–Ovid Version

Table B-8. EMBASE—Ovid Version

Table B-9. Global Health Library—World Health Organization

Table B-10. Pascal—Ovid Version

Table B-11. PeDRO—The Physical Therapy Evidence Database

Table B-12. ProQuest Dissertations and Theses–Full Text

Table B-13. Scopus—Elsevier B.V.

Table B-14. Web of Science—Institute for Scientific Information—Thomson Reuters

Table B-15. TOXLINE—ProQuest

Conference Proceedings

Table B-16. Conference Papers Index—ProQuest

Table B-17. OCLC Papers First—OCLC FirstSearch

Table B-18. ScienceDirect Tables of Contents

Table B-19. Conference Proceedings handsearched

Trials Registers

Table B-1. MEDLINE®—Ovid version

OvidSP_UI02.01.02.102 1950 to July Week 1 2009	Searched: 09Jul09 Results: 1061
1. exp Pain/ 2. exp "anesthesia and analgesia"/or exp analgesia/ 3. ((an?esthet$ or an?esthesia) adj4 (regional$ or local$ or general or spinal or epidural)).mp. 4. (block or analges*).mp. 5. or/2-4 6. exp Therapeutics/or exp "Outcome Assessment (Health Care)"/or exp "Length of Stay"/or "Quality of Life"/or "functional outcome".ti,ab. 7. ((pain* or discomfort* or ache* or aching or sore* or suffer*) adj3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")).mp. 8. exp Pain/rt, th, us, rh, dh, su, pc, dt 9. pain postoperative/pc, th 10. Pain Measurement/ 11. or/7-10 12. exp Hip Fractures/rh, nu, th, dt, dh 13. exp Hip Fractures/	14. ((intertrochanter* or petrochanter* or subtrochanter* or extracapsular or petrochant* or trochant* or hip or femoral neck) adj4 (hemiarthroplasty or fracture*)).mp. 15. ("neck of femur" adj4 fractur*).mp. 16. or/13-15 17. 5 and 16 18. 11 and 16 19. 1 and 16 20. 6 and 12 21. or/17-20 22. exp Arthroplasty, Replacement, Hip/ 23. THA.mp. 24. total hip*.mp. 25. or/22-24 26. 21 not 25 27. (pediatric* or child or children* or adolesc* or young or youth* or pregnan*).ti,ab,jw,kw,sh. 28. animals/or exp neoplasms/or case reports/or editorials/or exp Emergency Service, Hospital/ 29. or/27-28 30. 26 not 29 31. limit 30 to yr="1990 - 2009"

Table B-2. AMED (Allied and Complementary Medicine), Global Health and International Pharmaceutical Abstracts (IPAB)—Ovid version

OvidSP_UI02.01.02.102		Searched: 10Jul09
Database	**Dates Available**	**Results**
AMED	1985 to July 2009	340
Global Health	1910 to June 2009	157
IPAB	1970 to June 2009	95

1. exp Pain/
2. exp "anesthesia and analgesia"/or exp "Nerve Block"/or exp "anesthesiological techniques"/or exp "analgesic, antiinflammatory, antirheumatic and antigout agents"/or exp "agents interacting with transmitter, hormone or drug receptors"/
3. (block or analges*).mp.
4. (Therapy or therapeutics or "disease management" or "quality of life" or treatment or "outcome assessment" or "length of stay" or "functional outcome" or rehabilitation or traction or acupunct* or acupress* or stimulation or "continuous passive motion").ti,cw,cc,bt,id,hw,sh.
5. exp Pain Assessment/or exp Pain Measurement/
6. ((pain* or discomfort* or ache* or aching or sore* or suffer*) adj3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")).mp.
7. or/1-6
8. "fracture, hip"/or hip fracture/or hip fractures/or acetabulum fracture/or femur intertrochanteric fracture/or femur neck fracture/or femur pertrochanteric fracture/or exp femur subtrochanteric fracture/or femur trochanteric fracture/
9. ((intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or femoral neck or “neck of femur”) adj4 fracture*).mp.
10. ("neck of femur" adj4 fractur*).mp.
11. or/8-1012. 7 and 11
13. (THA or total hip*).mp. or exp "Arthroplasty, Replacement, Hip"/
14. (neoplasm* or cancer* or carcinoma* or lymphoma or sarcoma* or Emergency).ti,de,cw,cc,bt,id,hw,sh.
15. case report.ti,de,cw,cc,bt,id,hw,sh.
16. (pediatric* or child or children* or adolesc* or young or youth* or pregnan*).ti,ab,hw,de,cw,cc,tt,ed,sh.
17. or/13-16
18. 12 not 17
19. limit 18 to yr="1990 -Current"
20. remove duplicates from 19

Table B-3. BIOSIS previews—Institute for Scientific Information—Thomson Reuters

1926 to 2009 Searched: 14Jul09	Results: 206
# 3 #2 AND #1 Databases=PREVIEWS Timespan=1990-2009 # 2 TS=(intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") SAME TS=(fracture*) AND Taxa Notes=(Humans) # 1 TS=(pain* or discomfort* or ache* or aching or sore* or suffer*) SAME TS=(assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life") AND Taxa Notes=(Humans)	

Table B-4. CINAHL (Cumulative Index to Nursing & Allied Health Literature), Academic Search Complete, Health Source: nursing/academic edition—Ebsco version

1937 to 2009 (CINAHL) 1985 to 2009 (Academic Search Elite) Searched: 13Jul09	Results: 189
S11 S10 and S3 S10 (S9 or S8 or S7 or S6 or S5 or S4) S9 (safe or safety) or (adverse w1 effect* or adverse w1 event* or "side effect*") or (harm* or contraindicat* or contra-indicat*) S8 (cohort or observation* or control* or prospectiv* or volunteer* or "case-series" or "time-series" or "case-comparison" or "case-referent" or "cross-sectional" or risk* or efficacy) S7 (singl* w10 blind* or singl* w10 mask* or doubl* w10 blind* or doubl* w10 mask* or trebl* w10 blind* or trebl* w10 mask* or cross-over or placebo* or control* or random* or factorial or sham* or clin* w10 trial* intervention* w10 trial* or compar* w10 trial* or experiment* w10 trial* or preventive w10 trial* or therapeutic w10 trial*) S6 (clin* w25 trial* or random*) S5 PT clinical trial S4 ((MH "Random Assignment") or (MH "Random Sample") or (MH "Crossover Design") or (MH "Clinical Trials+") or (MH "Double-Blind Studies") or (MH "Single-Blind Studies") or (MH "Comparative Studies") or (MH "Control Group") or (MH "Factorial Design") or (MH "Quasi-Experimental Studies") or (MH "Experimental Studies") or (MH "One-Shot Case Study") or (MH "Study Design") or (MH "Placebos") or (MH "Clinical Nursing Research") or (MH "Clinical Research") or (MH "Community Trials") or (MH "Pretest-Postt ... S3 S2 not S1 Limiters - Exclude MEDLINE records S2 (MH "Hip Fractures") and (pain* or "drug therapy" or pharmacological OR "quality of life" OR acupunct* OR accupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) Limiters - Exclude MEDLINE records S1 TI (neoplasm* or cancer* or carcinoma* or lymphoma or sarcoma* or "total hip" or "THA" or arthroplasty or replacement) or TI case report* or TI (pediatric* or child or children* or adolesc* or young or youth* or pregnan*) Limiters - Exclude MEDLINE records	

Table B-5. Cochrane Complementary Medicine Trials Register and CAMPAIN (Complementary and Alternative Medicine and Pain Database) grant number R24-AT001293 from the National Center for Complementary and Alternative Medicine (NCCAM)

Searched: 23Jul09	Results: 263

ID	Search
#1	(SR-SYMPT)
#2	(hip OR "neck of femur" or "femoral neck" or extracapsular or intracapsular or intertrochanter* or petrochanter* or petrochant* or trochant*):ti,ab,kw
#3	(#1 AND #2)
#4	"total hip arthroplasty" OR replacement:ti
#5	(osteoarthr* OR cancer* or knee or carcinoma or sarcoma):ti
#6	MeSH descriptor Arthroplasty, Replacement, Hip explode all trees
#7	(child* or pediatric):ti,ab,kw
#8	(#4 OR #5 OR #6 OR #7)
#9	(#3 AND NOT #8)

Table B-6. Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects—Wiley version

OvidSP_UI02.01.02.102 3rd Quarter 2009	Searched: 27Jul09 Results: 36

#1 (hip OR "neck of femur" or "femoral neck" or extracapsular or intracapsular or intertrochanter* or petrochanter* or petrochant* or trochant*):ti,ab,kw
#2 (osteoarthr* OR cancer* or knee or carcinoma or sarcoma or "total hip arthroplasty" OR replacement):ti
#3 MeSH descriptor Arthroplasty, Replacement, Hip explode all trees
#4 (child* or pediatric):ti,ab,kw
#5 (#2 OR #3 OR #4)
#6 ((an?esthet$ or an?esthesia) near/4 (regional$ or local$ or general or spinal or epidural)) in Cochrane Reviews and Other Reviews
#7 (block or analges*) in Cochrane Reviews and Other Reviews
#8 (pain* or discomfort* or ache* or aching or suffer*) NEAR/3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life") in Cochrane Reviews and Other Reviews
#9 (#6 OR #7 OR #8)
#10 (#1 AND #8)
#11 (#10 AND NOT #5)

Table B-7. EBM reviews—Cochrane Central Register of Controlled Trials—Ovid version

OvidSP_UI02.01.02.102 2nd Quarter 2009	Searched: 09Jul09 Results: 263
1. exp Pain/ 2. exp Postoperative pain/ 3. exp "anesthesia and analgesia"/or exp "Nerve Block"/or exp "anesthesiological techniques"/or exp "analgesic, antiinflammatory, antirheumatic and antigout agents"/or exp "agents interacting with transmitter, hormone or drug receptors"/ 4. (block or analges*).mp. 5. exp Therapy/or exp therapeutics/or disease management/or exp "quality of life"/or exp treatment outcome/or exp "outcome assessment"/or "length of stay"/or "functional outcome".ti,ab. 6. exp Pain Assessment/or exp Pain Measurement/ 7. ((pain* or discomfort* or ache* or aching or sore* or suffer*) adj3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")).mp. 8. or/1-7	9. exp hip fracture/or exp hip fractures/or exp acetabulum fracture/or exp femur intertrochanteric fracture/or exp femur neck fracture/or exp femur pertrochanteric fracture/or exp femur subtrochanteric fracture/or exp femur trochanteric fracture/ 10. ((intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or femoral neck) adj4 fracture*).mp. 11. ("neck of femur" adj4 fractur*).mp. 12. or/9-11 13. 8 and 12 14. (THA or total hip*).mp. or exp "Arthroplasty, Replacement, Hip"/ 15. exp neoplasms/or exp Emergency Service, Hospital/ 16. (pediatric* or child or children* or adolesc* or young or youth* or pregnan*).ti,ab,hw,jn. 17. or/14-16 18. 13 not 17 19. limit 18 to yr="1990 -Current"

Table B-8. EMBASE—Ovid version

OvidSP_UI02.01.02.102 1980 to 2009 Week 28	Searched: 10Jul09 Results: 1179
1. exp Pain/ 2. exp Postoperative pain/ 3. (pain* or discomfort* or ache* or aching or sore* or suffer*).mp. 4. or/1-3 5. exp "Nerve Block"/or exp "anesthesiological techniques"/or exp "analgesic, antiinflammatory, antirheumatic and antigout agents"/or exp "agents interacting with transmitter, hormone or drug receptors"/ 6. (block or analges*).mp. 7. exp Therapy/or disease management/or exp "quality of life"/or exp treatment outcome/or exp outcome assessment/or "length of stay"/or "functional outcome".ti,ab. 8. or/5-7 9. 4 and 8 10. exp Pain/dt, rh, pc, th, dm, rt, su, dr 11. exp Pain Assessment/ 12. ((pain* or discomfort* or ache* or aching or sore* or suffer*) adj3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")).mp. 13. or/10-12 14. 9 or 13 15. exp hip fracture/dm, th, rh, dt 16. exp femur neck fracture/dm, th, rh, dt 17. or/15-16	18. exp hip fracture/or exp acetabulum fracture/or exp femur intertrochanteric fracture/or exp femur neck fracture/or exp femur pertrochanteric fracture/or exp femur subtrochanteric fracture/or exp femur trochanteric fracture/ 19. ((intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or femoral neck) adj4 fracture*).mp. 20. ("neck of femur" adj4 fractur*).mp. 21. or/18-20 22. 14 and 21 23. (4 or 8) and 17 24. or/22-23 25. exp "Total Hip Prosthesis"/ 26. THA.mp. 27. total hip*.mp. 28. or/25-27 29. 24 not 28 30. limit 29 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) 31. (pediatric* or child or children* or adolesc* or young or youth* or pregnan*).ti,ab,hw,jx. 32. "nonhuman"/or exp neoplasm/or cancer.hw. or case report/or emergency.af. 33. 29 not (30 or 31 or 32) 34. limit 33 to yr="1990 - 2009" 35. limit 34 to (article or conference paper or proceeding or report or "review")

Table B-9. Global Health Library—World Health Organization

Searched: 28Jul09	**Results: 110**
(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") AND fractur* AND (pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological OR acupunct* OR acupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) AND NOT (child* or adolesc* or young or youth or pediatric* or cancer* or replace* or "total hip arthroplasty" or nail or screw or "case reports" or osteoporosis)	

Table B-10. Pascal—Ovid version

OvidSP_UI02.01.02.102 1987 to Jan Week 4 2010	Searched: 03Feb10 Results: 169
1. exp Pain/ 2. exp "anesthesia and analgesia"/or exp "Nerve Block"/or exp "anesthesiological techniques"/or exp "analgesic, antiinflammatory, antirheumatic and antigout agents"/or exp "agents interacting with transmitter, hormone or drug receptors"/ 3. (block or analges*).mp. 4. exp Pain Assessment/or exp Pain Measurement/ 5. ((pain* or discomfort* or ache* or aching or sore* or suffer*) adj3 (assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")).mp. 6. or/1-5 7. "fracture, hip"/or hip fracture/or hip fractures/or acetabulum fracture/or femur intertrochanteric fracture/or femur neck fracture/or femur pertrochanteric fracture/or exp femur subtrochanteric fracture/or femur trochanteric fracture/	8. ((intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or femoral neck) adj4 fracture*).mp. 9. ("neck of femur" adj4 fractur*).mp. 10. or/7-9 11. 6 and 10 12. (THA or total hip*).mp. or exp "Arthroplasty, Replacement, Hip"/ 13. (neoplasm* or cancer* or carcinoma* or lymphoma or sarcoma* or Emergency).ti,de,cw,cc,bt,id,hw,sh. 14. case report.ti,de,cw,cc,bt,id,hw,sh. 15. (pediatric* or child or children* or adolesc* or young or youth* or pregnan*).ti,ab,hw,de,cw,cc,tt,ed,sh. 16. or/12-15 17. 11 not 16 18. limit 17 to yr="1990 -Current" 19. remove duplicates from 18

Table B-11. PEDro—The Physiotherapy Evidence Database

1929 to 2009 Searched: 14Jul09	Results: 256 of which 33 were selected
Problem: pain Body part: thigh or hip Published since 1990	

Table B-12. ProQuest dissertations and theses—full text

1637 to 2009 **Searched:** 24Jul09	**Results: 43**
(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") AND (fracture*) AND (pain* or "quality of life" or traction or "physical therapy" or acupunct* OR acupress* OR traction OR "electrical stimulation") AND NOT (child* or adolesc* or young or youth or pediatric* or cancer* or replace* or "total hip arthroplasty") Look for terms in: Citation and abstract; Publication type: All publication types (hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") AND (fracture*) AND ("passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) AND NOT (child* or adolesc* or young or youth or pediatric* or cancer* or replace* or "total hip arthroplasty") Look for terms in: Citation and abstract; Publication type: All publication types	

Table B-13. Scopus—Elsevier B.V.

1990 to July 2009	Searched: 13Jul09 Results: 900
(((((TITLE(pain*) OR KEY(pain*)) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1989) AND ((TITLE-ABS-KEY(assess* OR relief OR reliev* OR reduc* OR treat* OR manage* OR control* OR experience* OR medicat* OR duration OR evaluat* OR alleviat* OR level OR score* OR subjective OR felt OR prevent* OR duration OR outcome* OR heal OR healing OR therap* OR recover*) OR TITLE-ABS-KEY("quality of life" OR acupunct* OR accupress* OR traction OR "electrical stimulation" OR "passive motion")) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1989)) AND NOT ((TITLE-ABS-KEY("total hip replacement" OR "total hip arthroplasty" OR "THA") OR TITLE-ABS-KEY(cancer* OR carcinoma* OR neoplasm* OR pediatric* OR children* OR adolesc* OR "case report")) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1989)) AND (TITLE-ABS-KEY((hip* OR femur* OR femoral* OR trochant* OR pertrochant* OR intertrochant* OR subtrochant* OR intracapsular* OR extracapsular*) AND fractur*) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1989)) AND NOT (TITLE(diagnos* OR predictive OR accurac* OR specificity OR probability OR likelihood OR screen* OR test* OR "risk factors")) AND (EXCLUDE(DOCTYPE, "no") OR EXCLUDE(DOCTYPE, "sh") OR EXCLUDE(DOCTYPE, "ed")) AND (EXCLUDE(SUBJAREA, "BIOC") OR EXCLUDE(SUBJAREA, "VETE") OR EXCLUDE(SUBJAREA, "ENGI") OR EXCLUDE(SUBJAREA, "DENT") OR EXCLUDE(SUBJAREA, "CENG") OR EXCLUDE(SUBJAREA, "ENVI") OR EXCLUDE(SUBJAREA, "ECON") OR EXCLUDE(SUBJAREA, "COMP") OR EXCLUDE(SUBJAREA,	

Table B-14. Web of Science—Institute for Scientific Information—Thomson Reuters

1900 to 2009 Searched: 14Jul09	Results: 596
# 4 #2 AND #1 Refined by: [excluding] Subject Areas=(PEDIATRICS OR VETERINARY SCIENCES) Databases=SCI-EXPANDED, SSCI Timespan=1990-2009 # 3 #2 AND #1 # 2 TS=(intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") SAME TS=(fracture*) # 1 TS=(pain* or discomfort* or ache* or aching or sore* or suffer*) SAME TS=(assess* or relief or reliev* or reduc* or treat* or manage* or control* or experience* or medicat* or duration or evaluat* or alleviat* or level or score* or subjective or felt or prevent* or duration or outcome* or heal or healing or therap* or recover* or "quality of life")	

Table B-15. TOXLINE—ProQuest

1998 to 2009 Searched: 29Jul09	Results: 74
(TI=(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or "femoral neck") or DE=(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or "femoral neck") or AB=(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or "femoral neck")) and DE=fractur* and (DE=(pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological OR acupunct* OR acupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) or AB=(pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological OR acupunct* OR acupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) or TI=(pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological OR acupunct* OR acupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*)) not (DE=(child* or adolesc* or young or youth or pediatric* or cancer* or neoplasm* or carcinoma or anemia or alendronate or replace* or osteoporosis or "total hip arthroplasty" or "hip fractures: prevention control" or "hip fractures: epidemiology" OR"Hip Fractures: chemically induced"))	

Conference Proceedings

Table B-16. Conference papers index—ProQuest

1982 to 2009 **Searched:** 24Jul09	**Results: 97**
TI=(hip or intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") and DE=(pain* or heal or healing or therap* or recover* or "quality of life" or rehabilitat* or "drug therapy" or pharmacological OR acupunct* OR acupress* OR traction OR "electrical stimulation" OR "passive motion" or morphine OR acetaminophen or paracetamol or tylenol or anesth* or analges*) not TI=(child* or adolesc* or young or youth or pediatric* or cancer* or replace* or "total hip arthroplasty") Limits: 1990-2009	

Table B-17. OCLC papers first—OCLC FirstSearch

Searched: 24Jul09	Results: 12
((((ti: hip or ti: intertrochanter* or ti: petrochanter* or ti: subtrochanter* or ti: intracapsular or ti: extracapsular or ti: petrochant* or ti: trochant* or ti: hip or ti: femoral w neck)) and kw: pain*) and (kw: heal or kw: healing or kw: therap* or kw: recover* or kw: quality w1 life or kw: rehabilitat* or kw: drug w therapy or kw: pharmacological OR kw: acupunct* OR kw: acupress* OR kw: traction OR kw: electrical w stimulation OR kw: passive w motion or kw: morphine OR kw: acetaminophen or kw: paracetamol or kw: tylenol or kw: anesth* or kw: analges*) and yr: 1990-2009) not (ti: replacement or ti: total w hip) and yr: 1990-2009	

Table B-18. ScienceDirect tables of contents

Searched: 28Jul09	Results: 24
Regional Anesthesia and Pain Medicine Pain Management Nursing Acute Pain European Journal of Pain Journal of Pain and Symptom Management Techniques in Regional Anesthesia and Pain Management Anesthesiology Clinics Pain Searched tables of contents using the strategy below for the journals listed above: pub-date > 1989 and TITLE-ABSTR-KEY((intertrochanter* or petrochanter* or subtrochanter* or intracapsular or extracapsular or petrochant* or trochant* or hip or "femoral neck") AND fractur*) and SRCTITLEPLUS(pain)	

Table B-19. Conference proceedings hand searched

Searched: 28Jul09	
American Geriatric Society (AGS)	2005-2009
American Physical Therapy Association (APTA)	2005-2009
American Society of Regional Anesthesia and Pain Medicine (ASRA)	2007-2009
European Society of Regional Anesthesia (ESRA)	2005-2009
European Society of Anesthesiology (ESA)	2008-2009
International Anesthesia Research Society (IARS)	2005-2009

Trials Registers

Table B-20. ClinicalStudyResults.org

Searched: 03Sep09	Results: 0
Searched by Indication Word hip fracture	Searched by Study Indication/Disease: Hip Fracture Recovery; Pain, Postoperative; Pain, Postsurgical

Table B-21. ClinicalTrials.Gov—National Institutes of Health

Searched: 27Jul09	Results: 33
Pain* AND (hip OR intertrochanter* OR petrochanter* OR subtrochanter* OR intracapsular OR extracapsular OR petrochant* OR trochant* OR femoral neck) AND fracture*	

Table B-22. Current controlled trials—Biomed Central
Excluding Leukaemia Research Fund and ClinicalTrials.gov

Searched: 03Sep09	Results: 17
Pain* AND (hip OR intertrochanter* OR petrochanter* OR subtrochanter* OR intracapsular OR extracapsular OR petrochant* OR trochant* OR femoral neck) AND fracture*	

Table B-23. ICTRP search portal – World Health Organization

Searched: 03Sep09	Results: 199
(hip OR intertrochanter* OR petrochanter* OR subtrochanter* OR intracapsular OR extracapsular OR petrochant* OR trochant* OR femoral neck) AND fracture* ALL studies (not restricted to Recruiting)	

Table B-24. IFPMA clinical trials portal—International Federation of Pharmaceutical Manufacturers & Associations

Searched: 04Sep09	**Results: 37**
(hip OR intertrochanter* OR petrochanter* OR subtrochanter* OR intracapsular OR extracapsular OR petrochant* OR trochant* OR femoral neck) AND fracture*	

Table B-25. UMIN-CTR Clinical Trials—University Hospital Medical Information Network

Searched: 04Sep09	**Results: 7**
"hip fracture" "femoral neck"	

Appendix C. Sample Data Extraction and Quality Assessment Form

Comparative Effectiveness of Pain Management Interventions for Hip Fracture

Refid: **Study Name:**

Reviewer's name:

Study Demographics:

Publication type		***Study design***	
Type of hospital		***Country***	
Number of centers (n)		***Study period (month and year)***	
Main inclusion criteria		***Main exclusion criteria***	
Financial support		***Reported outcomes of interest to this review***	**Primary outcomes:** ☐ Acute pain ☐Chronic pain **Secondary outcomes:** ☐ Mortality ☐ Functional status ☐ Pain medication use; change in type and quantity **Adverse events:** ☐ AE related to the pain management interventions ☐ Mental status ☐ Health-related QoL ☐ Quality of sleep in hospital ☐ Ability to participate in rehabilitation ☐ Return to prefracture place of residence ☐ Length of stay for acute hospitalization, skilled nursing facility, subacute care facility ☐ Health service utilization

Reviewer's Comments:

Patient Baseline Demographics:

	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Classification				
Type of intervention				
Dosage				
Dosage Intervals				
Age (yr) ***Mean ± SD*** ***Range***				
Body weight (Kg) ***Mean ± SD*** ***Range***				
Height (cm) ***Mean ± SD*** ***Range***				
BMI (Kg/ m^2) ***Mean ± SD*** ***Range***				
Gender ***Females: n (%)*** ***Males: n (%)***				
Pre-fracture residence ***Community: n (%)*** ***Institutional: n (%)***				
Type of fractures ***Femoral neck: n (%)*** ***Intertrochanteric: n (%)*** ***Proximal femur: n (%)***				
Side of fracture ***Right: n (%)*** ***Left: n (%)***				
ASA Class ***ASA I (%)*** ***ASA II (%)*** ***ASA III (%)*** ***ASA IV (%)***				
Timing of intervention				

Time from fall to ER arrival (hr) ***Mean ± SD*** ***Range***				
Time from ER arrival to surgery (hr) ***Mean ± SD*** ***Range***				
Time from fall to surgery (hr) ***Mean ± SD*** ***Range***				
Type of surgery				
Type of anesthesia ***Epidural*** ***Spinal*** ***General***				
Duration of surgery (hr) ***Mean ± SD*** ***Range***				
Baseline pain score	***Scale name []***			
Mean ± SD ***Range***				

Reviewer's Comments:

Data available on subpopulations:

	Describe	***Outcomes available***
Sex		
Age		
Race		
Marital status		
Co-morbidities		
Body mass index		
Pre-fracture functional status		
Family distress		

Reviewer's Comments:

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?

□ a) yes, with independent validation ❋

□ b) yes, eg record linkage or based on self reports

□ c) no description

2) Representativeness of the cases

□ a) consecutive or obviously representative series of cases ❋

□ b) potential for selection biases or not stated

3) Selection of Controls

□ a) community controls ❋

□ b) hospital controls

□ c) no description

4) Definition of Controls

□ a) no history of disease (endpoint) ❋

□ b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis ❋

□ a) study controls for _____ ❋ (Select the most important factor.)

□ b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

□ a) secure record (eg surgical records) ❋

□ b) structured interview where blind to case/control status ❋

□ c) interview not blinded to case/control status

□ d) written self report or medical record only

□ e) no description

2) Same method of ascertainment for cases and controls

□ a) yes ❋

□ b) no

3) Non-Response rate

□ a) same rate for both groups ❋

□ b) non respondents described

□ c) rate different and no designation

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort

☐ a) truly representative of the average _____ (describe) in the community ❋

☐ b) somewhat representative of the average _____ in the community ❋

☐ c) selected group of users eg nurses, volunteers d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

☐ a) drawn from the same community as the exposed cohort ❋

☐ b) drawn from a different source

☐ c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

☐ a) secure record (eg surgical records) ❋

☐ b) structured interview ❋

☐ c) written self report

☐ d) no description

4) Demonstration that outcome of interest was not present at start of study

☐ a) yes ❋

☐ b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

☐ a) study controls for _____ (select the most important factor) ❋

☐ b) study controls for any additional factor ❋ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

☐ a) independent blind assessment ❋

☐ b) record linkage ❋

☐ c) self report

☐ d) no description

2) Was follow-up long enough for outcomes to occur

☐ a) yes (select an adequate follow up period for outcome of interest) ❋

☐ b) no

3) Adequacy of follow up of cohorts

☐ a) complete follow up -all subjects accounted for ❋

☐ b) subjects lost to follow up unlikely to introduce bias -small number lost -> ____ % (select an adequate %) follow up, or description provided of those lost) ❋

☐ c) follow up rate < ____% (select an adequate %) and no description of those lost

☐ d) no statement

RISK OF BIAS (ROB)
RANDOMIZED CONTROLLED TRIALS

Item	*Judgment*	*Description*
Adequate sequence generation?		
Allocation concealment?		
Blinding?		
Incomplete outcome data addressed?		
Free of selective reporting?		
Free of other bias?		

Primary outcome measures:

	Intervention (1)	*Intervention (2)*	*Intervention (3)*	*Intervention (4)*
Acute pain (% change from baseline)	***Scale name***			
Maximal pain relief				
Mean ± SD				
Range				
Time to max pain relief				
Mean ± SD				
Range				
Pain at rest				
Mean ± SD				
Range				
Pain on movement				
Mean ± SD				
Range				
Acute pain (post-treatment means)	***Scale name***			
Maximal pain relief				
Mean ± SD				
Range				
Time to max pain relief				
Mean ± SD				
Range				
Pain at rest				
Mean ± SD				
Range				
Pain on movement				
Mean ± SD				
Range				

Is there acute pain?				
Day 1				
Day 2				
Day ≥7 – 30				
Pain at rest				
Pain on movement				
Chronic pain (% change from baseline)	***Scale name***			
Maximal pain relief				
Mean ± SD				
Range				
Time to max pain relief				
Mean ± SD				
Range				
Pain at rest				
Mean ± SD				
Range				
Pain on movement				
Mean ± SD				
Range				
Chronic pain (post-treatment means)	***Scale name***			
Maximal pain relief				
Mean ± SD				
Range				
Time to max pain relief				
Mean ± SD				
Range				
Pain at rest				
Mean ± SD				

Range				
Pain on movement Mean ± SD				
Range				
Is there chronic pain?				
Pain is present				
Pain at rest				
Pain on movement				

Reviewer's Comments:

Secondary outcome measures:

	Intervention (1)	*Intervention (2)*	*Intervention (3)*	*Intervention (4)*
Mortality (30 days)				
Mortality (1-year)				
Functional status (describe)				
Additional pain medication				
Another medication used				
Time interval before use Mean ± SD				
Range				
Type and Quantity of additional pain medication				
Change in type (explain)				

Reviewer's Comments:

Adverse events related to the pain management intervention:

	Intervention (1)	*Intervention (2)*	*Intervention (3)*	*Intervention (4)*
Any adverse event				
Incidence of pressure sores				
Peroneal palsy				

	Intervention (1)	*Intervention (2)*	*Intervention (3)*	*Intervention (4)*
Allergic reactions				
Respiratory distress				
Damage to surrounding structures				
GI symptoms				
Bleeding				
Infection at site of injection				
Headache				
Delirium				
Other mental health issues (describe:)				
Health-related QoL	***Scale name***			
Quality of sleep in hospital	***Scale name***			
Ability to participate in rehabilitation				

	Intervention (1)	*Intervention (2)*	*Intervention (3)*	*Intervention (4)*
Return to pre-fracture place of residence ***Overall*** ***Community*** ***Institutional***				
Length of stay for acute hospitalization				
Length of stay at skilled nursing facility				
Length of stay at sub-acute care facility				
Other health service utilization (describe)				

Reviewer's Comments:

Reviewer's Overall Comments:

Appendix D. Excluded Studies

Publication Type/Study Design

1. Ahmed T, Ullah H. Paramedian technique of spinal anaesthesia in elderly patients for hip fracture surgery. J Coll Physicians Surg Pak 2007;17(3):184.
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Appendix E. Description of Included Studies

Table E-1. Systemic analgesia

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Apostolopoulos 2006[41]	Study design: RCT Study period: Jan-03 to Jul-04 Type of hospital: General hospital Country: Switzerland Financial support: NR	Intervention #1: Classification: IV analgesia Intervention: Parecoxib IV Dosage: 40mg Intervals: Every 12hrs Intervention #2: Classification: IM analgesia Intervention: Diclofenac IM; Pethidine IM Dosage: 75mg; NR Intervals: Every 12hrs; on demand	Main inclusion criteria: Pts operated for fracture of hip joint Main exclusion criteria: NR
Baker 2004[42]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Intrathecal analgesia Intervention: Clonidine (Isotonic) Dosage: 150ug Intervals: Single administration Intervention #2: Classification: Intrathecal analgesia Intervention: Clonidine (Hypertonic) Dosage: 150ug Intervals: Single administration	Main inclusion criteria: Elderly pts undergoing surgery after traumatic hip fractures under general anesthesia Main exclusion criteria: Contraindications to spinal anesthesia, unable to understand study protocol, severe deformities of spine, history of untreated hypertensive disease, or receiving treatment with β-adrenergic blockers
Poitevin 1999[55]	Study design: Randomized controlled trials Study period: NR to NR Type of hospital: University hospital Country: Argentina Financial support: NR	Intervention #1: Classification: Analgesia Intervention: Lysine clonixinate Dosage: 125mg Intervals: every 8 hr Intervention #2: Classification: Analgesia Intervention: Metamizole Dosage: 400mg Intervals: every 8 hr	Main inclusion criteria: Patients aged 50-85 years old; <3 days since trauma leading to hip fracture; undergoing surgery Main exclusion criteria: Patients with allergies to investigational drug; GI problems; psychiatric disorders; any other use of anti-inflammatory analgesic drugs

IM = intramuscular; IV = intravenous; NR = NR; RCT = randomized controlled trial

Table E-2. Anesthesia

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Adams 1990[56]	Study design: Randomized controlled trials Study period: NR to NR Type of hospital: University hospital Country: Germany Financial support:	Intervention #1: Classification: Spinal anesthesia Intervention: Bupivacaine 0.5%/Mepivacaine 4% Dosage: NR Intervals: NR Intervention #2: Classification: General anesthesia Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: age 60+, proximal hip fracture Main exclusion criteria: Patients who insisted on a specific type of anesthesia or who were not eligible for the anesthesia types used in the study
Alonso Chico 2003[57]	Study design: Randomized controlled trials Study period: NR to NR Type of hospital: University hospital Country: Spain Financial support: NR	Intervention #1: Classification: Spinal anesthesia Intervention: Bupivacaine 0.5%/ Fenantyl Dosage: 5mg/15ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia Intervention: Bupivacaine 0.5% Dosage: 7.5mg Intervals: Single administration	Main inclusion criteria: Patients aged >75 years; ASA II-III; pro-trochanteric fracture Main exclusion criteria: Patients with contraindications to subarachnoid anesthesia or uncontrolled cardiac; respiratory; or neurologic disease
Ben-David 2000[58]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Israel Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine/Fentanyl Dosage: 4mg/20ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 10mg Intervals: Single administration	Main inclusion criteria: Pts >70yr presenting for open surgical repair of hip fracture Main exclusion criteria: NR

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Bredahl 1991[59]	Study design: Randomized Controlled Trial Study period: NR Type of hospital: University Hospital Country: Denmark Financial support: NR	Intervention #1: Classification: Spinal Anaesthesia Intervention: Bupivacainc 0.5% Dosage: 2.5-3 ml Intervals: NR Intervention #2: Classification: General Anaesthesia Intervention: Thiopentone Dosage: 2-4 mg/kg Intervals: once	Main inclusion criteria: female patients, more than 60 years old, with hip fracture, otherwise healthy (ASA class I or 11) Main exclusion criteria: NR
Casati 2003[60]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Italy Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 7.5mg Intervals: Single administration Intervention #2: Classification: General anesthesia Intervention: None Dosage: NA Intervals: NA	Main inclusion criteria: Pts ASA II-III undergoing hemiarthroplasty for repair of fractured femur Main exclusion criteria: Contraindications to spinal anesthesia or laryngeal mask placement, severe cardiovascular or pulmonary disease, or psychiatric pathology
Danelli 2008[61]	Study design: RCT Study period: May-06 to Jul-06 Type of hospital: University hospital Country: Italy Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Levobupivacaine 0.5% Dosage: 15mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Levobupivacaine 0.75% Dosage: 15mg Intervals: Single administration	Main inclusion criteria: ASA I-III; >18 yrs Main exclusion criteria: Unable to understand, cooperate, or communicate with investigators, any contraindication to spinal anesthesia, or had a known history of hypersensitivity to local anesthetics

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Favarel-Garrigues 1996[62]	Study design: RCT Study period: Sep-92 to Apr-94 Type of hospital: University hospital Country: France Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: Bolus: Bupivacaine 5mg (1ml); Maintenance: Bupivacaine 2.5mg (0.5ml) Intervals: Single administration; Continuous administration on demand Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: Based on age and ht (15mg between 70 and 79 yr and/or >170 cm height, 12.5mg between 80 and 90 yr and/or between 150 and 170 cm, 10mg >90 yr and/or <150 cm) Intervals: Single administration	Main inclusion criteria: Pts ≥ 70 yrs, ASA I-III, undergoing hip fracture surgery Main exclusion criteria: Pts did not accept regional anesthesia, or had contraindications for spinal anesthesia, or severely altered mental status
Hooda 2006[63]	Study design: RCT Study period: NR Type of hospital: University hospital Country: India Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Fentanyl Dosage: 4mg (0.8ml)/20mg (0.4ml) Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Fentanyl Dosage: 5mg (1.0ml)/20mg (0.4ml) Intervals: Single administration Intervention #3: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Fentanyl Dosage: 6mg (1.2ml)/20mg (0.4ml) Intervals: Single administration	Main inclusion criteria: Pts of either sex, ≥60 yrs, scheduled to undergo open surgical repair of hip fractures Main exclusion criteria: <60 yrs, ASA III or more, contraindications to spinal anesthesia (e.g., peripheral neuropathy, coagulopathy, spinal deformity, infection at the injection site), or known hypersensitivity to amide local anesthetics or fentanyl

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Juelsgaard 1998[64]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Denmark Financial support: NR	Intervention #1: Classification: Spinal anesthesia (incremental) Intervention: Bupivacaine 0.5% Dosage: 1.6ml Intervals: Incremental dosage Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 2.5ml Intervals: Single administration Intervention #3: Classification: General anesthesia Intervention: Fentanyl Dosage: Bolus: 1-2ug per kg/Maintainence: 25-50ug Intervals: Single administration/Continuous administration (on demand)	Main inclusion criteria: Pts with known CAD scheduled for osteosynthesis of a femoral neck fracture Main exclusion criteria: Uncooperative pts, recent myocardial infarction, unstable angina pectoris, significant aortic stenosis, or contraindication to spinal anesthesia, or had factors that adversely affect the quality of the Holter analysis or had failure of monitoring for 36hrs

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Klimscha 1995[65]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% plus clonidine Dosage: 1ml bupivacaine/1ml Clonidine Intervals: Continuous administration (3 repetitive doses) Intervention #2: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 10ml bupivacaine Intervals: Continuous administration (3 repetitive doses) Intervention #3: Classification: Epidural anesthesia (continuous) Intervention: Bupivacaine 0.5%/clonidine Dosage: 10ml bupivacaine/1ml Clonidine Intervals: Continuous administration (3 repetitive doses) Intervention #4: Classification: Epidural anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 10ml bupivacaine Intervals: Continuous administration (3 repetitive doses)	Main inclusion criteria: Elderly pts undergoing hip surgery after traumatic fractures Main exclusion criteria: Pts with usual contraindications to spinal or epidural anesthesia, had senile dementia and those with severe deformities of the spinal column

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Koval 1999[78]	Study design: Prospective Cohort Study Study period: July 1987 to June 1995 Type of hospital: University Hospital Country: USA Financial support: NR	Intervention #1: Classification: Spinal Anaesthesia Intervention: NR Dosage: NR Intervals: NR Intervention #2: Classification: General Anaesthesia Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: age>=65, previously ambulatory and home dwelling, and had femoral neck or intertrochanteric hip fracture of non-pathologic origin Main exclusion criteria: moderate to severe dementia
Krobot 2006[77]	Study design: nRCT Study period: NR Type of hospital: General hospital Country: Croatia Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Levobupivacaine/Fentanyl Dosage: 7.5mg/0.01mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Levobupivacaine Dosage: 10mg Intervals: Single administration	Main inclusion criteria: Elderly pts undergoing hip fracture repair Main exclusion criteria: NR
Kwan 1997[66]	Study design: RCT Study period: Jul-95 to Dec-95 Type of hospital: General hospital Country: Hong Kong Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Morphine Dosage: 2.2ml/0.2mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 2.2ml Intervals: Single administration	Main inclusion criteria: Pts, ASA I-IV, scheduled for emergency surgery for a fractured hip Main exclusion criteria: Pts who had contraindications to regional anesthesia, or an allergy to the study drugs (bupivacaine, morphine)

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Labaille 1992[79]	Study design: Prospective cohort study Study period: NR Type of hospital: General hospital Country: France Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.125%/Bupivacaine 0.125% Dosage: Bolus: 3ml/Maintaninence: 1ml Intervals: Single administration/Continuous administration (on demand) Intervention #2: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5%/Bupivacaine 0.5% Dosage: Bolus: 3ml/Maintaninence: 1ml Intervals: Single administration/Continuous administration (on demand)	Main inclusion criteria: Pts, ASA I-II, aged 70-97 yrs old without any known CVD who were scheduled for repair of femoral neck or trochanteric fracture under spinal anesthesia Main exclusion criteria: NR
Malek 2004[67]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Czech Republic Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Fentanyl Dosage: 3ml/50ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Sufentanil Dosage: 3ml/5ug Intervals: Single administration Intervention #3: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 3ml Intervals: Single administration	Main inclusion criteria: Pts scheduled to be operated on for hip fracture Main exclusion criteria: Pts with suspected allergy to opiates, common contraindications of spinal anesthesia and inability to perform dural puncture in L3—L4 or L2—L3 vertebral interspaces

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Martyr 2001[68]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Australia Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivaciane/Fentanyl Dosage: 7.5mg/20ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 12.5mg Intervals: Single administration	Main inclusion criteria: Pts with a fractured neck of femur requiring internal fixation with a Richards pin and plate Main exclusion criteria: NR
Martyr 2005[69]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Australia Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine/Fentanyl Dosage: 9.0mg/20ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 11.0mg Intervals: Single administration	Main inclusion criteria: >70 yrs with fractured neck of femur requiring internal fixation with a DHS or hemiarthroplasty and < 70 kg estimated body weight Main exclusion criteria: NR
Maurette 1993[70]	Study design: RCT Study period: NR Type of hospital: University hospital Country: France Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bolus: lidocaine 1.6%/meperidine 1%; Maintainence: lidocaine 1.6% Dosage: NA/4ml (200mg); NA Intervals: Continuous administration Intervention #2: Classification: Spinal anesthesia (continuous) Intervention: Bolus: lidocaine 1.6%; Maintainence: lidocaine 1.6% Dosage: NA Intervals: Continuous administration	Main inclusion criteria: Pts undergoing elective surgery for fracture of the neck of the femur and able to describe their pain with accuracy Main exclusion criteria: Bedridden pts or suffering from severe dehydration or senile dementia

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Miller 1990[81]	Study design: Retrospective cohort study Study period: 30317 to 32478 Type of hospital: General hospital Country: Germany Financial support:	Intervention #1: Classification: Spinal anesthesia Intervention: Mepivacaine 4 % Dosage: 2ml (80 mg) Intervals: NR Intervention #2: Classification: General anesthesia Intervention: Fentanyl Dosage: 3-5mg per kg Intervals: NR	Main inclusion criteria: Proximal hip fracture Main exclusion criteria: NR
Minville 2006[71]	Study design: RCT Study period: Nov-03 to Nov-04 Type of hospital: University hospital Country: France Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine Dosage: 2.5mg Intervals: Continuous administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 7.5mg Intervals: Single administration	Main inclusion criteria: 75 yrs who underwent surgery for open surgical repair of hip fracture Main exclusion criteria: Contraindication to spinal anesthesia or continuous spinal anesthesia including patient refusal, intracranial hypertension, major hemostasis anomalies or local infection, dementia, allergic reaction to local anesthetics, anemia (hemoglobin <10 g/dL), as well as being treated with aspirin

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Minville 2008[82]	Study design: Retrospective cohort study Study period: Jan-01 to Dec-04 Type of hospital: University hospital Country: France Financial support: No external funding	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 2.5mg Intervals: Continuous administration Intervention #2: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 5mg Intervals: Continuous administration Intervention #3: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: NR Intervals: Single administration Intervention #4: Classification: General anesthesia Intervention: Sulfentanil Dosage: NR Intervals: NR	Main inclusion criteria: Pts over 75 yrs old who underwent surgical repair of femoral neck fractures Main exclusion criteria: NR
Navas 2008[72]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Spain Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.15-0.25% Dosage: NR Intervals: Continuous administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: NR Intervals: Single administration	Main inclusion criteria: Pts undergoing surgery for hip fracture Main exclusion criteria: NR

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Olofsson 2004[73]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Sweden Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine/sufentanil Dosage: 7.5mg/5mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 15mg Intervals: Single administration	Main inclusion criteria: Pts, ASA II, scheduled for surgery after hip fracture, who could understand oral information Main exclusion criteria: Uncooperative pts, unstable angina, significant aortic stenosis, recent myocardial infarction, coagulation disorders, contraindications to spinal anesthesia
Qamarul Hoda 2007[146]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Pakistan Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine/Fentanyl Dosage: 6mg/20ug Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine/Fentanyl Dosage: 8mg/20ug Intervals: Single administration Intervention #3: Classification: Spinal anesthesia (single) Intervention: Bupivacaine Dosage: 10mg Intervals: Single administration	Main inclusion criteria: Elderly pts, ASA I-III, 65 yrs and scheduled for surgical repair of hip fracture. Main exclusion criteria: Pts with any contraindication for spinal anesthesia

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Rais 2008[75]	Study design: RCT Study period: NR Type of hospital: Orthopedic hospital Country: Tunisia Financial support: NR	Intervention #1: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 2.5mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (continuous) Intervention: Bupivacaine 0.5% Dosage: 5mg Intervals: Single administration	Main inclusion criteria: Pts with no contraindication to continuous spinal anesthesia Main exclusion criteria: NR
Said-Ahmed 2006[76]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Egypt Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Fentanyl Dosage: 5mg/20mcg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5%/Sufentanil Dosage: 5mg/5mcg Intervals: Single administration Intervention #3: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 10mg Intervals: Single administration	Main inclusion criteria: Pts, ASA I-II, aged 70 yrs or older, undergoing either insertion of Austin-Moore prosthesis or DHS for fixation of femur neck fractures Main exclusion criteria: NR

Table E-2. Anesthesia (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Sen 2007[83]	Study design: Retrospective cohort study Study period: Aug-00 to Oct-01 Type of hospital: University hospital Country: Turkey Financial support: NR	Intervention #1: Classification: Spinal anesthesia (single - lateral) Intervention: Bupivacaine 0.5% Dosage: 10mg Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single - supine) Intervention: Bupivacaine 0.5% Dosage: 10mg Intervals: Single administration	Main inclusion criteria: Elderly pts, ASA I-II, who had undergone spinal anesthesia for hip surgery and who had ejection fraction < 50% Main exclusion criteria: NR
Shih 2010[84]	Study design: Retrospective Cohort Study Study period: 2002 to 2006 Type of hospital: University Hospital Country: Taiwan Financial support: NR	Intervention #1: Classification Spinal Anaesthesia Intervention: Bupivacaine Dosage: 8-15 mg Intervals: once Intervention #2: Classification: General Anaesthesia Intervention: Thiopental Dosage: NR Intervals: NR	Main inclusion criteria: NR Main exclusion criteria: Patients with multiple fractures, with pathologic fractures, with other acute diseases when admitted, or with patient-controlled analgesia, or received both spinal and general anesthesia
Sutcliffe 1994[85]	Study design: Prospective Cohort Study Study period: NR Type of hospital: University Hospital Country: England Financial support: NR	Intervention #1: Classification: Spinal Anaesthesia Intervention: Bupivacaine Dosage: NR Intervals: NR Intervention #2: Classification: General Anaesthesia Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: NR Main exclusion criteria: NR

ASA = American Society of Anesthesiology; IM = intramuscular; IV = intravenous; NR = NR; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Table E-3. Complementary and alternative medicine (CAM)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Barker 2006[43]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: Auricular acupressure Intervention: 1-mm plastic acupressure beads Dosage: 3 true auricular acupressure points Intervals: Single administration Intervention #2: Classification: Sham Control Intervention: 1-mm acupressure plastic beads Dosage: 3 sham auricular acupressure points Intervals: Single administration	Main inclusion criteria: Pts aged 80–95 yrs, ASA II–III, who sustained an isolated hip fracture without any additional trauma Main exclusion criteria: Not fluent in German, with ear deformity, severe neurologic or psychiatric disorders, long-term use of sedatives or analgesics
Martin 1991[54]	Study design: RCT Study period: 1988 to 1989 Type of hospital: General hospital Country: US Financial support: NR	Intervention #1: Classification: Relaxation Intervention: Jacobson relaxation technique/ Meperidine/ Morphine Dosage: NA Intervals: Instruction given prior to surgery Intervention #2: Classification: Analgesia Intervention: Meperidine/Morphine Dosage: NR Intervals: NR	Main inclusion criteria: Pts, 60 yrs old and older with a fractured hip to be surgically repaired by internal fixation Main exclusion criteria: Pts with known psychiatric illness or mental retardation, pathologic fractures as a result of metastasis to bone, inability to cooperate or follow instructions, and multiple trauma

ASA = American Society of Anesthesiology; IM = intramuscular; IV = intravenous; NR = NR; RCT = randomized controlled trial

Table E-4. Multimodal pain management

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Milisen 2001[86]	Study design: Prospective cohort study Study period: Sep-96 to Mar-97 Type of hospital: University hospital Country: Belgium Financial support: NR	Intervention #1: Classification: Multimodal pain management Intervention: Bolus: Tramadol IV; Maintainence (48hrs): Tramdol IV + propacetamol IV; Maintainence (Day 3-5): oral tramadol + oral paracetamol Dosage: 3mg/ kg; 6mg/k/ 24hrs; 120mg per kg per 24hours/NA Intervals: Continuous administration Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Dutch-speaking and verbally testable pts admitted with a traumatic frature of proximal femur within 24 hrs of surgery Main exclusion criteria: Pts with multiple trauma, concussion, pathological fractures, surgery occurring > 72 hrs after admission, aphasia, blindness, deafness, and < 9 yrs formal education
Ogilvie-Harris 1993[87]	Study design: Prospective cohort study Study period: NR Type of hospital: University hospital Country: Canada Financial support: NR	Intervention #1: Classification: Mutlimodal pain management Intervention: Skin Traction/Morphine/Acetaminophen Dosage: NA/2.5-5mg/1000mg Intervals: Rewrap every 8hrs/every 4hrs/every 4hrs Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Geriatric pts with hip fractures Main exclusion criteria: NR

ASA = American Society of Anesthesiology; IM = intramuscular; IV = intravenous; NR = NR; RCT = randomized controlled trial

Table E-5. Nerve blocks

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Antonopoulou 2006[88]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Greece Financial support: NR	Intervention #1: Classification: Femoral nerve block Intervention: Bolus: Levobupivacaine 0.25%; Maintanence: Levobupivacaine 0.12% Dosage: 18ml Intervals: Single administration; Continuous administration Intervention #2: Classification: Analgesia Intervention: Paracetamol; Pethidine Dosage: 500mg; NR Intervals: Every 8hrs; on demand	Main inclusion criteria: Pts with hip fracture Main exclusion criteria: NR
Chudinov 1999[89]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Israel Financial support: NR	Intervention #1: Classification: Psoas Compartment Block (continuous) Intervention: Bupivacaine 0.25% Dosage: Bolus: 2mg per kg; Maintainence: 2mg per kg Intervals: Single administration/Maintainence: every 12hrs Intervention #2: Classification: IM analgesia Intervention: Meperidine IM Dosage: 1mg per kg Intervals: On demand (max every 5hrs)	Main inclusion criteria: Pts with unilateral fractures of the neck of the femur Main exclusion criteria: Severe cardiac, pulmonary, renal, or liver dysfunction, systemic infection, decubitus ulcers, dementia, aspirin or anticoagulant treatment, or known hypersensitivity to local anesthetic agents

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Coad 1991[90]	Study design: RCT Study period: NR Type of hospital: General hospital Country: UK Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block Intervention: Bupivacaine 0.5% Dosage: 15ml Intervals: Single administration Intervention #2: Classification: Lateral cutaneous Nerve Block Intervention: Bupivacaine 0.5% Dosage: 15ml Intervals: Single administration Intervention #3: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Pts undergoing either pin-and-plate or compression-screw fixation of the femoral neck Main exclusion criteria: Pts who were receiving analgesic drugs, were suffering from dementia, or if regional anesthesia was thought to be indicated
Cuvillon 2007[91]	Study design: Randomized controlled trials Study period: 36404 to 37408 Type of hospital: University hospital Country: France Financial support: Fondation de l'avenir (Paris)	Intervention #1: Classification: 3-in-1 nerve block (NS) Intervention: Ropivacaine Dosage: Catheter attached to pump allowing continuous ropivacaine 0.2% at 10 mL/hr x 48 hr Intervals: Continuous Intervention #2: Classification: Analgesia Intervention: Paracetamol Dosage: 1st dose 2g then 2g Intervals: every 6 hours Intervention #3: Classification: Analgesia Intervention: Morphine Dosage: 2 mg q5min in post-op until VAS <30 then 0.1 mg/kg q4 hr; if VAS >30 dosage increased by 50% Intervals: NA	Main inclusion criteria: Pts ≥70 yrs; operation for traumatic fracture sup. femur under spinal anesthetic Main exclusion criteria: Patient refusal to participate; > 72 hr delay between fall and surgery; Pts < 70 yrs; weight < 40 kg; ASA score > 4; contraindications to locoregional analgesia; neuropathy; severe renal or hepatic insufficiency; noncooperative patients; mini mental score less than 15/30

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
de Visme 2000[92]	Study design: RCT Study period: NR Type of hospital: University hospital Country: France Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Combined lumbar/sacral plexus block (NS) Intervention: Lidocaine 1.33% Dosage: 45mL Intervals: Single administration Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 3mL Intervals: Single administration	Main inclusion criteria: Pts > 65 yrs with proximal femoral fracture Main exclusion criteria: Pts with evidence of cognitive deficit (MMSE <5), contraindication to spinal anesthesia, or peripheral nerve block
Del Rosario 2008[117]	Study design: Retrospective cohort study Study period: Oct-04 to Oct-05 Type of hospital: General hospital Country: Spain Financial support: NR	Intervention #1: Classification: Femoral nerve block (NS)/IV analgesia Intervention: Bolus: Bupivacaine 0.25%; Maintainence: bupivaine 0.1%; PCA: Paracetamol IV/metamizol IV Dosage: 30ml/5ml/1g/2g Intervals: Single administration; Maintainence: every hr; Patient controlled bolus: every 6hrs/every 8hrs Intervention #2: Classification: IV analgesia Intervention: Paracetamol IV; metamizol IV Dosage: 1g; 2g Intervals: Every 6hrs; every 8hrs	Main inclusion criteria: Pts > 50 yrs who underwent hip fracture surgery with intradural anesthesia Main exclusion criteria: Pts who received general or epidural analgesia, presented failure of femoral analgesia, or had localized infection or coagulopathy

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Eyrolle 1998[93]	Study design: RCT Study period: NR Type of hospital: University hospital Country: France Financial support: NR	Intervention #1: Classification: Posterior lumbar plexus block Intervention: Lidocaine 2%/Bupivacaine 0.5% Dosage: NR Intervals: NR Intervention #2: Classification: Spinal anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: NR Intervals: Single administration	Main inclusion criteria: Pts undergoing femoral neck osteosynthesis Main exclusion criteria: NR
Fletcher 2003[94]	Study design: RCT Study period: Feb to Aug Type of hospital: General hospital Country: UK Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 20mL Intervals: Single administration Intervention #2: Classification: IV analgesia Intervention: Morphine IV Dosage: 5-10mg Intervals: On demand	Main inclusion criteria: Pts with all types of fractured neck of femur Main exclusion criteria: Confused, with a bleeding diathesis, taking warfarin, local or systemic infection, or previous hypersensitivity to local anesthetics

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Foss 2005[95]	Study design: RCT Study period: Jan-03 to Apr-04 Type of hospital: University hospital Country: Denmark Financial support: Financial support provided by governmental sources	Intervention #1: Classification: Epidural analgesia (continuous) Intervention: Bupivacaine 0.125%/morphine Dosage: 4ml of 50ug per ml per hr Intervals: Continuous infusion (four days) Intervention #2: Classification: Placebo Intervention: Saline Dosage: NA Intervals: Continuous inusion (four days)	Main inclusion criteria: ≥65 yrs living in own home, intact cognitive status, able to provide written informed consent, New Mobility Score of ≥3 (indicating independent indoor ambulation) Main exclusion criteria: Refused to participate, prefracture hospitalization, contraindications to epidural analgesia, regular prefracture opioid or glucocorticoid therapy, alcohol or substance abuse, morphine intolerance, and postoperative restrictions for ambulation
Foss 2007[96]	Study design: Randomized controlled trials Study period: May-03 to Jan-06 Type of hospital: University hospital Country: Denmark Financial support: Imk Almene Fond	Intervention #1: Classification: Fascia iliaca compartment nerve block (CT) Intervention: 1.0% mepivacaine Dosage: 40 mL 1.0% mepivacaine with 1:200 000 epinephrine; 0.02 mL/kg placebo IM injection of 0.9% saline Intervals: Single dose Intervention #2: Classification: Analgesia Intervention: Morphine Dosage: 40 mL placebo FICB with 0.9% saline; 0.02 mL/kg 5.0 mg/mL morphine Intervals: Single dose	Main inclusion criteria: Clinical signs of hip fracture as assessed by the ED staff; intact cognitive status on admission; and the ability to provide written informed consent. Main exclusion criteria: Refusal to participate in the study; previous surgery in the affected hip; regular prefracture opioid or glucocorticoid therapy; alcohol or substance abuse; infection at the injection site; morphine intolerance; or any previous opioid administration for the acute pain and nonconfirmation of the hip fracture suspicion on x-ray

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Gille 2006[97]	Study design: Randomized controlled trials Study period: NR to NR Type of hospital: University hospital Country: Germany Financial support: No industry funding	Intervention #1: Classification: Femoral nerve block Intervention: Prilocaine 1%/ Ropivacaine 0.2% Dosage: 40ml/ 30ml Intervals: Single administration/ Continuous (every 6hrs) Intervention #2: Classification: Analgesia Intervention: Metamizol/ Tilidine; Ibuprofen Dosage: 1g / 100mg; 400mg Intervals: Single administration/ single administration; every 8hrs	Main inclusion criteria: Isolated hip fracture Main exclusion criteria: Open fracture or fracture associated with neurological injury; age<18 years; inability to swallow pills; contraindication for regional anesthesia or medications in trial; ongoing opiod analgesic therapy; multiple injuries; repeat intervention
Graham 2008[98]	Study design: RCT Study period: Apr-00 to Oct-01 Type of hospital: General hospital Country: UK Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 30ml Intervals: Single administration Intervention #2: Classification: IV analgesia Intervention: Morphine IV Dosage: 0.1mg per kg Intervals: Single administration	Main inclusion criteria: Pts > 16 yrs presenting with clinical or radiological evidence of fractured hip Main exclusion criteria: Pts with suspected allergy or contraindication to either morphine or bupivacaine, or if they had an abbreviated mental test score <9
Haddad 1995[99]	Study design: RCT Study period: NR Type of hospital: General hospital Country: UK Financial support: No external funding	Intervention #1: Classification: Femoral nerve block (CT) Intervention: Bupivacaine 0.25% Dosage: 0.3ml per kg Intervals: Single administration Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Pts with extracapsular fractures of the femoral neck Main exclusion criteria: Pts who were unable to score their pain due to dementia

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Henderson 2008[100]	Study design: RCT Study period: NR Type of hospital: General hospital Country: US Financial support: NR	Intervention #1: Classification: Femoral nerve block/Opioids Intervention: Bupivacaine 0.5% Dosage: NR/NR Intervals: Continuous/On demand Intervention #2: Classification: Standard care Intervention: Opioids Dosage: NR Intervals: Intermittent	Main inclusion criteria: ≥55 yrs presenting to the ED with acute hip fractures Main exclusion criteria: NR
Hood 1991[101]	Study design: RCT Study period: NR Type of hospital: General hospital Country: UK Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block Intervention: Prilocaine 0.75% Dosage: 43ml Intervals: Single administration Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: > 60 yrs with intertrochanteric fractures of neck of femur requiring surgical correction with compression screw or pin and plate devices Main exclusion criteria: Contraindication to a regional technique, allergy to local anesthetic agents, or systemic disease that indicated an alternative method of anesthesia
Kocum 2007[118]	Study design: Retrospective cohort study Study period: Sep-04 to Aug-05 Type of hospital: University hospital Country: Turkey Financial support: NR	Intervention #1: Classification: Lumbar plexus plus sciatic block (NS) Intervention: Ropivacaine 0.25% Dosage: 60ml Intervals: Single administration Intervention #2: Classification: Lumbar plexus plus sciatic block (NS) Intervention: Bupivacaine 0.25% Dosage: 60ml Intervals: Single administration	Main inclusion criteria: Pts, ASA III-IV, who underwent unilateral femur or hip surgery with lumbar plexus and sciatic nerve blockade Main exclusion criteria: Pts ASA I-II and those who received additional anesthesia modalities or who had other fractures

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Mannion 2005[102]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Ireland Financial support: NR	Intervention #1: Classification: Psoas compartment block (NS) Intervention: Levobupivacaine 0.5%/Clonidine IV Dosage: 0.4mL per kg/1ug per kg Intervals: Single administration Intervention #2: Classification: Psoas compartment block (NS) Intervention: Levobupivacaine 0.5%/Clonidine (peripheral) Dosage: 0.4mL per kg/1ug per kg Intervals: Single administration Intervention #3: Classification: Psoas compartment block (NS) Intervention: Levobupivacaine 0.5% Dosage: 0.4mL per kg Intervals: Single administration	Main inclusion criteria: Pts scheduled for surgical repair of traumatic hip fractures Main exclusion criteria: Concurrent medication with adrenoceptor agonists, antagonists, or contraindications to regional anesthesia
Marhofer 1997[103]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (US) Intervention: Bupivacaine 0.5% Dosage: 20ml Intervals: Single administration Intervention #2: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 20ml Intervals: Single administration	Main inclusion criteria: Pts undergoing hip surgery after trauma Main exclusion criteria: Pts who refused to participate or had contraindication to local anesthetics or puncture in the inguinal area, or unable to understand the study protocol

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Marhofer 1998[104]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (US) Intervention: Bupivacaine 0.5% Dosage: 20ml Intervals: Single administration Intervention #2: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 20ml Intervals: Single administration Intervention #3: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 30ml Intervals: Single administration	Main inclusion criteria: Pts, ASA II-III, scheduled for surgery of nondislocated hip fractures following trauma Main exclusion criteria: Refusal by the patient, allergies to local anesthetics, or general contraindications against puncture in the inguinal area, or unable to understand the study protocol because of language or other difficulty
Marhofer 2000[105]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (NS) Intervention: Ropivacaine 0.5% Dosage: 20ml Intervals: Single administration Intervention #2: Classification: 3-in-1 nerve block (NS) Intervention: Bupivacaine 0.5% Dosage: 20ml Intervals: Single administration	Main inclusion criteria: ASA I–III, scheduled for hip surgery after trauma Main exclusion criteria: Refusal by the patient, inability to understand study protocol, allergies to local anesthetics, and contraindications against puncture in the inguinal area

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Matot 2003[106]	Study design: RCT Study period: Oct-98 to Sep-98 Type of hospital: University hospital Country: Israel Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Epidural analgesia (continuous) Intervention: Bolus: Bupivacaine 0.25%/Methadone; Maintainence: Bupivacaine 0.5%/Methadone Dosage: 7-10mL/4mg; 45mg/16mg Intervals: Continous (24hrs) Intervention #2: Classification: IM analgesia Intervention: Meperidine IM Dosage: 1mg per kg Intervals: Every 6hrs	Main inclusion criteria: ≥60 yrs with traumatic hip fracture, able to sign informed consent, known CAD or at high risk for CAD Main exclusion criteria: Contraindications to epidural analgesia, suspected allergy to study drugs, acute coronary insufficiency, ECG evidence of left bundle branch block, or ≥ 10 hrs from the time of injury
Monzon 2010[107]	Study design: Randomized Controlled Trial Study period: June 2006 to Jan 2008 Type of hospital: University Hospital Country: Argentina Financial support: No conflicts of interest	Intervention #1: Classification: Fasciailiaca compartment block Intervention: 0.25% bupivacaine Dosage: 0.3 ml/kg Intervals: NR Intervention #2: Classification: General Anaesthesia Intervention: IV NSAID analgesics Dosage: NR Intervals: NR	Main inclusion criteria: adult patients more than 65 years old who presented to the ED because of a previously undiagnosed and untreated hip fracture Main exclusion criteria: anatomical abnormalities in the inguinal area different from fracture, known coagulation disorders, a history of allergy to any of the active ingredients used during the study and refusal to participate
Mouzopoulos 2009[108]	Study design: RCT Study period: Jul-04 to Mar-08 Type of hospital: General hospital Country: Greece Financial support: NR	Intervention #1: Classification: Fascia iliaca compartment nerve block (CT) Intervention: Bupivacaine Dosage: 0.25mg dose of 0.3mL per kg Intervals: every 24h before and after surgery Intervention #2: Classification: Placebo Intervention: Saline Dosage: NA Intervals: Every 24h before and after surgery	Main inclusion criteria: ≥ 70 yrs, admitted for hip fracture Main exclusion criteria: Delirium at admission, metastatic hip cancer, hx bupivacaine allergy, use of cholinesterase inhibitors, severe coagulopathy, Parkinsonism, epilepsy, levodopa treatment, delay of surgery > 72 hrs after admission, inability to participate in interviews (e.g. dementia, respiratory isolation, intubation, aphasia, coma or terminal illness)

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Murgue 2006[109]	Study design: Randomized controlled trials Study period: 37622 to 37987 Type of hospital: General hospital Country: France Financial support: NR	Intervention #1: Classification: Femoral nerve block Intervention: Mepivacaine Dosage: 20 cc Intervals: NA Intervention #2: Classification: Analgesia Intervention: IV morphine Dosage: 2 mg Intervals: 1 mg q5 min until p<=4 Intervention #3: Classification: Analgesia Intervention: IV paracetamol + ketoprofen Dosage: 1 g P + 100 mg K Intervals: NA	Main inclusion criteria: Patients with suspected fractured neck of femur admitted to ED; cognitive functioning to assess pain >27 high SES >24 low SES Main exclusion criteria: Contraindications to equimolar mix of nitrous oxide/O2; contraindications to femoral block; allergy to morphine and/or paracetamol/ketoprofene; known renal insufficiency; already receiving morphine Rx
Pedersen 2008[119]	Study design: Retrospective cohort study Study period: Jan-03 to Mar-04 Type of hospital: University hospital Country: Denmark Financial support: No external funding	Intervention #1: Classification: 3-in-1 nerve block Intervention: Bupivacaine Dosage: Bolus: 100mg; Maintainence: 50mg Intervals: Single administration; continuous (every 8hrs) Intervention #2: Classification: Analgesia Intervention: Preoperative: Morphine SC or tablets; Postoperative: Morphine SR tablets/acetaminophen or ibuprofen Dosage: 2.5-5mg/10-20mg; 1g/or 400mg Intervals: Every 12hrs; every 8hr/or every 12hrs	Main inclusion criteria: Pts undergoing surgery for a nonpathological, low-energy hip fracture Main exclusion criteria: Pts who did not receive a femoral nerve catheter or were not admitted to hip fracture unit

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Scheinin 2000[110]	Study design: RCT Study period: Jan-95 to Jan-97 Type of hospital: University hospital Country: Finland Financial support: Financial support provided by institutional, departmental and/or governmental sources	Intervention #1: Classification: Epidural analgesia (continuous) Intervention: Bupivacaine/Fentanyl Dosage: 1mg per ml + 10ug per ml Intervals: Continuous administration Intervention #2: Classification: IM analgesia Intervention: Oxycodone IM Dosage: 0.1-0.15mg per kg Intervals: On demand (max every 6hrs)	Main inclusion criteria: Elderly pts admitted for surgical repair of a traumatic hip fracture Main exclusion criteria: Known coagulation abnormalities, progressive neurologic diseases, sepsis and skin infections in lumbar region, restless or uncooperative (e.g., dementia), or significant conduction abnormalities or no sinus rhythm
Segado Jiménez 2009[111]	Study design: RCT Study period: May 2008 to Dec 2008 Type of hospital: University hospital Country: Spain Financial support: NR	Intervention #1: Classification: Obturator/ Femoral cutaneous nerve block Intervention: NR Dosage: NR Intervals: NR Intervention #2: Classification: Obturator nerve block Intervention: NR Dosage: NR Intervals: NR Intervention #3: Classification: IV analgesia Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Patients undergoing hip surgery with subarachnoid blockage Main exclusion criteria: General anesthesia, IV analgesic drugs during surgery, untreated chronic pain, arrythmias/MI, or neurological disorders

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Segado Jimenez 2010[112]	Study design: Randomized Controlled Trial Study period: 2009 to 2010 Type of hospital: University Hospital Country: Spain Financial support: No funding	Intervention #1: Classification: Fascia iliaca compartment block Intervention: Bupivacaine 0.5% Dosage: 30 ml Intervals: NR Intervention #2: Classification: Obturator /femoralcutaneous nerves block Intervention: Bupivacaine 0.5% Dosage: 15ml / 5 ml Intervals: NR Intervention #3: Classification: General Anaesthesia Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: patients with hip surgery, total or partial arthroplasty, and osteosynthesis of femor Main exclusion criteria: patients with previous traetment for chronic pain, ischemic cardiopathic, or arrhythmia, psychiatric and neurodegenerative diseases, poor collaboration and comprehension, allergy to local anaethetics, and contraindication to local/regional anaethetics
Spansberg 1996[113]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Denmark Financial support: NR	Intervention #1: Classification: Lumbar plexus block (NS) Intervention: Bolus: Bupivacaine 0.5%; Maintenence: Bupivacaine 0.25% Dosage: 0.4mL per kg; 0.14mL per kg per hr Intervals: Single administration; Continuous administration Intervention #2: Classification: Placebo Intervention: Bolus: Saline; Maintainence: Saline Dosage: 0.4mL per Kg; 0.14mL per kg per hr Intervals: Continuous administration	Main inclusion criteria: Pts with femoral neck fractures Main exclusion criteria: NR

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Tuncer 2003[114]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Turkey Financial support: NR	Intervention #1: Classification: 3-in-1 nerve block (NS) Intervention: Bolus: Lidocaine 2%/Maintainence: Bupivacaine 0.125%; PCA bolus: Bupivaciane 0.125% Dosage: 30ml; 4ml per hr; 3ml Intervals: Single administration; Continuous administration; Patient cotrolled bolus on demand Intervention #2: Classification: IV analgesia Intervention: Morphine IV Dosage: 1mg Intervals: On demand	Main inclusion criteria: Pts, ASA I–II, scheduled for trochanteric fracture repair Main exclusion criteria: Pts with coagulation abnormalities, <18 or >80 yrs, wt <50 or >100 kg, suspected allergy to bupivacaine or opioids, previous analgesic treatment with opioids, inability to understand pain scales or use a patient controlled analgesia device
Turker 2003[115]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Turkey Financial support: NR	Intervention #1: Classification: Psoas compartment block (NS) Intervention: Bupivacaine 0.5% Dosage: 30ml Intervals: Single administration Intervention #2: Classification: Epidural anesthesia (single) Intervention: Bupivacaine 0.5% Dosage: 15ml Intervals: Single administration	Main inclusion criteria: Pts, ASA I–III, scheduled for unilateral hip surgery Main exclusion criteria: Contraindications to regional anesthesia, suspected allergy to any local anesthetic, dementia preventing proper comprehension, and refusal of the procedure

Table E-5. Nerve blocks (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Yun 2009[116]	Study design: Randomized controlled trials Study period: 39264 to 39417 Type of hospital: University hospital Country: Korea Financial support: NR	Intervention #1: Classification: Fascia iliaca compartment nerve block (CT) Intervention: Ropivacaine Dosage: 30 mL 3.75 mg/mL 2-3 min Intervals: Single dose Intervention #2: Classification: Analgesia Intervention: Alfentanil Dosage: 10 ug/kg bolus; 0.25 ug/kg/min 2 min Intervals: Single dose	Main inclusion criteria: Patients with an isolated femoral neck fracture scheduled to undergo either compression hip screw or hip replacement surgery. Main exclusion criteria: A suspected allergy to amide local anaesthetics; haemorrhagic diathesis; periperal neuropathy or mental disorders.

ASA = American Society of Anesthesiology; CT = clinical touch; IM = intramuscular; IV = intravenous; NR = NR; NS = nerve stimulation; RCT = randomized controlled trial; US = ultrasound

Table E-6. Neurostimulation

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Gorodetskyi 2007[120]	Study design: RCT Study period: Feb-05 to Nov-05 Type of hospital: University hospital Country: Russia Financial support: Financial support provided by a commercial party	Intervention #1: Classification: Neurostimualtion Intervention: InterX 5000 device Dosage: high peak amplitude averaging 17 volts on skin with low current of 6 mA, and damped biphasic electrical impulses Intervals: Every 24hrs Intervention #2: Classification: Sham Control Intervention: NA Intervals: Every 24hrs	Main inclusion criteria: Between 60 and 75 yrs, undergone stabilization of A2 femoral trochanteric fracture Main exclusion criteria: Lmitations that interfere with electrical stimulation (e.g., insulin pumps, pacemakers, neurostimulation implants), hx epilepsy or seizure, bilateral fractures, fractures of pathological origin, excluding osteoporosis
Lang 2007[121]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Austria Financial support: NR	Intervention #1: Classification: Neurostimulation Intervention: Transcutaneous electrical nerve stimulation Dosage: 70 mA, frequency range: 0.5 to 120 Hz, pulse width: 60 to 300 us, Intervals: Single administration Intervention #2: Classification: Sham Control Intervention: NA Intervals: Single administration	Main inclusion criteria: >19 yrs, acute pain (>60 mm VAS) in region of hip Main exclusion criteria: Analgesics in previous 48 hr, neurologic impairment of legs, cognitive impairment or inability to communicate, potentially dangerous internal diseases (ASA score >3), or hip pain from causes other than fracture

ASA = American Society of Anesthesiology; IM = intramuscular; IV = intravenous; NR = not reported; RCT = randomized controlled trial

Table E-7. Rehabilitation

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Di Lorenzo 2007[122]	Study design: RCT Study period: Jan-02 to Oct-06 Type of hospital: General hospital Country: Italy Financial support: NR	Intervention #1: Classification: Rehabilitation Intervention: Stretching/strengthening of spinal and psoas muscles Dosage: 1 hr of training Intervals: Every 12 hrs for 4 wk Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Pts with extracapuslar unstable hip fracture who underwent surgery and have back pain on ipsilateral side of fracture despite standard rehabilitation Main exclusion criteria: Previous chronic back pain, back surgery, spinal stenosis, spondylolisthesis or anxiety and depression

NR = Not reported; RCT = randomized controlled trial

Table E-8. Traction

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Anderson 1993[128]	Study design: nRCT Study period: Nov-91 to Jul-93 Type of hospital: General hospital Country: UK Financial support: No external funding	Intervention #1: Classification: Skin traction Intervention: Hamilton-Russell skin traction Dosage: 5lb (2.3kg) Intervention #2: Classification: Standard care Intervention: NR Dosage: NR	Main inclusion criteria: Pts with fractures of the proximal femur Main exclusion criteria: Refused informed consent or consent could not be obtained (e.g., dementia), contraindications for use of skin traction (e.g., poor skin, ulceration of lower limb, peripheral arterial disease, severe edema and lower limb deformities)
Finsen 1992[123]	Study design: RCT Study period: NR Type of hospital: General hospital Country: Norway Financial support: NR	Intervention #1: Classification: Skin traction Intervention: Elastic bandages Dosage: 3kg Intervention #2: Classification: Skeletal traction Intervention: Steinman pin Dosage: 10% of the patient's body weight Intervention #3: Classification: Pillow Intervention: Standard pillow	Main inclusion criteria: > 50 yrs admitted with recent cervical, trochanteric or subtrochanteric hip fractures Main exclusion criteria: NR
Ghnaimat 2005[129]	Study design: nRCT Study period: Feb-02 to Oct-04 Type of hospital: General hospital Country: Jordan Financial support: NR	Intervention #1: Classification: Skin traction Intervention: Skin traction Dosage: 6lb Intervals: NA Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Pts admitted with fractures of the proximal femur Main exclusion criteria: Allergy to adhesive bandages, ulceration in lower limbs, peripheral arterial disease, severe ederna or lower limb deformities, or refused to be part of the study

Table E-8. Traction (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Jerre 2000[124]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Sweden Financial support: NR	Intervention #1: Classification: Skin traction Intervention: Foam rubber boot with straps around the lower leg Dosage: 3Kg Intervals: NA Intervention #2: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR Intervention #3: Classification: Skin traction Intervention: Foam rubber boot with straps around the lower leg Dosage: 3Kg Intervals: NA Intervention #4: Classification: Standard care Intervention: NR Dosage: NR Intervals: NR	Main inclusion criteria: Pts with cervical or trochanteric hip fractures Main exclusion criteria: Pts unwilling or unable to provide consent for enrollment
Needoff 1993[125]	Study design: RCT Study period: NR Type of hospital: General hospital Country: UK Financial support: NR	Intervention #1: Classification: Skin traction Intervention: Ventilated foam strap secured by means of a crepe bandage Dosage: 2.5kg Intervals: NA Intervention #2: Classification: Pillow Intervention: Standard pillow Dosage: NA Intervals: NA	Main inclusion criteria: > 60 yrs with cervical or pertrochanteric femoral fractures undergoing surgical hip fracture repair Main exclusion criteria: Cognitively impaired pts on the Mini-Mental State Examination

Table E-8. Traction (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Resch 1998[126]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Sweden Financial support: Financial support provided by governmental sources	Intervention #1: Classification: Skin traction Intervention: Foam boot Dosage: 3kg Intervals: NA Intervention #2: Classification: Skeletal traction Intervention: K-wire Dosage: 3-5kg (5-10% body weight) Intervals: NA	Main inclusion criteria: Displaced hip fractures Main exclusion criteria: Pts who could not give consent, declined participation or had local skin problems (e.g., leg ulcers)
Resch 2005[26]	Study design: RCT Study period: NR Type of hospital: University hospital Country: Sweden Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Skin traction Intervention: Foam rubber boot Dosage: 3kg Intervals: NA Intervention #2: Classification: Pillow Intervention: Lasse Pillow Dosage: NA Intervals: NA Intervention #3: Classification: Pillow Intervention: Standard pillow Dosage: NA Intervals: NA	Main inclusion criteria: Pts who had a dislocated cervical or trochanteric hip fracture, ability to give informed consent, and no local problems which would prohibit the use of skin traction, such as ulcers, eczema, or peripheral vascular disease Main exclusion criteria: NR
Rosen 2001[127]	Study design: RCT Study period: Jun-95 to Feb-97 Type of hospital: University hospital Country: US Financial support: No external funding	Intervention #1: Classification: Skin traction Intervention: Foam traction boot Dosage: 5lb Intervals: NA Intervention #2: Classification: Pillow Intervention: Standard pillow Dosage: NA Intervals: NA	Main inclusion criteria: Pts with an isolated femoral neck or intertrochanteric hip fracture Main exclusion criteria: < 50 yrs, underlying dementia, other concomitant injury, delayed hospital presentation (e.g., >24 hrs after the initial injury)

Table E-8. Traction (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Saygi 2010[130]	Study design: Retrospective cohort study Study period: NR Type of hospital: General hospital Country: Turkey Financial support: No external funding	Intervention #1: Classification: Skin traction Intervention: Traction bandages Dosage: 2kg Intervals: NA Intervention #2: Classification: Sham traction Intervention: Traction bandages Dosage: 0kg Intervals: NA Intervention #3: Classification: Pillow Intervention: Standard pillow Dosage: NA Intervals: NA	Main inclusion criteria: Pts with hip fracture Main exclusion criteria: Refusal to participate in the study or a cognitive inadequacy detected in their simple mental scores
Vermeiren 1995[132]	Study design: Prospective cohort study Study period: Jul-87 to Jun-89 Type of hospital: General hospital Country: Belgium Financial support: NR	Intervention #1: Classification: Skeletal traction Intervention: Skeletal traction with pillows for foot elevation Dosage: 1 kg traction weight/10 kg body weight Intervals: NA Intervention #2: Classification: Skeletal traction Intervention: Skeletal traction with metal splint Dosage: 1 kg traction weight/10 kg body weight Intervals: NA	Main inclusion criteria: Pts admitted with an intertrochanteric or subtrochanteric hip fracture Main exclusion criteria: NR

Table E-8. Traction (continued)

Study	Study characteristics	Interventions	Inclusion/Exclusion criteria
Yip 2002[131]	Study design: nRCT Study period: Aug-95 to Dec-97 Type of hospital: University hospital Country: Hong Kong Financial support: Financial support provided by institutional and/or departmental sources	Intervention #1: Classification: Skin traction Intervention: Foam boot Dosage: 2kg Intervals: NA Intervention #2: Classification: Pillow Intervention: Standard pillow Dosage: NA Intervals: NA	Main inclusion criteria: Pts with proximal femur fracture and consenting to enrollment Main exclusion criteria: Pts that were senile or had been taking regular analgesia prior to admission

NA = not applicable; NR = n; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Appendix F. Characteristics of Interventions

Table F-1. Systemic analgesia

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Apostolopoulos 2006[41]	Classification	IV analgesia	IM analgesia	NA	NA
	Type of intervention	Parecoxib IV	Diclofenac IM; Pethidine IM		
	Dosage	40mg	75mg; NR		
	Dosage Intervals	Every 12hrs	Every 12hrs; on demand		
	Timing of intervention	Postoperative	Postoperative		
	Type of intervention	Clonidine (Isotonic)	Clonidine (Hypertonic)		
	Dosage	150 ug	150 ug		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Postoperative	Postoperative		
	Baseline pain score (VAS) Mean ± SD (n)	6.51 ± 0.63 (15)	7.18 ± 0.37 (15)		
Poitevin 1999[55]	Classification	Analgesia	Analgesia	NA	NA
	Type of intervention	Lysine clonixinate	Metamizole		
	Dosage	125mg	400mg		
	Dosage Intervals	every 8 hr	every 8 hr		
	Age (yr) Mean ± SD	76.91 ± 6.00	77.60 ± 6.10		
	Gender				
	Females: n (%)	35/48 (72.92%)	35/46 (76.09%)		
	Males: n (%)	13/48 (27.08%)	9/46 (19.57%)		

IM = intramuscular; IV = intravenous; NA = not applicable; NR = not reported; VAS = visual analogue scale

Table F-2. Anesthesia

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Adams 1990[56]	Classification	Spinal anesthesia	General anesthesia	NA	NA
	Type of intervention	Bupivacaine 0.5%/ Mepivacaine 4%	NR		
	Dosage	NR	NR		
	Dosage Intervals	NR	NR		
	Age (yr)				
	Mean	81	79		
	Range	(70 – 88)	(63 – 96)		
	Body weight (Kg)				
	Mean	63	58		
	Range	(45 – 100)	(40 – 80)		
	Height (cm)				
	Mean ± SD	161.00 ± 178	161.00 ± 178		
	Range	(150 –182)	(150 – 178)		
	BMI (Kg/ m^2)				
	Mean	24.3	22.4		
	Gender				
	Females: n (%)	18/ 24 (75.00%)	28/ 32 (87.50%)		
	Males: n (%)	6/ 24 (25.00%)	4/ 32 (12.50%)		
	Type of fractures				
	Femoral neck: n (%)	24/ 24 (100.00%)	32/ 32 (100.00%)		
	Intertrochanteric: n (%)	0/ 24 (0.00%)	0/ 32 (0.00%)		
	Proximal femur: n (%)	0/ 24 (0.00%)	0/ 32 (0.00%)		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Ben-David 2000[58]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine/Fentanyl	Bupivacaine		
	Dosage	4mg/20ug	10mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Richard's platescrew internal fixation of femoral neck fx in 8/10 ; Austin–Moore hemiarthroplasty for subcapital fx of femoral neck in 2/10	Richard's platescrew internal fixation of femoral neck fx and Austin–Moore hemiarthroplasty for subcapital fx of femoral neck in all		
	Type of anesthesia				
	Epidural	0/10 (0%)	0/10 (0%)		
	Spinal	10/10 (100%)	10/10 (100%)		
	General	0/10 (0%)	0/10 (0%)		
Bredahl 1991[59]	Classification	Spinal anaesthesia	General anaesthesia	NA	NA
	Type of intervention	Bupivacainc 0.5%	Thiopentone		
	Dosage	2.5-3 ml	2-4 mg/kg		
	Dosage Intervals	NR	Once		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	internal fixation/hemiarthroplasty	internal fixation/hemiarthroplasty		
	Type of anesthesia				
	Epidural	0/15 (0%)	0/15 (0%)		
	Spinal	15/15 (100%)	0/15(0%)		
	General	0/15(0%)	13/13(100%)		
	Duration of surgery (hr)				
	Mean ± SD	1.00 ± 0.40	1.10 ± 0.40		
	(Range)	(0.50 –2.00)	(0.60 –1.75)		
	Age (yr)				
	Mean ± SD	80.00± 5.81	79.00 ± 7.93		
	(Range)	(72 – 93)	(60 – 90)		
	Body weight (Kg)				
	Mean ± SD	56.00 ± 6.97	56.00 ± 7.93		
	Range	(40 – 65)	(45 – 70)		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Gender				
	Females: n (%)	15/15 (100%)	13/13 (100%)		
	Males: n (%)	0/15 (0%)	0/13 (0%)		
	Type of fractures				
	Femoral neck: n (%)	12/15 (80%)	8/13 (61.50%)		
	Intertrochanteric: n (%)	3/15 (20%)	5/13 (38.50%)		
	Proximal femur: n (%)	0/15 (0%)	0/13 (0%)		
Casati 2003[60]	Classification	Spinal anesthesia (single)	General anesthesia	NA	NA
	Type of intervention	Bupivacaine 0.5%	None		
	Dosage	7.5mg	NA		
	Dosage Intervals	Single administration	NA		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of anesthesia				
	Epidural	0/15 (0%)	0/15 (0%)		
	Spinal	15/15 (100%)	0/15 (0%)		
	General	0/15 (0%)	15/15 (100%)		
	Duration of surgery (hr)				
	Range	(0.75 –1.83)	(0.83 –1.67)		
	Baseline pain score	Scale name [NRS (1-5)]			
	Mean ± SD (n)	1.67 ± 0.49 (15)	2.13 ± 0.74 (15)		
	(Range)	(1.00 – 2.00)	(1.00 – 3.00)		
Danelli 2008[61]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Levobupivacaine 0.5%	Levobupivacaine 0.75%		
	Dosage	15mg	15mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Gamma-nail fixation or hip hemiarthroplasty in all	Gamma-nail fixation or hip hemiarthroplasty in all		
	Type of anesthesia				
	Epidural	0/29 (0%)	0/31 (0%)		
	Spinal	29/29 (100%)	31/31 (100%)		
	General	0/29 (0%)	0/31 (0%)		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Favarel-Garrigues 1996[62]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	Bolus: Bupivacaine 5mg (1ml); Manintainence: Bupivacaine 2.5mg (0.5ml)	Based on age and ht: 15mg 70-79 yr or >170 cm;12.5mg 80-90 yr or 150-170 cm; 10mg >90 yr or <150 cm		
	Dosage Intervals	Single administration; Continuous administration on demand	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of anesthesia				
	Epidural	0/30 (0%)	0/30 (0%)		
	Spinal	30/30 (100%)	30/30 (100%)		
	General	0/30 (0%)	0/30 (0%)		
	Duration of surgery (hr)				
	Mean ± SD	1.42 ± 0.71	1.38 ± 0.55		
Hooda 2006[63]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	Spinal anesthesia (single)	
	Type of intervention	Bupivacaine 0.5%/Fentanyl	Bupivacaine 0.5%/Fentanyl	Bupivacaine 0.5%/Fentanyl	
	Dosage	4mg (0.8ml)/20mg (0.4ml)	5mg (1.0ml)/20mg (0.4ml)	6mg (1.2ml)/20mg (0.4ml)	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of anesthesia				
	Epidural	0/30 (0%)	0/30 (0%)	0/30 (0%)	
	Spinal	30/30 (100%)	30/30 (100%)	30/30 (100%)	
	General	0/30 (0%)	0/30 (0%)	0/30 (0%)	
	Duration of surgery (hr)				
	Mean ± SD	0.98 ± 0.27	1.00 ± 0.41	1.03 ± 0.21	
	(Range)	(0.42 –1.42)	(0.50 –2.67)	(0.67 –1.50)	
Juelsgaard 1998[64]	Classification	Spinal anesthesia (incremental)	Spinal anesthesia (single)	General anesthesia	
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%	Fentanyl	
	Dosage	1.6ml	2.5ml	Bolus: 1-2ug/kg/ Maintainence: 25-50ug	

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage Intervals	Incremental dosage	Single administration	Single administration/ Continuous administration (on demand)	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of surgery	Internal fixation in 4/14; hemiarthroplasty in 10/14	Internal fixation in 5/15; hemiarthroplasty in 10/15	Internal fixation in 3/14; hemiarthroplasty in 11/14	
	Type of anesthesia				
	Epidural	0/14 (0%)	0/15 (0%)	0/14 (0%)	
	Spinal	14/14 (100%)	15/15 (100%)	0/14 (0%)	
	General	0/14 (0%)	0/15 (0%)	14/14 (100%)	
	Duration of surgery (hr)				
	Mean	1.09	1.17	1.13	
	(Range)	(0.45 –2.00)	(0.45 –2.40)	(0.45 –1.20)	
Klimscha 1995[65]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (continuous)	Epidural anesthesia (continuous)	Epidural anesthesia (continuous)
	Type of intervention	Bupivacaine 0.5% plus clonidine	Bupivacaine 0.5%	Bupivacaine 0.5%/clonidine	Bupivacaine 0.5%
	Dosage	1ml bupivacaine/1ml Clonidine	10ml bupivacaine	10ml bupivacaine/ 1ml Clonidine	10ml bupivacaine
	Dosage Intervals	Continuous administration (3 repetitive doses)	Continuous administration (3 repetitive doses)	Continuous administration (3 repetitive doses)	Continuous administration (3 repetitive doses)
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	Intra-operative
	Type of anesthesia				
	Epidural	0/10 (0%)	0/10 (0%)	10/10 (100%)	10/10 (100%)
	Spinal	10/10 (100%)	10/10 (100%)	0/10 (0%)	0/10 (0%)
	General	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Koval 1999[78]	Classification	Spinal anaesthesia	General anaesthesia	NA	NA
	Type of intervention	NR	NR		
	Dosage	NR	NR		
	Dosage Intervals	NR	NR		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Internal fixation, Prosthetic replacement	Internal fixation, Prosthetic replacement		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of anesthesia				
	Epidural	0/280 (0%)	0/362 (0%)		
	Spinal	143/280 (51.07%)	196/362 (54.14%)		
	General	137/280 (48.93%)	166/362 (48.86%)		
	Age (yr)				
	Mean ± SD	81.00	78.50		
	(Range)	(65 – 105)	(65 – 104)		
	Gender				
	Females: n (%)	213/280 (76.07%)	62/362 (17.13%)		
	Males: n (%)	67/280 (23.93%)	300/362 (82.87%)		
	Type of fractures				
	Femoral neck: n (%)	143/280(51.07%)	196/362(54.14%)		
	Intertrochanteric: n (%)	137/280(48.93%)	166/362(45.86%)		
	Proximal femur: n (%)	0/280(0%)	0/362(0%)		
Krobot 2006[77]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Levobupivacaine/Fentanyl	Levobupivacaine		
	Dosage	7.5mg/0.01mg	10mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
Kwan 1997[66]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine 0.5%/Morphine	Bupivacaine 0.5%		
	Dosage	2.2ml/0.2mg	2.2ml		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Austin Moore arthroplasty or compression hip screw	Austin Moore arthroplasty or compression hip screw		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	4.68 ± 2.14 (20)	5.40 ± 2.76 (20)		
Labaille 1992[79]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (continuous)	NA	NA
	Type of intervention	Bupivacaine 0.125%/Bupivacaine 0.125%	Bupivacaine 0.5%/Bupivacaine 0.5%		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage	Bolus: 3ml/Maintaninence: 1ml	Bolus: 3ml/Maintaninence: 1ml		
	Dosage Intervals	Single administration/ Continuous administration (on demand)	Single administration/ Continuous administration (on demand)		
	Timing of intervention	Intra-operative	Intra-operative		
Malek 2004[67]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	Spinal anesthesia (single)	NA
	Type of intervention	Bupivacaine 0.5%/Fentanyl	Bupivacaine 0.5%/Sufentanil	Bupivacaine 0.5%	
	Dosage	3ml/50ug	3ml/5ug	3ml	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of anesthesia				
	Epidural	0/21 (0%)	0/21 (0%)	0/21 (0%)	
	Spinal	21/21 (100%)	21/21 (100%)	21/21 (100%)	
	General	0/21 (0%)	0/21 (0%)	0/21 (0%)	
	Duration of surgery (hr)				
	Mean ± SD	1.57 ± 0.43	1.75 ± 0.33	1.60 ± 0.50	
Martyr 2001[68]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivaciane/Fentanyl	Bupivacaine		
	Dosage	7.5mg/20ug	12.5mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Richards pin and plate in all	Richards pin and plate in all		
	Type of anesthesia				
	Epidural	0/20 (0%)	0/22 (0%)		
	Spinal	20/20 (100%)	22/22 (100%)		
	General	0/20 (0%)	0/22 (0%)		
	Duration of surgery (hr)				
	Mean ± SD	1.27 ± 0.50	1.10 ± 0.24		
Martyr 2005[69]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine/Fentanyl	Bupivacaine		
	Dosage	9.0mg/20ug	11.0mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of surgery	DHS in 13/20 pts; hemianhroplasty in 7/20 pts	DHS in 11/20 pts; hemianhroplasty in 9/20 pts		
	Type of anesthesia				
	Epidural	0/20 (0%)	0/20 (0%)		
	Spinal	20/20 (100%)	20/20 (100%)		
	General	0/20 (0%)	0/20 (0%)		
	Duration of surgery (hr)				
	Mean ± SD	0.85 ± 0.40	0.78 ± 0.33		
Maurette 1993[70]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (continuous)	NA	NA
	Type of intervention	Bolus: lidocaine 1.6%/ meperidine 1%; Maintainence: lidocaine 1.6%	Bolus: lidocaine 1.6%; Maintainence: lidocaine 1.6%		
	Dosage	NA/4ml (200mg); NA	NA		
	Dosage Intervals	Continuous administration	Continuous administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of anesthesia				
	Epidural	0/19 (0%)	0/15 (0%)		
	Spinal	19/19 (100%)	15/15 (100%)		
	General	0/19 (0%)	0/15 (0%)		
	Duration of surgery (hr)				
	Mean ± SD	1.33 ± 0.60	1.35 ± 0.40		
Miller 1990[81]	Classification	Spinal anesthesia	General anesthesia		
	Type of intervention	Mepivacaine 4 %	Fentanyl		
	Dosage	2ml (80 mg)	3-5mg per kg		
	Dosage Intervals	NR	NR		
	Age (yr)				
	Mean	79.8	80.5		
	Type of fractures				
	Femoral neck: n (%)	0/ 180 (0.00%)	0/ 137 (0.00%)		
	Intertrochanteric: n (%)	0/ 180 (0.00%)	0/ 137 (0.00%)		
	Proximal femur: n (%)	180/ 180 (100.00%)	137/ 137 (100.00%)		
Minville 2006[71]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine	Bupivacaine		
	Dosage	2.5mg	7.5mg		
	Dosage Intervals	Continuous administration	Single administration		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	DHS in 12/36 pts; Austin-Moore arthroplasty in 18/36; hip hemiarthroplasty in 6/36	DHS in 10/37 pts; Austin-Moore arthroplasty in 22/37; hip hemiarthroplasty in 5/37		
	Type of anesthesia				
	Epidural	0/36 (0%)	0/37 (0%)		
	Spinal	36/36 (100%)	37/37 (100%)		
	General	0/36 (0%)	0/37 (0%)		
	Duration of surgery (hr)				
	Mean ± SD	0.87 ± 0.30	0.85 ± 0.28		
Minville 2008[82]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (continuous)	Spinal anesthesia (single)	General anesthesia
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%	Bupivacaine 0.5%	Sulfentanil
	Dosage	2.5mg	5mg	NR	NR
	Dosage Intervals	Continuous administration	Continuous administration	Single administration	NR
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	Intra-operative
	Time from ED arrival to surgery (hr)				
	Mean ± SD	24.00 ± 10.00	17.00 ± 12.00	18.00 ± 10.00	23.00 ± 7.00
	Type of surgery	Ostheosynthesis in 76/121; intermediate prosthesis in 33/12; total hip replacement in 12/121	ostheosynthesis 34/61; intermediate prosthesis 19/61; total hip replacement 8/61	ostheosynthesis 52/109; intermediate prosthesis 41/109; total hip replacement 16/109	ostheosynthesis 20/42; intermediate prosthesis 8/42; total hip replacement 14/42
	Type of anesthesia				
	Epidural	0/121 (0%)	0/61 (0%)	0/109 (0%)	0/42 (0%)
	Spinal	121/121 (100%)	61/61 (100%)	109/109 (100%)	0/42 (0%)
	General	0/121 (0%)	0/61 (0%)	0/109 (0%)	42/42 (100%)
	Duration of surgery (hr)				
	Mean ± SD	1.00 ± 0.33	1.03 ± 0.32	1.10 ± 0.48	1.30 ± 0.48
Navas 2008[72]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine 0.15-0.25%	Bupivacaine 0.5%		
	Dosage	NR	NR		
	Dosage Intervals	Continuous administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
Olofsson 2004[73]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	NA	NA

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of intervention	Bupivacaine/sufentanil	Bupivacaine		
	Dosage	7.5mg/5mg	15mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	internal fixation of femoral neck fractures with two parallel screws or DHS for subcapital fractures of the femoral neck in all pts	internal fixation of femoral neck fractures with two parallel screws or DHS for subcapital fractures of the femoral neck in all		
	Type of anesthesia Epidural Spinal General	 0/25 (0%) 25/25 (100%) 0/25 (0%)	 0/25 (0%) 25/25 (100%) 0/25 (0%)		
	Duration of surgery (hr) Mean ± SD	 0.82 ± 0.13	 0.65 ± 0.08		
Qamarul Hoda 2007[146]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	Spinal anesthesia (single)	NA
	Type of intervention	Bupivacaine/Fentanyl	Bupivacaine/Fentanyl	Bupivacaine	
	Dosage	6mg/20ug	8mg/20ug	10mg	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
Rais 2008[75]	Classification	Spinal anesthesia (continuous)	Spinal anesthesia (continuous)	NA	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	2.5mg	5mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
Said-Ahmed 2006[76]	Classification	Spinal anesthesia (single)	Spinal anesthesia (single)	Spinal anesthesia (single)	NA
	Type of intervention	Bupivacaine 0.5%/Fentanyl	Bupivacaine 0.5%/Sufentanil	Bupivacaine 0.5%	
	Dosage	5mg/20mcg	5mg/5mcg	10mg	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of surgery	Austin-Moore prosthesis in 14/20 pts; DHS in 6/20 pts	Austin-Moore prosthesis in 14/20; DHS in 6/20	Austin-Moore prosthesis 14/20; DHS 6/20	
	Type of anesthesia Epidural	 0/20 (0%)	 0/20 (0%)		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Spinal General	20/20 (100%) 0/20 (0%)	20/20 (100%) 0/20 (0%)		
Sen 2007[83]	Classification	Spinal anesthesia (single - lateral)	Spinal anesthesia (single - supine)	NA	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	10mg	10mg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of anesthesia Epidural Spinal General	 0/23 (0%) 23/23 (100%) 0/23 (0%)	 0/18 (0%) 18/18 (100%) 0/18 (0%)		
Shih 2010[84]	Classification	Spinal anaesthesia	General anaesthesia	NA	NA
	Type of intervention	Bupivacaine	Thiopental		
	Dosage	8-15 mg	NR		
	Dosage Intervals	NR	NR		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	NR	NR		
	Type of anesthesia Epidural Spinal General	 0/168 (0%) 168/168 (100%) 0/168 (0%)	 0/167 (0%) 0/167 (0%) 167/167(100%)		
	Duration of surgery (hr) Mean ± SD Range	 NR (1.33 –4.92)	 NR (1.42 –8.53)		
	Age (yr) Mean ± SD (Range)	 84.93 ± 4.04 (80 – 99)	 83.96 ± 3.71 (80 – 99)		
	Gender Females: n (%) Males: n (%)	 74/168 (44.05%) 94/168 (55.95%)	 72/167 (43.11%) 95/167 (56.89%)		

Table F-2. Anesthesia (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	ASA Class				
	ASA I (%)	0/168 (0%)	0/167 (0%)		
	ASA II (%)	45/168 (26.79%)	47/167 (28.14%)		
	ASA III (%)	120/168 (71.43%)	115/167 (68.86%)		
	ASA IV (%)	2/168 (1.19%)	1/167 (0.60%)		
Sutcliffe 1994[85]	Classification	Spinal anaesthesia	General anaesthesia	NA	NA
	Type of intervention	Bupivacaine	NR		
	Dosage	NR	NR		
	Dosage Intervals	NR	NR		
	Timing of intervention	Intra-operative	Intra-operative		
	Time from fall to surgery (hr)				
	Mean ± SD	57.00 ± NR	56.00 ± NR		
	Type of surgery	internal fixation, hemiarthroplasty, dynamic hip screw or nail plate fixation, other fixation devices	internal fixation, hemiarthroplasty, dynamic hip screw or nail plate fixation, other fixation devices		
	Type of anesthesia				
	Epidural	0/383 (0%)	0/950 (0%)		
	Spinal	383/383 (100%)	0/950 (100%)		
	General	0/383 (0%)	950/950 (0%)		
	Age (yr)				
	Mean ± SD	80.00 ± NR	79.00 ± NR		
	Gender				
	Females: n (%)	303/383 (79.11%)	788/950 (82.95%)		
	Males: n (%)	80/ 383 (20.89%)	162/ 950 (17.05%)		
	Pre-fracture residence				
	Community: n (%)	92/383 (24.00)	266/950 (28.00)		
	Institutional: n (%)	291/383 (76.00)	684/950 (72.00)		

NA = not applicable; NR = not reported; NRS = numeric rating scale; VAS = visual analogue scale

Table F-3. Complementary and alternative medicine (CAM)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Barker 2006[43]	Classification	Auricular acupressure	Sham Control	NA	NA
	Type of intervention	1-mm plastic acupressure beads	1-mm acupressure plastic beads		
	Dosage	3 true auricular acupressure points	3 sham auricular acupressure points		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Pre-operative	Pre-operative		
	Time from fall to ED arrival (hr)				
	Mean ± SD	0.48 ± 0.20	0.53 ± 0.25		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	6.39 ± NR (18)	6.56 ± NR (20)		
Martin 1991[54]	Classification	Relaxation	Analgesia	NA	NA
	Type of intervention	Jacobson relaxation technique/Meperidine/Morphine	Meperidine/Morphine		
	Dosage	NA	NR		
	Dosage Intervals	Instruction given prior to surgery	NR		
	Timing of intervention	Pre-operative	Pre-operative		

NA = not applicable; NR = not reported; VAS = Visual analogue scale

Table F-4. Multimodal pain management

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Milisen 2001[86]	Classification	Multimodal pain management	Standard care	NA	NA
	Type of intervention	Bolus: Tramadol IV; Maintainence (48hrs): Tramdol IV + propacetamol IV; Maintainence (Day 3-5): oral tramadol + oral paracetamol	NR		
	Dosage	3mg/ kg; 6mg/ kg/ 24hrs; 120mg/ kg/ 24hours/NA	NR		
	Dosage Intervals	Continuous administration	NR		
	Timing of intervention	Postoperative	Postoperative		
Ogilvie-Harris 1993[87]	Classification	Mutlimodal pain management	Standard care	NA	NA
	Type of intervention	Skin Traction/ Morphine/Acetaminophen	NR		
	Dosage	NA/2.5-5mg/1000mg	NR		
	Dosage Intervals	Rewrap every 8hrs/every 4hrs/every 4hrs	NR		
	Timing of intervention	Preoperative	Preoperative		

IV = intravenous; NA = not applicable; NR = not reported

Table F-5. Nerve blocks

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Antonopoulou 2006[88]	Classification	Femoral nerve block	Analgesia	NA	NA
	Type of intervention	Bolus: Levobupivacaine 0.25%; Maintanence: Levobupivacaine 0.12%	Paracetamol; Pethidine		
	Dosage	18ml	500mg; NR		
	Dosage Intervals	Single administration; Continuous administration	Every 8hrs; on demand		
	Timing of intervention	Postoperative	Postoperative		
	Type of anesthesia Epidural Spinal General	 0/49 (0%) 49/49 (100%) 0/49 (0%)	 0/35 (0%) 35/35 (100%) 0/35 (0%)		
Chudinov 1999[89]	Classification	Psoas Compartment Block (continuous)	IM analgesia	NA	NA
	Type of intervention	Bupivacaine 0.25%	Meperidine IM		
	Dosage	Bolus: 2mg/kg; Maintainence: 2mg/kg	1mg/kg		
	Dosage Intervals	Single administration/ Maintainence: every 12hrs	On demand (max every 5hrs)		
	Timing of intervention	Preoperative	Preoperative		
	Type of anesthesia Epidural Spinal General	 0/20 (0%) 11/20 (55%) 1/20 (5%)	 0/20 (0%) 19/20 (95%) 1/20 (5%)		
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		4.30 ± 0.60 (20)	4.30 ± 0.70 (20)		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Coad 1991[90]	Classification	3-in-1 nerve block	Lateral cutaneous nerve block	Standard care	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%	NR	
	Dosage	15ml	15ml	NR	
	Dosage Intervals	Single administration	Single administration	NR	
	Timing of intervention	Postoperative	Postoperative	Postoperative	
	Type of surgery	Compresion screw 12/17 pts; pin and plate 5/17	Compresion screw 13/17 pts; pin and plate 4/17	Compresion screw 11/17; pin and plate 5/17	
	Type of anesthesia Epidural Spinal General	 0/17 (0%) 0/17 (0%) 17/17 (100%)	 0/17 (0%) 0/17 (0%) 17/17 (100%)	 0/16 (0%) 0/16 (0%) 16/16 (100%)	
Cuvillon 2007[91]	Classification	3-in-1 nerve block (NS)	Analgesia	Analgesia	
	Type of intervention	Ropivacaine	Paracetamol	Morphine	
	Dosage	Catheter attached to pump allowing continuous ropivacaine 0.2% at 10 mL/hr x 48 hr	1st dose 2g then 2g	2 mg q5min in post-op until VAS <30 then 0.1 mg/kg q4 hr; if VAS >30 dosage increased by 50%	
	Dosage Intervals	Continuous	Every 6 hours		
	Age (yr) Mean ± SD	 83 ± 5.00	 83 ± 7.00	 81.00 ± 8.00	
	Body weight (Kg) Mean ± SD	 60.00 ± 11.00	 57.00 ± 10.00	 59.00 ± 13.00	
	Height (cm) Mean ± SD	 159.00 ± 10.00	 158.00 ± 10.00	 159.00 ± 10.00	
	Gender Females: n (%) Males: n (%)	 18/ 21 (85.71%) 3/ 21 (14.29%)	 19/ 21 (90.48%) 2/ 21 (9.52%)	 16/ 20 (80.00%) 4/ 20 (20.00%)	
de Visme 2000[92]	Classification	Combined lumbar/sacral plexus block (NS)	Spinal anesthesia (single)	NA	NA
	Type of intervention	Lidocaine 1.33%	Bupivacaine 0.5%		
	Dosage	45mL	3mL		
	Dosage Intervals	Single administration	Single administration		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Gamma nail osteosynthesis 9/15; Moore prosthesis 2/15; intermediary prosthesis 0/15; pinnings 4/15	Gamma nail osteosynthesis 11/14; Moore prosthesis 1/14; intermediary prosthesis 2/14; pinnings 0/14		
	Type of anesthesia Epidural Spinal General	 0/15 (0%) 0/15 (0%) 0/15 (0%)	 0/14 (0%) 14/14 (100%) 0/14 (0%)		
	Duration of surgery (hr) Mean ± SD (Range)	0.73 ± NR (0.32 –1.30)	1.02 ± NR (0.53 –2.67)		
Del Rosario 2008[117]	Classification	Femoral nerve block (NS)/IV analgesia	IV analgesia	NA	NA
	Type of intervention	Bolus: Bupivacaine 0.25%; Maintainence: bupivaine 0.1%; PCA: Paracetamol IV/metamizol IV	Paracetamol IV; metamizol IV		
	Dosage	30ml/5ml/1g/2g	1g; 2g		
	Dosage Intervals	Single administration; Maintainence: every hour; Patient controlled bolus: every 6hrs/every 8hrs	Every 6hrs; every 8hrs		
	Timing of intervention	Postoperative	Postoperative		
	Type of anesthesia Epidural Spinal General	 0/49 (0%) 49/49 (100%) 0/49 (0%)	 0/50 (0%) 50/50 (100%) 0/50 (0%)		
Eyrolle 1998[93]	Classification	Posterior lumbar plexus block	Spinal anesthesia (single)	NA	NA
	Type of intervention	Lidocaine 2%/Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	NR	NR		
	Dosage Intervals	NR	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of anesthesia Epidural Spinal General	 0/25 (0%) 0/25 (0%) 0/25 (0%)	 0/25 (0%) 25/25 (100%) 0/25 (0%)		
Fletcher 2003[94]	Classification	3-in-1 nerve block (NS)	IV analgesia	NA	NA
	Type of intervention	Bupivacaine 0.5%	Morphine IV		
	Dosage	20mL	5-10mg		
	Dosage Intervals	Single administration	On demand		
	Timing of intervention	Preoperative	Preoperative		
	Time from fall to ED arrival (hr) Mean ± SD	29.30 ± 20.80	27.40 ± 16.50		
	Baseline pain score Mean ± SD (n)	Scale name [NRS (0-3)]			
		2.80 ± 0.40 (24)	2.70 ± 0.60 (26)		
Foss 2005[95]	Classification	Epidural analgesia (continuous)	Placebo	NA	NA
	Type of intervention	Bupivacaine 0.125%/morphine	Saline		
	Dosage	4ml of 50ug per ml per hr	NA		
	Dosage Intervals	Continuous infusion (four days)	Continuous inusion (four days)		
	Timing of intervention	Postoperative	Postoperative		
	Type of surgery	Arthroplasty 10/28; intramedullar nailing 0/28; partial screws 6/28; sliding screws 12/28	Arthroplasty 8/2; intramedullar nailing 4/27; partial screws 4/27; sliding screws 11/27		
	Type of anesthesia Epidural Spinal General	 28/28 (100%) 0/28 (0%) 0/28 (0%)	 27/27 (100%) 0/27 (0%) 0/27 (0%)		
Foss 2007[96]	Classification	Fascia iliaca compartment nerve block (CT)	Analgesia	NA	NA
	Type of intervention	1.0% mepivacaine	Morphine		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage	40 mL 1.0% mepivacaine with 1:200 000 epinephrine; 0.02 mL/kg placebo IM injection of 0.9% saline	40 mL placebo FICB with 0.9% saline; 0.02 mL/kg 5.0 mg/mL morphine		
	Dosage Intervals	Single dose	Single dose		
	Age (yr) Mean Range	 83 (75 – 88)	 77 (69 – 88)		
	Body weight (Kg) Mean Range	 60.00 (50 – 80)	 60.00 (50 – 65)		
	BMI (Kg/ m^2) Mean Range	 22.80 (20 – 28)	 21.30 (19 – 21)		
	Gender Females: n (%) Males: n (%)	 14/ 24 (58.33%) 10/ 24 (41.67%)	 21/ 24 (87.50%) 3/ 24 (12.50%)		
	ASA Class ASA I (%) ASA II (%) ASA III (%) ASA IV (%)	 0/24 (0.00%) 13/24 (54.17%) 11/24 (45.83%) 0/24 (0.00%)	 3/ 24 (12.50%) 15/ 24 (62.50%) 6/ 24(25.00%) 0/24 (0.00%)		
Gille 2006[97]	Classification	Femoral nerve block	Analgesia	NA	NA
	Type of intervention	Prilocaine 1%/ Ropivacaine 0.2%	Metamizol/Tilidine; Ibuprofen		
	Dosage	40ml/ 30ml	1g / 100mg; 400mg		
	Dosage Intervals	Single administration/ Continuous (every 6hrs)	Single administration/single administration; every 8hrs		
	Age (yr) Mean ± SD Range	 82 ± 8.85 (61 – 103)	 78 ± 13.16 (35 – 93)		
	Body weight (Kg) Mean ± SD	 64.00 ± 13.41	 67.00 ± 14.54		
	Height (cm) Mean	 163.00	 165.00		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	BMI (Kg/ m^2) Mean	24.10	24.60		
	Gender Females: n (%) Males: n (%)	39/ 50 (78.00%) 11/ 50 (22.00%)	38/ 50 (76.00%) 12/ 50 (24.00%)		
	Type of fractures Femoral neck: n (%) Intertrochanteric: n (%) Proximal femur: n (%)	0/ 50 (0.00%) 0/ 50 (0.00%) 50/ 50 (100.00%)	0/ 50 (0.00%) 0 /50 (0.00%) 50/ 50 (100.00%)		
Graham 2008[98]	Classification	3-in-1 nerve block (NS)	IV analgesia	NA	NA
	Type of intervention	Bupivacaine 0.5%	Morphine IV		
	Dosage	30ml	0.1mg per kg		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Preoperative	Preoperative		
Haddad 1995[99]	Classification	Femoral nerve block CT)	Standard care	NA	NA
	Type of intervention	Bupivacaine 0.25%	NR		
	Dosage	0.3ml per kg	NR		
	Dosage Intervals	Single administration	NR		
	Timing of intervention	Preoperative	Preoperative		
	Type of surgery	Internal fixation with DHS in all pts	Internal fixation with DHS in all pts		
	Baseline pain score	Scale name [VAS]			
	Mean (n) (Range)	7.40 (25) (2.00 – 10.00)	7.10 (25) (3.00 – 10.00)		
Henderson 2008[100]	Classification	Femoral nerve block/ Opioids	Standard care	NA	NA
	Type of intervention	Bupivacaine 0.5%	Opioids		
	Dosage	NR/NR	NR		
	Dosage Intervals	Continuous/On demand	Intermittent		
	Timing of intervention	Preoperative	Preoperative		
Hood 1991[101]	Classification	3-in-1 nerve block	Standard care	NA	NA
	Type of intervention	Prilocaine 0.75%	NR		
	Dosage	43ml	NR		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage Intervals	Single administration	NR		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Compression screw or pin and plate device	Compression screw or pin and plate device		
	Type of anesthesia General	25/25 (100%)	25/25 (100%)		
Kocum 2007[118]	Classification	Lumbar plexus plus sciatic block (NS)	Lumbar plexus plus sciatic block (NS)	NA	NA
	Type of intervention	Ropivacaine 0.25%	Bupivacaine 0.25%		
	Dosage	60ml	60ml		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Duration of surgery (hr) Mean ± SD	1.05 ± 0.39	1.03 ± 0.29		
Mannion 2005[102]	Classification	Psoas compartment block (NS)	Psoas compartment block (NS)	Psoas compartment block (NS)	NA
	Type of intervention	Levobupivacaine 0.5%/Clonidine IV	Levobupivacaine 0.5%/Clonidine (peripheral)	Levobupivacaine 0.5%	
	Dosage	0.4mL per kg/1ug per kg	0.4mL per kg/1ug/kg	0.4mL/ kg	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of surgery	Hemiarthroplasty in 6/12 pts; DHS in 6/12 pts	Hemiarthroplasty in 7/12 pts; DHS in 5/12 pts	Hemiarthroplasty in 5/12 pts; DHS in 7/12 pts	
	Type of anesthesia General	12/12 (100%)	12/12 (100%)	12/12 (100%)	
Marhofer 1997[103]	Classification	3-in-1 nerve block (US)	3-in-1 nerve block (NS)	NA	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	20ml	20ml		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Preoperative	Preoperative		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of anesthesia Epidural Spinal General	 0/20 (0%) 20/20 (100%) 0/20 (0%)	 0/20 (0%) 20/20 (100%) 0/20 (0%)		
Marhofer 1998[104]	Classification	3-in-1 nerve block (US)	3-in-1 nerve block (NS)	3-in-1 nerve block (NS)	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%	Bupivacaine 0.5%	
	Dosage	20ml	20ml	30ml	
	Dosage Intervals	Single administration	Single administration	Single administration	
	Timing of intervention	Pre-operative	Pre-operative	Pre-operative	
Marhofer 2000[105]	Classification	3-in-1 nerve block (NS)	3-in-1 nerve block (NS)	NA	NA
	Type of intervention	Ropivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	20ml	20ml		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Preoperative	Preoperative		
Matot 2003[106]	Classification	Epidural analgesia (continuous)	IM analgesia	NA	NA
	Type of intervention	Bolus: Bupivacaine 0.25%/ Methadone; Maintainence: Bupivacaine 0.5%/ Methadone	Meperidine IM		
	Dosage	7-10mL/4mg; 45mg/16mg	1mg/ kg		
	Dosage Intervals	Continous (24hrs)	Every 6hrs		
	Timing of intervention	Preoperative	Preoperative		
	Time from fall to ED arrival (hr) Mean ± SD	 4.38 ± 2.50	 4.18 ± 2.21		
	Time from ED arrival to surgery (hr) Mean ± SD	25.90 ± 16.70	28.60 ± 18.20		
	Type of surgery	DHS and plate fixation 20/34; hemiarthroplasty 12/34; cannulated hip screw 2/34	DHS and plate fixation 17/34; hemiarthroplasty 11/34; cannulated hip screw 2/34		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Type of anesthesia Epidural Spinal General	 30/34 (88.24%) 0/34 (0%) 4/34 (11.76%)	 0/34 (0%) 27/34 (79.41%) 3/34 (8.82%)		
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		5.16 ± 1.74 (34)	4.91 ± 2.03 (34)		
Monzon 2010[107]	Classification	Fascia iliaca compartment block	General anaethesia	NA	NA
	Type of intervention	0.25% bupivacaine	IV NSAID analgesics		
	Dosage	0.3 ml/kg	NR		
	Dosage Intervals	NR	NR		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	NR	NR		
	Type of anesthesia Epidural Spinal General	 0/92 (0%) 92/92 (100%) 0/92 (0%)	 0/62 (0%) 0/62 (0%) 62/62 (100%)		
	Baseline pain score Scale name [VAS] Mean ± SD (n)	 8.50 ± 0.72 (n = 92)	 7.60 ± 0.22 (n = 62)		
	Gender Females: n (%) Males: n (%)	 59/92 (64.13%) 33/92 (35.87%)	 37/62 (59.68%) 25/62 (40.32%)		
Mouzopoulos 2009[108]	Classification	Fascia iliaca compartment nerve block (CT)	Placebo	NA	NA
	Type of intervention	Bupivacaine	Saline		
	Dosage	0.25mg dose of 0.3mL/ kg	NA		
	Dosage Intervals	every 24h pre-/post surgery	Every 24h pre-/post surgery		
	Timing of intervention	Preoperative	Preoperative		
	Baseline pain score Mean ± SD (n)	Scale name [Visual analogue scale]			
		6.14 ± NR (102)	6.82 ± NR (105)		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Murgue 2006[109]	Classification	Femoral nerve block	Analgesia	Analgesia	NA
	Type of intervention	Mepivacaine	IV morphine	IV paracetamol + ketoprofen	
	Dosage	20 cc	2 mg	1 g P + 100 mg K	
	Dosage Intervals		1 mg q5 min until p<=4		
	Age (yr) Mean ± SD Range	 85.90 ± 6.60 (70 – 96)	 85.90 ± 6.60 (70 – 96)	 85.90 ± 6.60 (70 – 96)	
Pedersen 2008[119]	Classification	3-in-1 nerve block	Analgesia	NA	NA
	Type of intervention	Bupivacaine	Preoperative: Morphine SC or tablets; Postoperative: Morphine SR tablets/ acetaminophen/ ibuprofen		
	Dosage	Bolus: 100mg; Maintainence: 50mg	2.5-5mg/10-20mg; 1g/or 400mg		
	Dosage Intervals	Single administration; continuous (every 8hrs)	Every 12hrs; every 8hr/or every 12hrs		
	Timing of intervention	Preoperative	Preoperative		
	Time from ED arrival to surgery (hr) Mean ± SD	26.40 ± 19.30	27.60 ± 29.10		
	Type of surgery	Screws 39/178; DHS 50/178; intramedullary hip screw 43/178; Hemialloplasty 44/178; total hip arthroplasty 2/178	Screws 66/357; DHS 109/357; intramedullary hip screw 81/357; hemialloplasty 101/357; total hip arthroplasty 0/357		
	Type of anesthesia Epidural Spinal General	 0/178 (0%) 42/178 (23.60%) 136/178 (76.40%)	 0/357 (0%) 48/357 (13.45%) 309/357 (86.55%)		
Scheinin 2000[110]	Classification	Epidural analgesia (continuous)	IM analgesia	NA	NA
	Type of intervention	Bupivacaine/Fentanyl	Oxycodone IM		
	Dosage	1mg per ml + 10ug/ ml	0.1-0.15mg/ kg		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage Intervals	Continuous administration	On demand (max every 6hrs)		
	Timing of intervention	Preoperative	Preoperative		
	Type of surgery	Screw, lamina or prothesis in all pts	Screw, lamina or prothesis in all pts		
	Type of anesthesia Epidural Spinal General	 0/38 (0%) 38/38 (100%) 0/38 (0%)	 0/39 (0%) 39/39 (100%) 0/39 (0%)		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	3.40 ± 2.40 (38)	4.20 ± 2.90 (39)		
Segado Jiménez 2009[111]	Classification	Obturator/ Femoral cutaneous nerve block	Obturator nerve block	IV analgesia	
	Type of intervention	NR	NR	Opioid analgesia	
	Dosage	NR	NR	NR	
	Dosage Intervals	NR	NR	NR	
	Timing of intervention	Postoperative	Postoperative	Postoperative	
Segado Jiménez 2010[112]	Classification	Fascia iliaca compartment block	Obturator /femoralcutaneous nerves block	General anaesthesia	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%	NR	
	Dosage	30 ml	15ml / 5 ml	NR	
	Dosage Intervals	NR	NR	NR	
	Timing of intervention	Intra-operative	Intra-operative	Intra-operative	
	Type of surgery	total/partial arthroplasty, osteosynthesis, Richards osteosynthesis	total/partial arthroplasty, osteosynthesis, Richards osteosynthesis	total/partial arthroplasty, osteosynthesis, Richards osteosynthesis	
	Type of anesthesia Epidural Spinal General	 0/30 (0%) 30/30 (100%) 0/30 (0%)	 0/30 (0%) 30/30 (100%) 0/30 (0%)	 0/30 (0%) 0/30 (0%) 30/30 (100%)	

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Baseline pain score Scale name [VAS] Mean ± SD	0.84 (n = 30)	0.84 (n = 30)	7.47 (n = 30)	
	Age (yr) Mean ± SD	71.30 ± 12.60	74.60 ± 10.10	71.10 ± 10.20	
	Body weight (Kg) Mean ± SD	69.70 ± 8.60	68.60± 10.20	68.20 ± 9.60	
	Height (cm) Mean ± SD	157.00 ± 6.00	158.00± 7.00	157.00 ± 6.00	
	BMI (Kg/ m2) Mean ± SD	28.20 ± 4.20	27.30 ± 4.20	27.6 ± 3.80	
Spansberg 1996[113]	Classification	Lumbar plexus block (NS)	Placebo	NA	NA
	Type of intervention	Bolus: Bupivacaine 0.5%; Maintenence: Bupivacaine 0.25%	Bolus: Saline; Maintainence: Saline		
	Dosage	0.4mL per kg; 0.14mL/kg/hr	0.4mL per Kg; 0.14mL/kg/hr		
	Dosage Intervals	Single administration; Continuous administration	Continuous administration		
	Timing of intervention	Postoperative	Postoperative		
	Type of anesthesia Spinal	10/10 (100%)	10/10 (100%)		
	Duration of surgery (hr) Mean ± SD (Range)	0.96 ± NR (0.50 –1.83)	1.18 ± NR (0.75 –2.08)		
Tuncer 2003[114]	Classification	3-in-1 nerve block (NS)	IV analgesia	NA	NA
	Type of intervention	Bolus: Lidocaine 2%/Maintainence: Bupivacaine 0.125%; PCA bolus: Bupivaciane 0.125%	Morphine IV		
	Dosage	30ml; 4ml/hr; 3ml	1mg		

Table F-5. Nerve blocks (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Dosage Intervals	Single administration; Continuous administration; Patient cotrolled bolus on demand	On demand		
	Timing of intervention	Postoperative	Postoperative		
Turker 2003[115]	Classification	Psoas compartment block (NS)	Epidural anesthesia (single)	NA	NA
	Type of intervention	Bupivacaine 0.5%	Bupivacaine 0.5%		
	Dosage	30ml	15ml		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Intra-operative	Intra-operative		
	Type of surgery	Partial hip replacement	Partial hip replacement		
	Type of anesthesia Epidural Spinal General	 0/15 (0%) 0/15 (0%) 15/15 (100%)	 15/15 (100%) 0/15 (0%) 15/15 (100%)		
	Duration of surgery (hr) Mean ± SD	 2.19 ± 0.31	 2.15 ± 0.44		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	1.56 ± 0.97 (15)	1.23 ± 1.05 (15)		
Yun 2009[116]	Classification	Fascia iliaca compartment nerve block (CT)	Analgesia		
	Type of intervention	Ropivacaine	Alfentanil		
	Dosage	30 mL 3.75 mg/mL 2-3 min	10 ug/kg bolus; 0.25 ug/kg/min 2 min		
	Dosage Intervals	Single dose	Single dose		
	Age (yr) Mean ± SD Range	 75 (69 – 85)	 75.10 (62 – 88)		
	Body weight (Kg) Mean ± SD	 60.60 ± 7.20	 60.30 ± 11.30		
	Height (cm) Mean	 156.20	 160.80		

Table F-5. Nerve blocks (continued)

	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Gender				
Females: n (%)	13/ 20 (65.00%)	13/ 20 (65.00%)		
Males: n (%)	5/ 20 (25.00%)	7/ 20 (35.00%)		

CT = clinical touch; FICB = fascia iliaca compartment block; IM = intramuscular; IV = intravenous; NA = not applicable; NR = not reported; NRS = numeric rating scale; NS = nerve stimulation; NSAID = non-steroidal anti-inflamatory drugs; US = ultrasound; VAS = visual analogue scale

Table F-6. Neurostimulation

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Gorodetskyi 2007[120]	Classification	Neurostimualtion	Sham Control	NA	NA
	Type of intervention	InterX 5000 device	NA		
	Dosage	High peak amplitude 17 volts , low current 6 mA, damped biphasic electrical impulses	NA		
	Dosage Intervals	Every 24hrs	Every 24hrs		
	Timing of intervention	Postoperative	Postoperative		
	Type of surgery	DHS/dynamic condylar screw for noncomplex fractures 25/30; Gorodnichenko external fixation method for complex fractures 5/30	DHS/dynamic condylar screw for noncomplex fractures 27/30; Gorodnichenko external fixation method for complex fractures 3/30		
	Type of anesthesia General	30/30 (100%)	30/30 (100%)		
	Baseline pain score Mean ± SD (n) Range	Scale name [VAS]			
		9.00 ± NR (30) (7.50 – 10.00)	8.80 ± NR (30) (7.50 – 10.00)		
Lang 2007[121]	Classification	Neurostimulation	Sham Control	NA	NA
	Type of intervention	Transcutaneous electrical nerve stimulation	NA		
	Dosage	70 mA, range: 0.5-120 Hz, pulse width: 60 to 300 us	NA		
	Dosage Intervals	Single administration	Single administration		
	Timing of intervention	Preoperative	Preoperative		
	Time from fall to ED arrival (hr) Mean ± SD	29.80 ± 8.50	28.20 ± 12.30		
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		8.90 ± 0.90 (30)	8.60 ± 1.20 (33)		

NA = not applicable; VAS = visual analogue scale

Table F-7. Rehabilitation

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Di Lorenzo 2007[122]	Classification	Rehabilitation	Standard care	NA	NA
	Type of intervention	Stretching-strengthening of spinal and psoas muscles	NR		
	Dosage	1 hr of training	NR		
	Dosage Intervals	Every 12 hrs for four wk	NR		
	Timing of intervention	Postoperative	Postoperative		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n) Range	7.94 ± 0.80 (18) (7.00 – 9.00)	7.94 ± 0.82 (19) (7.00 – 9.00)		

NA = not applicable; NR = not reported; VAS = visual analogue scale

Table F-8. Traction

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Anderson 1993[128]	Classification	Skin traction	Standard care	NA	NA
	Type of intervention	Hamilton-Russell skin traction	NR		
	Dosage	5lb (2.3kg)	NR		
	Dosage Intervals	NA	NR		
	Timing of intervention	Preoperative	Preoperative		
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		5.11 ± NR (101)	5.42 ± NR (151)		
Finsen 1992[123]	Classification	Skin traction	Skeletal traction	Pillow	NA
	Type of intervention	Elastic bandages	Steinman pin	Standard pillow	
	Dosage	3Kg	10% of patient's wt	NA	
	Dosage Intervals	NA	NA	NA	
	Timing of intervention	Preoperative	Preoperative	Preoperative	
	Time from ED arrival to surgery (hr) Mean ± SD (Range)	24.00 ± NR (10.00 – 52.00)	23.00 ± NR (8.00 – 68.00)	26.00 ± NR (10.00 – 90.00)	
	Type of surgery	Hip compression screws or uncemented endoprosthesis	Hip compression screws or uncemented endoprosthesis	Hip compression screws, uncemented endoprosthesis 24/25; cemented endoprosthesis 1/25	
Ghnaimat 2005[129]	Classification	Skin traction	Standard care	NA	NA
	Type of intervention	Skin traction	NR		
	Dosage	6lb	NR		
	Dosage Intervals	NA	NR		
	Timing of intervention	Preoperative	Preoperative		

Table F-8. Traction (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Jerre 2000[124]	Classification	Skin traction	Standard care	Skin traction	Standard care
	Type of intervention	Foam rubber boot with straps around lower leg	NR	Foam rubber boot with straps around lower leg	NR
	Dosage	3Kg	NR	3Kg	NR
	Dosage Intervals	NA	NR	NA	NR
	Timing of intervention	Preoperative	Preoperative	Preoperative	Preoperative
	Time from ED arrival to surgery (hr) Mean ± SD	21.50 ± 37.70	18.50 ± 9.40	16.30 ± 8.20	15.20 ± 9.30
	Time from fall to surgery (hr) Mean ± SD	34.50 ± 44.30	27.20 ± 10.00	25.00 ± 9.30	28.60 ± 18.80
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		4.10 ± 2.70 (30)	4.50 ± 2.60 (30)	4.30 ± 2.40 (30)	3.90 ± 2.70 (30)
Needoff 1993[125]	Classification	Skin traction	Pillow	NA	NA
	Type of intervention	Ventilated foam strap secured by means of a crepe bandage	Standard pillow		
	Dosage	2.5kg	NA		
	Dosage Intervals	NA	NA		
	Timing of intervention	Preoperative	Pre-operative		
	Duration of surgery (hr) Mean ± SD	0.69 ± NR	0.77 ± NR		
	Baseline pain score Mean ± SD (n)	Scale name [VAS]			
		6.82 ± NR (30)	6.32 ± NR (34)	NA	NA
Resch 1998[126]	Classification	Skin traction	Skeletal traction	NA	NA
	Type of intervention	Foam boot	K-wire		
	Dosage	3kg	3-5kg (5-10% body weight)		
	Dosage Intervals	NA	NA		
	Timing of intervention	Preoperative	Preoperative		
	Time from ED arrival to surgery (hr) Mean ± SD (Range)	24.00 ± 13.00 (20.00 – 28.00)	21.00 ± 9.00 (18.00 – 24.00)		

Table F-8. Traction (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Duration of surgery (hr) Mean ± SD (Range)	0.80 ± 0.40 (0.68 – 0.92)	0.97 ± 0.60 (0.78 – 1.15)		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n) Range	4.80 ± 2.50 (40) (4.00 – 5.60)	3.80 ± 2.00 (38) (3.20 – 4.40)		
Resch 2005[26]	Classification	Skin traction	Pillow	Pillow	NA
	Type of intervention	Foam rubber boot	Lasse Pillow	Standard pillow	
	Dosage	3kg	NA	NA	
	Timing of intervention	Preoperative	Preoperative	Preoperative	
	Time from ED arrival to surgery (hr) Mean ± SD	22.00 ± 6.70	24.00 ± 6.50	23.00 ± 6.60	
	Duration of surgery (hr) Mean ± SD	0.88 ± 0.52	1.08 ± 0.95	0.98 ± 0.55	
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	4.30 ± 2.20 (49)	3.30 ± 2.50 (21)	3.90 ± 1.90 (53)	
Rosen 2001[127]	Classification	Skin traction	Pillow	NA	NA
	Type of intervention	Foam traction boot	Standard pillow		
	Dosage	5lb	NA		
	Timing of intervention	Preoperative	Preoperative		
	Time from ED arrival to surgery (hr) Mean ± SD	28.80 ± 15.36	31.44 ± 25.44		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	5.86 ± 2.73 (50)	6.12 ± 2.08 (50)		
Saygi 2010[130]	Classification	Skin traction	Sham traction	Pillow	NA
	Type of intervention	Foam traction boot	Standard pillow	Standard pillow	
	Dosage	2kg	0kg	NA	
	Timing of intervention	Preoperative	Preoperative	Preoperative	
	Time from fall to surgery (hr) Mean	52.8	52.6	54.2	
	Baseline pain score	Scale name [Visual analogue scale]			
	Mean ± SD (n)	6.93 ± 1.14 (36)	7.04 ± 1.08 (36)	6.85 ± 1.29 (36)	

Table F-8. Traction (continued)

		Intervention 1	Intervention 2	Intervention 3	Intervention 4
Vermeiren 1995[132]	Classification	Skeletal traction	Skeletal traction	NA	NA
	Type of intervention	Skeletal traction with pillows for foot elevation	Skeletal traction with metal splint		
	Dosage	1 kg traction weight/10 kg body weight	1 kg traction weight/10 kg body weight		
	Dosage Intervals	NA	NA		
	Timing of intervention	Preoperative	Preoperative		
	Type of surgery	Nail-plates or screw plates 62/64; sliding hip nials 4/64	Nail-plates or screw-plates 46/68; sliding hip nails 16/68; Ender nails 5/68; cancellous screw fixation 1/68		
Yip 2002[131]	Classification	Skin traction	Pillow	NA	NA
	Type of intervention	Foam boot	Standard pillow		
	Dosage	2kg	NA		
	Dosage Intervals	NA	NA		
	Timing of intervention	Preoperative	Preoperative		
	Time from fall to ED arrival (hr) Mean ± SD (Range)	 17.52 ± 14.16 (0.00 – 96.00)	 17.52 ± 14.88 (0.00 – 72.00)		
	Time from ED arrival to surgery (hr) Mean ± SD	 113.52 ± 51.84	 112.56 ± 71.76		
	Type of surgery	Hemiarthroplasty 52/166; DHS 99/166; percutaneous hip screws 10/166; other types of surgeries 4/166	Hemiarthroplasty in 45/145; DHS 78/145; percutaneous hip screws 16/145; other types of surgeries 5/145		
	Baseline pain score	Scale name [VAS]			
	Mean ± SD (n)	0.24 ± NR (166)	0.30 ± NR (145)		

NA = not applicable; NR = not reported; VAS = visual analogue scale

Appendix G. Risk of Bias Assessment for Randomized Controlled Trials and Nonrandomized Controlled Trials

Guidelines and Decision Rules for Risk of Bias Assessments

Sequence Generation:

- If computer-generated, random number list, flipping coins, randomly picking envelopes, etc. is specified → YES
- If the description only includes 'random,' 'randomly generated,' 'randomized,' etc., do not assume additional details → UNCLEAR
- If the description is quasi-randomized (e.g. alternate randomization, day of the year, day of the month, birth date, birth month, beginning letter of last name, availability of investigator or specialist, etc.) → NO

Allocation Concealment:

- If the assignment is conducted by central telephone, pharmacy, etc. → YES
- If dark (or opaque), sealed, sequentially numbered envelopes are used → YES
- If the envelopes are not stated to dark and sealed, or sequentially numbered → UNCLEAR

Note: sequential numbering of the envelopes is only required for adequate allocation concealment if the method of randomization was anything other than randomly picking envelopes (i.e., the envelopes were only used for allocation concealment and not as part of the randomization process).

Blinding:

- If the study was stated to be blinded (masked) and the blinding is considered to be possible, and not likely to be broken → YES
- If the study is only stated to be blinded, double-blinded, double-dummy, etc. without any further details → UNCLEAR
- If the study states the use of a placebo (dummy) but with no further details → UNCLEAR
- If no mention of blinding → NO

Incomplete Outcome Data:

- Look for intention-to-treat analysis (all randomized pts. are analyzed) → YES
- If all participants were accounted for (i.e. no drop-outs or censored analysis conducted) → YES
- If the numbers and reasons for withdrawal/dropouts were described and comparable across groups (and ≤ approximately 10 percent) → YES
- If there is between 10 percent and 30 percent dropout and no ITT analysis → UNCLEAR

- If there is greater 30 percent dropout and no ITT analysis → NO

Selective Outcome Reporting:

- If the study protocol is available (referenced in the manuscript), compare the outcomes reported in the publication to those specified in the protocol. If they match → YES
- If the study protocol is available (referenced in the manuscript), compare the outcomes reported in the publication to those specified in the protocol. If they do not match, but there is reference to another publication with this information presented → YES
- If the study protocol is not available, compare the outcomes reported in the Methods and Results sections. If they match → YES

Other Sources of Bias:

- Assess for baseline imbalances that could have biased the results (or were not accounted for).
- Assess for early stopping for benefit.
- Assess for appropriateness of cross-over design (e.g., inadequate washout period).
- Assess for inappropriate influence of funders that could have biased the results:
  - If sponsor is acknowledged and there is a clear statement regarding no involvement of sponsor in trial conduct or data management/analysis, or coauthorship → YES
  - If sponsor is acknowledged with no further information provided or (co)author works for a pharmaceutical company → NO
  - If there is no mention of funding source → UNCLEAR
- Note any “other” sources of bias.

Risk of Bias (RoB) Assessments

Table G-1. Pharmacologic Analgesia

Study	Item	Judgment	Description
Apostolopoulos 2006[41]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of selective reporting?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of other bias?	UNCLEAR	No information on baseline characteristics or any information on financial support.
Baker 2004[42]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported as a double-blind trial and that the study solutions were freshly prepared by an anesthesiologist who had no further part in the study. Also reported that the anesthesiologist who injected the study solution and the investigator were blinded to the baricity of the clonidine solution administered
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional
Poitevin 1999[55]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	NR
	Blinding?	YES	Reported as a double-blind study using identical matching placebos
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics are balanced but there is no source of funding declared

Table G-2. Anesthesia

Study	Item	Judgment	Description
Adams 1990[56]	Adequate sequence generation?	NO	Quasi-randomization based on the date of admission
	Allocation concealment?	NO	Based on even or odd calendar dates of admission
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics are balanced but there is no source of funding declared
Alonso Chico 2003[57]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	NR
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics are balanced but there is no source of funding declared
Ben-David 2000[58]	Adequate sequence generation?	UNCLEAR	Reported the use of a sealed-envelope technique with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed-envelope technique with no further details
	Blinding?	YES	Reported that all pts received the same injectate volume. Additionally the syringes were prepared by one researcher and administered by a second who remained blinded to its contents. Patient assessment and care were conducted and study data were recorded by the second blinded researcher. Finally, the protocol allowed for conversion to general anesthesia as deemed necessary by the blinded anesthesiologist. No mention of patient blinding was reported.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
Bredahl1991[59]	Adequate sequence generation?	Unclear	Reported as a randomized trial without any further details
	Allocation concealment?	Unclear	No description of allocation concealment reported
	Blinding?	Unclear	NR
	Incomplete outcome data addressed?	Unclear	No ITT. 13.3% exclusion in general a. group due to the incomplete data and sampling.
	Free of selective reporting?	Yes	Protocol not available, but the outcomes in the methods match those in the results.
	Free of other bias?	Unclear	Baseline characteristics are balanced but there is no source of funding declared.
Casati 2003[60]	Adequate sequence generation?	UNCLEAR	Reported the use of a sealed-envelope technique with no further details
	Allocation concealment?	UNCLEAR	Reported that Allocation concealment was via a sealed-envelope technique with no further details
	Blinding?	NO	Reported that the orthopedic and rehabilitation staff who assessed the clinical criteria prior to discharge from hospital were blinded to the anesthesia technique used during surgery. There is no mention of clinicians or patients being blinded. Additionally since pts in the spinal group were awake, while the pts in the general anesthesia group were unconscious, pt blinding was not possible. Finally, no mention of any procedure to blind the clinicians performing the surgery or anesthesia.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Danelli 2008[61]	Adequate sequence generation?	YES	Reported that randomization was performed using a computer-generated sequence of random numbers
	Allocation concealment?	YES	Reported that allocation concealment was ensured using sequentially numbered, sealed opaque envelopes
	Blinding?	YES	Reported as a double-blind study with an independent observer, who was blinded to group allocation, recording the observations.
	Incomplete outcome data addressed?	YES	Principle of Intention-to-treat not used in the analyses with 9% of randomized pts were excluded with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Favarel-Garrigues 1996[62]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All patient completed the study and followed up for one month post-operatively (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Hooda 2006[63]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported as a double-blind trial and that In order to facilitate blinding; spinal anesthesia was administered by a fellow colleague and observer did not know the amount of drug received by the patient
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Juelsgaard 1998[64]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported that the investigator was blinded to the randomization
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 11/54 (%) of randomized pts excluded from the analyses with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Klimscha 1995[65]	Adequate sequence generation?	YES	Reported that randomization was performed by having an assistant blindly pick from an envelope a piece of paper with the name of the study solution and route of administration written on it

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Allocation concealment?	UNCLEAR	Reported as using envelopes with no further details
	Blinding?	YES	Reported that an assisting anesthesiologist inserted the catheters, prepared the fresh study solution, injected it, and covered the injection port with a cotton towel to blind the other anesthesiologist to the group assignment.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared. There was mention of 'valuable support' from an employee of a pharmaceutical company with no further explanation
Krobot 2006[77]	Adequate sequence generation?	NO	NR to be a randomized trial
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics not provided nor any disclosure on sources of funding
Kwan 1997[66]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	YES	Injections were prepared by another investigator who was not performing the block.
	Blinding?	YES	Reported as double-blind design. Two different investigators prepared the solutions and administered them. An assessment of pain level conducted by investigator who was unaware of the constituents of the allocation
	Incomplete outcome data addressed?	YES	Intention-to-treat analysis was not used with 10% of participants dropped-out of the trial with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Malek 2004[67]	Adequate sequence generation?	UNCLEAR	Reported the use of a sealed-envelope technique with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed-envelope technique with no further details

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Blinding?	UNCLEAR	Reported that only the anesthesiologist and anesthetic nurse were aware of the allocation, but there is no reporting on how was in charge of monitoring the patients and recording the outcomes
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional
Martyr 2001[68]	Adequate sequence generation?	UNCLEAR	Reported that for each patient a numbered syringe was chosen at random from the supply kept in the Pharmacy Department with no further details
	Allocation concealment?	YES	Reported that the coded syringes were chosen at random
	Blinding?	YES	Reported that the syringes were prepared by Baxter Healthcare and the study solution syringes were the same volume as the standard solution syringes and were all numbered and coded such that the administering anesthetist was blinded to their contents.
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 6/48 (12.50%) of randomized pts excluded from the analyses with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Martyr 2005[69]	Adequate sequence generation?	YES	Reported that randomization was performed using a computer-generated randomization
	Allocation concealment?	YES	Reported that randomization was performed by a third-party and syringes were sequentially numbered and administered
	Blinding?	YES	Reported that the syringes were prepared by a third party and stored in the hospital pharmacy, and that the anesthesiologists and nurses that administered and monitored the patients were not aware of the allocation
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced, and disclosure of institutional financial support is provided, but the interventions were provided by Baxter Healthcare and it is not clear if they were provided as a type of financial support for the trial or were co
Maurette 1993[70]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported as double-blind, and that the investigator that administered the medications was different from the one that prepared them
	Incomplete outcome data addressed?	YES	Intention-to-treat principle was not used with 1/35 (2.86%) of randomized pts were excluded with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Minville 2006[71]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	Reported that a blinded observer assessed the dermatome level of sensory blockade, but no details of who assessed the outcome measures
	Incomplete outcome data addressed?	YES	Intention-to-treat principle was not used in the analyses with one pt not completing the investigation and not included in the analyses
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Navas 2008[72]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Olofsson 2004[73]	Adequate sequence generation?	UNCLEAR	Reported the use of a sealed-envelope technique with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed-envelope technique with no further details

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Blinding?	YES	Reported that the study was double-blind and that all pts received the same injectate volume which was prepared by a nurse not involved in the study
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional
Qamarul Hoda 2007[146]	Adequate sequence generation?	UNCLEAR	Reported that randomization was performed using the sealed envelope technique with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed envelopes with no further details
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Rais 2008[75]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Said-Ahmed 2006[76]	Adequate sequence generation?	UNCLEAR	Reported the use of randomization using sealed envelopes with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed envelopes with no further details
	Blinding?	YES	Reported that the syringes were prepared by a researcher and passed to a second investigator who was blinded to its content. The second investigator was reported to have administered the drug and collected the study data.

Table G-2. Anesthesia (continued)

Study	Item	Judgment	Description
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-3. Complementary and alternative medicine (CAM)

Study	Item	Judgment	Description
Barker 2006[43]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	Reported using a sealed envelope to determine the patient's group assignment without any further details
	Blinding?	YES	Reported that the trial was double-blind and that following the administration of the intervention, one paramedic covered the ears of all subjects with ear patches to assure blinding of the other paramedic, who was involved in the outcome assessment
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Martin 1991[54]	Adequate sequence generation?	YES	Reported that randomization was performed using a table of random numbers coding system
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	Reported that the researcher that was instructing the patients on the use of the intervention was also the one measuring outcomes; including subjective assessments of pain.
	Incomplete outcome data addressed?	UNCLEAR	Pts were randomized before receiving confirmation of inclusion in the study with no mention of the number excluded after randomization
	Free of selective reporting?	NO	Protocol not available, but methods section numerates differing outcomes than were presented in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-4. Nerve blocks

Study	Item	Judgment	Description
Antonopoulou 2006[88]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of selective reporting?	NO	Protocol not available, but methods section numerates differing outcomes than were presented in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Chudinov 1999[89]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Coad 1991[90]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported that the nurses who prescribed rescue analgesia were unaware of the patients' allocation
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	NO	Protocol not available, but it was noted that the authors abandoned a pilot study for measuring pain score using VAS due to unsatisfactory results.
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
Cuvillon 2007[91]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed, numbered envelopes with no further details
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics are balanced and the source of funding was declared to be institutional
de Visme 2000[92]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	YES	Randomization was performed in the hospital pharmacy (third party)
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 11/29 (37.93%) of randomized pts excluded from analysis
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional
Eyrolle 1998[93]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	NO	Protocol is not available and the intended outcomes were not clearly described in the methods section
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Fletcher 2003[94]	Adequate sequence generation?	YES	Reported that randomization was performed using a random number generator
	Allocation concealment?	YES	Reported the use of sealed opaque envelopes
	Blinding?	NO	Reported that data collectors and outcome assessors were blinded but patients were not blinded to group allocation
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Free of selective reporting?	NO	Protocol not available, but one of the outcomes in the methods is not presented in the results (i.e., time to discharge)
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Foss 2005[95]	Adequate sequence generation?	YES	Reported that randomization was performed using a computer-generated randomization list
	Allocation concealment?	YES	Reported that randomization was performed by a third party
	Blinding?	YES	Reported that it was a double-blind trials and that the epidural cassettes were packed by the local pharmacy and blinded and supplied with a randomization number by a person not affiliated with the project
	Incomplete outcome data addressed?	YES	Intention-to-treat principle was not used in the analyses with 5/60 (8.33%) pts excluded from the analyses with reasons given
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and source of funding declared as governmental
Foss 2007[96]	Adequate sequence generation?	YES	Reported that randomization was performed using computer-generated list
	Allocation concealment?	YES	Reported that the medicine used for each individual patient was prepared by a nurse not otherwise involved with the collection of patient data
	Blinding?	YES	Reported that the study was double blind with placebo injections given along with the intervention studied in each group
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	The outcomes reported in the publication match those in the protocol (NCT00162630)
	Free of other bias?	YES	Gender is imbalanced between the groups but this is unlikely to introduce bias; Funding provided by IMK Almene Fond, a private research fund
Gille 2006[97]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	NR
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	UNCLEAR	Not clear if all pts completed the trial and were included in the analyses
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Free of other bias?	YES	Baseline characteristics are balanced and the source of funding was declared to be institutional
Graham 2008[98]	Adequate sequence generation?	UNCLEAR	Reported the use of numbered, sequential, sealed opaque envelopes with no further details
	Allocation concealment?	YES	Reported that allocation concealment was ensured using numbered, sequential, sealed opaque envelopes
	Blinding?	NO	Reported as an 'open-label' trial
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 7/40 (17.50%) of randomized pts excluded from analyses with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Haddad 1995[99]	Adequate sequence generation?	UNCLEAR	Reported as randomized by using sealed envelopes with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed-envelope technique with no further details
	Blinding?	YES	Reported that the staff that monitored the patients and provided rescue analgesia were unaware of the patients' allocation
	Incomplete outcome data addressed?	YES	Intention-to-treat principle was not used with 5/50 (10%) of randomized pts were excluded with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Henderson 2008[100]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	No information on baseline characteristics or any information on financial support.
Hood 1991[101]	Adequate sequence generation?	UNCLEAR	Reported the use of unmarked envelopes with no further details
	Allocation concealment?	UNCLEAR	Reported the use of sealed-envelope technique with no further details

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Blinding?	YES	Reported that all the patients had their skin prepared and an elastoplast placed over the possible injection site to minimize bias, while staff providing rescue analgesia administration and assessing the quality of analgesia after operation were blinded to the patients' allocation
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Mannion 2005[102]	Adequate sequence generation?	YES	Reported that randomization was performed using a randomization table restricted to blocks of 12 (block randomization)
	Allocation concealment?	UNCLEAR	Reported as using sealed envelopes without any further details
	Blinding?	YES	Reported as a double-blind trial and that the drug solutions to be administered were prepared by an anesthesiologist not involved in block performance, patient care, or data collection.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Marhofer 1997[103]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Marhofer 1998[104]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Blinding?	YES	Reported that all blocks were performed by one anesthesiologist while another anesthesiologist unaware of the group assignment performed the monitoring
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Marhofer 2000[105]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	Reported as a double-blind trial without any further details
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Matot 2003[106]	Adequate sequence generation?	YES	Reported that randomization was performed using random numbers
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and the source of funding was declared to be institutional
Monzon 2010[107]	Adequate sequence generation?	Yes	Computer-generated
	Allocation concealment?	Yes	The randomization list was kept by one of the authors who did not interact with the patients. He gave instructions to the patient's ED nurse about which treatment should be administered.
	Blinding?	Unclear	NR
	Incomplete outcome data addressed?	Unclear	No ITT, and 13.6 exclusion.

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Free of selective reporting?	Yes	Protocol not available, but the outcomes in the methods match those in the results.
	Free of other bias?	Yes	Baseline characteristics are balanced; no funding
Mouzopoulos 2009[108]	Adequate sequence generation?	YES	Reported that randomization was performed using a computer-generated randomization code
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported that patients were blinded to the treatment using a placebo with identical appearance and route of administration to the study medication
	Incomplete outcome data addressed?	YES	Intention-to-treat principle was not used in the analyses with 12/219 (5.48%) of randomized pts not included in the analyses
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Murgue 2006[109]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	NR
	Blinding?	UNCLEAR	NR
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics are balanced but there is no source of funding declared
Scheinin 2000[110]	Adequate sequence generation?	YES	Reported that randomization was performed using permuted blocks with strata
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	Reported as an “open-label” trial
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 18/77 (23.38%) of randomized pts excluded from the analyses
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	NO	Baseline characteristics were unbalanced with more males allocated to the parenteral analgesia group, but the source of funding is declared to be governmental and institutional.

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
Segado Jiménez 2009[111]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	Reported as double-blind without any further details
	Incomplete outcome data addressed?	UNCLEAR	Not enough information provided in the text to make a precise decision
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were not presented and there is no source of funding declared
Segado Jimenez 2010[112]	Adequate sequence generation?	Unclear	Reported as a randomized trial without any further details
	Allocation concealment?	Unclear	NR
	Blinding?	No	Surgeons and evaluators were independants. nothing is reported about patients.
	Incomplete outcome data addressed?	Yes	All patients completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	Yes	Protocol not available, but the outcomes in the methods match those in the results.
	Free of other bias?	Unclear	Baseline characteristics are balanced. No conflict of interest for funding.
Spansberg 1996[113]	Adequate sequence generation?	YES	Reported that randomization was performed using a computer-generated randomization.
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	YES	Reported as a double-blind trial and reported the use of a placebo (saline) to blind patients, recovery staff and observers.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Tuncer 2003[114]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design

Table G-4. Nerve blocks (continued)

Study	Item	Judgment	Description
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Turker 2003[115]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	UNCLEAR	Reported that the outcomes assessment was blinded (single-blind)
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Yun 2009[116]	Adequate sequence generation?	YES	'using an allocation sequence (which was generated by Y.H. Kim using a computer)'
	Allocation concealment?	UNCLEAR	'The random allocation sequence was concealed until group was assigned' - no further details.
	Blinding?	NO	Although the anaesthesiologist who performed the spinal block and reocrded the UAS scores during patient positioning was unaware of group assignments the clinical effects of i.v. alfentanil were evident in most patients which may have introduced a bias'
	Incomplete outcome data addressed?	YES	All the patients in both groups were included in the statistical analysis'
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics are balanced but source of funding is not declared

Table G-5. Neurostimulation

Study	Item	Judgment	Description
Gorodetskyi 2007[120]	Adequate sequence generation?	UNCLEAR	Reported as randomized using a fixed randomization scheme with sealed envelopes with no further details.
	Allocation concealment?	UNCLEAR	Reported as using sealed envelopes with no further details
	Blinding?	YES	Reported that all the assessing surgeons, patients and research personnel involved in determining and recording outcome measurements were blinded. Additionally reported that the sham device had an identical appearance and application to the active device, but did not produce interactive neurostimulation
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	NO	Baseline characteristics were balanced but there is financial support from a commercial party
Lang 2007[121]	Adequate sequence generation?	YES	Reported that randomization was performed using computer-generated codes
	Allocation concealment?	YES	Reported that they used sealed, sequentially-numbered, opaque envelopes
	Blinding?	YES	Reported that the investigator that recorded the data was not aware of the allocation, neither was the patient (use of a sham procedure)
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 9/72 (12.50%) of randomized pts excluded from analyses with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-6. Rehabilitation

Study	Item	Judgment	Description
Di Lorenzo 2007[122]	Adequate sequence generation?	YES	Reported that randomization was performed using a random numerical table (simple dichotomized admission table)
	Allocation concealment?	UNCLEAR	Reported that the allocation was performed by a 'blinded' nurse but without any further details
	Blinding?	NO	Reported as an 'open' trail.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-7. Traction

Study	Item	Judgment	Description
Finsen 1992[123]	Adequate sequence generation?	YES	Reported that randomization was performed using random numbers
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	NO	Intention-to-treat principle was not used in the analyses with 38/118 (32.20%) of randomized pts excluded with reasons provided
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Jerre 2000[124]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared
Needoff 1993[125]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were balanced but there is no source of funding declared

Table G-7. Traction (continued)

Study	Item	Judgment	Description
Resch 1998[126]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and source of funding declared as governmental
Resch 2005[26]	Adequate sequence generation?	UNCLEAR	Reported as a randomized trial without any further details
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	UNCLEAR	Baseline characteristics were not described for the groups, but the source of funding was declared to be institutional. Additionally, reasons for the 1:2:1 randomization scheme was not provided
Rosen 2001[127]	Adequate sequence generation?	YES	Reported that randomization was performed using computer-generated randomization
	Allocation concealment?	UNCLEAR	No description of allocation concealment reported
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and declaration made of no external funding

Table G-7. Traction (continued)

Saygi 2010[130]	Adequate sequence generation?	NO	Reported as allocation according to the order of adminission to the hospital
	Allocation concealment?	NO	Quasi-randomization
	Blinding?	NO	NR, but also not possible with the study design
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics were balanced and declaration made of no external funding
Yip 2002[131]	Adequate sequence generation?	NO	Patients were randomised into the two study arms depending on whether their hospital admission number was an even or an odd number.
	Allocation concealment?	NO	Patients were randomised into the two study arms depending on whether their hospital admission number was an even or an odd number.
	Blinding?	NO	There was no blinding.
	Incomplete outcome data addressed?	YES	All pts completed the study and were included in the analyses (intention-to-treat)
	Free of selective reporting?	YES	Protocol not available, but the outcomes in the methods match those in the results
	Free of other bias?	YES	Baseline characteristics are balanced and declaration of a noncomercial source of funding is provided

Appendix H. Summary Risk of Bias Assessments

Table H-1. Pharmacological analgesia

Domain	High	Unclear	Low
Adequate sequence generation	0 (0%)	3 (100%)	0 (0%)
Allocation concealment	0 (0%)	3 (100%)	0 (0%)
Blinding	0 (0%)	1 (33.33%)	2 (66.67%)
Incomplete outcome data addressed	0 (0%)	1 (33.33%)	2 (66.67%)
Free of selective reporting	0 (0%)	1 (33.33%)	2 (66.67%)
Free of other bias	0 (0%)	2 (66.67%)	1 (33.33%)

Table H-2. Anesthesia

Domain	High	Unclear	Low
Adequate sequence generation	2 (9.09%)	17 (77.27%)	3 (13.64%)
Allocation concealment	1 (4.55%)	17 (77.27%)	4 (18.18%)
Blinding	1 (4.55%)	10 (45.45%)	11 (50.00%)
Incomplete outcome data addressed	2 (9.09%)	3 (13.64%)	17 (77.27%)
Free of selective reporting	0 (0%)	0 (0%)	22 (100%)
Free of other bias	0 (0%)	19 (86.36%)	3 (13.64%)

Table H-3. Complementary and alternative medicine (CAM)

Domain	High	Unclear	Low
Adequate sequence generation	0 (0%)	1 (50%)	1 (50%)
Allocation concealment	0 (0%)	2 (100%)	0 (0%)
Blinding	1 (50%)	0 (0%)	1 (50%)
Incomplete outcome data addressed	0 (0%)	0 (0%)	2 (100%)
Free of selective reporting	0 (0%)	0 (0%)	2 (100%)
Free of other bias	0 (0%)	2 (100%)	0 (0%)

Table H-4. Nerve blocks

Domain	High	Unclear	Low
Adequate sequence generation	0 (0%)	19 (65.52%)	10 (34.48%)
Allocation concealment	0 (0%)	23 (79.31%)	6 (20.69%)
Blinding	7 (24.14%)	13 (44.83%)	9 (31.03%)
Incomplete outcome data addressed	3 (10.35%)	3 (10.35%)	23 (79.31%)
Free of selective reporting	4 (13.79%)	0 (0%)	25 (86.21%)
Free of other bias	1 (3.45%)	21 (72.41%)	7 (24.14%)

Table H-5. Neurostimulation

Domain	High	Unclear	Low
Adequate sequence generation	0 (0%)	1 (50%)	1 (50%)
Allocation concealment	0 (0%)	1 (50%)	1 (50%)
Blinding	0 (0%)	0 (0%)	2 (100%)
Incomplete outcome data addressed	1 (50%)	0 (0%)	1 (50%)
Free of selective reporting	0 (0%)	0 (0%)	2 (100%)
Free of other bias	1 (50%)	1 (50%)	0 (0%)

Table H-6. Rehabilitation

Domain	High	Unclear	Low
Adequate sequence generation	0 (0%)	0 (0%)	1 (100%)
Allocation concealment	0 (0%)	1 (100%)	0 (0%)
Blinding	1 (100%)	0 (0%)	0 (0%)
Incomplete outcome data addressed	0 (0%)	0 (0%)	1 (100%)
Free of selective reporting	0 (0%)	0 (0%)	1 (100%)
Free of other bias	0 (0%)	1 (100%)	0 (0%)

Table H-7. Traction

Domain	High	Unclear	Low
Adequate sequence generation	4 (40.00%)	4 (40.00%)	2 (20.00%)
Allocation concealment	4 (40.00%)	6 (60.00%)	0 (0%)
Blinding	10 (100%)	0 (0%)	0 (0%)
Incomplete outcome data addressed	1 (10.00%)	0 (0%)	9 (90.00%)
Free of selective reporting	1 (10.00%)	0 (0%)	9 (90.00%)
Free of other bias	0 (0.00%)	5 (50.00%)	5 (50.00%)

Appendix I. Newcastle-Ottawa Scale Assessment of Cohort Studies

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?

- ☐ a) yes, with independent validation ❋
- ☐ b) yes, e.g., record linkage or based on self reports
- ☐ c) no description

2) Representativeness of the cases

- ☐ a) consecutive or obviously representative series of cases ❋
- ☐ b) potential for selection biases or not stated

3) Selection of Controls

- ☐ a) community controls ❋
- ☐ b) hospital controls
- ☐ c) no description

4) Definition of Controls

- ☐ a) no history of disease (endpoint) ❋
- ☐ b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis ❋

- ☐ a) study controls for _____ ❋ (Select the most important factor.)
- ☐ b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure

- ☐ a) secure record (eg surgical records) ❋
- ☐ b) structured interview where blind to case/control status ❋
- ☐ c) interview not blinded to case/control status
- ☐ d) written self report or medical record only
- ☐ e) no description

2) Same method of ascertainment for cases and controls

- ☐ a) yes ❋
- ☐ b) no

3) Non-Response rate

- ☐ a) same rate for both groups ❋
- ☐ b) nonrespondents described
- ☐ c) rate different and no designation

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort

□ a) truly representative of the average _____ (describe) in the community ❋

□ b) somewhat representative of the average _____ in the community ❋

□ c) selected group of users eg nurses, volunteers d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

□ a) drawn from the same community as the exposed cohort ❋

□ b) drawn from a different source

□ c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

□ a) secure record (eg surgical records) ❋

□ b) structured interview ❋

□ c) written self report

□ d) no description

4) Demonstration that outcome of interest was not present at start of study

□ a) yes ❋

□ b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

□ a) study controls for _____ (select the most important factor) ❋

□ b) study controls for any additional factor ❋ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome

□ a) independent blind assessment ❋

□ b) record linkage ❋

□ c) self report

□ d) no description

2) Was followup long enough for outcomes to occur

□ a) yes (select an adequate follow up period for outcome of interest) ❋

□ b) no

3) Adequacy of follow up of cohorts

□ a) complete follow up -all subjects accounted for ❋

□ b) subjects lost to followup unlikely to introduce bias -small number lost -> ____ % (select an adequate %) followup, or description provided of those lost) ❋

□ c) followup rate < ____% (select an adequate %) and no description of those lost

□ d) no statement

Table I-1. Anesthesia

		Selection				Compara-bility	Outcome			
Author, year	Study design	Repre-sentative-ness of cohort	Selec-tion of non-exposed cohort	Ascertain-ment of exposure	Outcome of interest	Compara-bility of cohorts	Assess-ment of outcome	Ade-quate duration of followup	Ade-quate follow-up of cohort	Total stars
Koval 1999[78]	Prospective cohort study	B (1*)	A (1*)	D (0)	A (1*)	B (1*)	D (0)	A (1*)	C (0)	5
Labaille 1992[79]	Prospective cohort study	B (1*)	A (1*)	B (1*)	A (1*)	A (1*)	B (1*)	A (1*)	A (1*)	8
Miller 1990[81]	Retrospective cohort study	A (1*)	A (1*)	D (0)	A (1*)	A (1*)	B (1*)	A (1*)	A (1*)	7
Minville 2008[71]	Retrospective cohort study	B (1*)	A (1*)	A (1*)	A (1*)	B (1*)	B (1*)	A (1*)	A (1*)	8
Sen 2007[83]	Retrospective cohort study	B (1*)	A (1*)	A (1*)	B (0)	A (1*)	B (1*)	A (1*)	A (1*)	7
Shih 2010[84]	Retrospective cohort study	B (1*)	A (1*)	A (1*)	A (1*)	B (1*)	B (1*)	A (1*)	A (1*)	8
Sutcliffe 1994[85]	Prospective cohort study	B (1*)	B (0)	D (0)	A (1*)	B (1*)	D (0)	A (1*)	A (1*)	5

Table I-2. Multimodal pain management

		Selection				Compara-bility	Outcome			
Author, year	Study design	Repre-sentative-ness of cohort	Selec-tion of non-exposed cohort	Ascertain-ment of exposure	Outcome of interest	Compara-bility of cohorts	Assess-ment of outcome	Ade-quate duration of followup	Ade-quate follow-up of cohort	Total stars
Milisen 2001[86]	Prospective cohort study	B (1*)	A (1*)	A (1*)	A (1*)	A,B (2*)	C (0)	A (1*)	A (1*)	8
Ogilvie-Harris 1993[87]	Prospective cohort study	D (0)	C (0)	A (1*)	A (1*)	B (1*)	B (1*)	A (1*)	D (0)	5

Table I-3. Nerve blocks

		Selection				Compara-bility	Outcome			
Author, year	Study design	Repre-sentative-ness of cohort	Selec-tion of non-exposed cohort	Ascertain-ment of exposure	Outcome of interest	Compara-bility of cohorts	Assess-ment of outcome	Ade-quate duration of followup	Ade-quate follow-up of cohort	Total stars
Del Rosario 2008[117]	Retrospective cohort study	B (1*)	A (1*)	A (1*)	B (0)	B (1*)	B (1*)	A (1*)	A (1*)	7
Kocum 2007[118]	Retrospective cohort study	B (1*)	A (1*)	A (1*)	A (1*)	A (1*)	B (1*)	A (1*)	B (1*)	8
Pedersen 2008[119]	Retrospective cohort study	A (1*)	A (1*)	A (1*)	A (1*)	A,B (2*)	B (1*)	A (1*)	A (1*)	9

Table I-4. Traction

		Selection				Compara-bility	Outcome			
Author, year	Study design	Repre-sentative-ness of cohort	Selec-tion of non-exposed cohort	Ascertain-ment of exposure	Outcome of interest	Compara-bility of cohorts	Assess-ment of outcome	Ade-quate duration of followup	Ade-quate follow-up of cohort	Total stars
Vermeiren 1995[132]	Prospective cohort study	A (1*)	A (1*)	A (1*)	A (1*)	(0)	B (1*)	A (1*)	B (1*)	7

Appendix J. GRADE Tables: Assessing the Strength of Evidence

Each major outcome was provided a summary of the body of evidence (e.g., number of studies, study designs), the quality of the evidence, the results of pooling (if performed), and an overall grade for the quality of evidence for each outcome using the AHRQ GRADE approach. Randomized trials were considered to high quality unless downgraded as a result of concerns of important limitations (e.g., high risk of bias, inconsistent results, etc.). Cohorts were considered to be lower quality unless upgraded as a result of both confidence in the lack of any major limitations and characterized by having special strengths (e.g., large effect size).

Table J-1. Analgesia for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) - IM Analgesia (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Precise	Publication bias: Not investigated	35	55	-	MD 0.7 lower (1.04 to 0.36 lower)	INSUFFICIENT
Acute pain (post-treatment means) - Oral analgesia (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	48	46	-	MD 0.43 lower (1.3 lower to 0.44 higher)	INSUFFICIENT
Acute pain (post-treatment means) - Intrathecal analgesia (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Precise	Publication bias: Not investigated	15	15	-	MD 1.69 lower (2.01 to 1.37 lower)	INSUFFICIENT
Acute pain (rest) - Oral analgesia (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	48	46	-	MD 0.43 lower (1.3 lower to 0.44 higher)	INSUFFICIENT
Delirium - Oral analgesia											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	1/48 (2.1%)	1/46 (2.2%)	OR 0.96 (0.06 to 15.77)	1 fewer per 1,000 (from 20 fewer to 238 more)	INSUFFICIENT

RCT = randomized controlled trial; IM = intramuscular; MD = mean difference; OR = odds ratio

Table J-2. Spinal versus general anesthesia for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) - Spinal anesthesia (single) (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	15	15	-	MD 0.86 lower (1.3 to 0.42 lower)	INSUFFICIENT
Delirium - Spinal anesthesia (single)											
3	1 RCT; 2 Cohorts	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	8/15 (53.3%)	9/15 (60%)	OR 0.76 (0.18 to 3.24)	67 fewer per 1,000 (from 387 fewer to 229 more)	INSUFFICIENT
Mortality 30 days											
4	2 RCTs; 5 Cohorts	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	10/53 (18.9%)	5/46 (10.9%)	OR 1.73 (0.53 to 5.68)	66 more per 1,000 (from 48 fewer to 301 more)	LOW
Myocardial Infarction											
2	1 RCT; 1 Cohort	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	1/29 (3.4%)	0/14 (0%)	OR 1.55 (0.06 to 42.91)	0 more per 1,000 (from 0 fewer to 0 more)	INSUFFICIENT
Renal failure											
1	Cohort	High	Unkown	Direct	Imprecise	Publication bias: Not investigated	1/168 (0.6%)	2/167 (1.2%)	OR 0.49 (0.04 to 5.5)	6 fewer per 1,000 (from 11 fewer to 51 more)	INSUFFICIENT
Stroke											
2	Cohorts	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	3/448 (0.7%)	4/529 (0.8%)	3/448 (0.7%)	0 fewer per 1,000 (from 6 fewer to 23 more)	INSUFFICIENT

Table J-3. Spinal anesthesia (continuous vs. single administration) for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Delirium											
2	RCTs	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	5/67 (7.5%)	4/67 (6%)	OR 1.27 (0.32 to 4.99)	15 more per 1,000 (from 40 fewer to 181 more)	LOW
Mortality 30 days											
4	3 RCTs; 1 Cohort	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	2/81 (2.5%)	4/82 (4.9%)	OR 0.46 (0.07 to 3.02)	26 fewer per 1,000 (from 45 fewer to 85 more)	INSUFFICIENT
Myocardial Infarction											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	0/14 (0%)	1/15 (6.7%)	OR 0.33 (0.01 to 8.88)	44 fewer per 1,000 (from 66 fewer to 321 more)	INSUFFICIENT
Stroke											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	0/37 (0%)	0/37 (0%)	not pooled	not pooled	INSUFFICIENT

Table J-4. Spinal anesthesia (single): addition of fentanyl for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	20	20	-	not pooled	INSUFFICIENT

Table J-4. Spinal anesthesia (single): addition of fentanyl for hip fracture (continued)

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Day 1 pain											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	6/40 (15%)	5/40 (12.5%)	OR 1.24 (0.34 to 4.48)	not pooled	INSUFFICIENT

Table J-5. Spinal anesthesia (single): addition of morphine for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
1	RCTs	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	20	20	-	MD 0.36 lower (1.11 lower to 0.39 higher)	INSUFFICIENT
Delirium											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	1/20 (5%)	0/20 (0%)	OR 3.15 (0.12 to 82.16)	0 more per 1,000 (from 0 fewer to 0 more)	INSUFFICIENT

Table J-6. Spinal anesthesia (single): addition of sufentanil for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	25	25	-	not pooled	INSUFFICIENT

Table J-7. Spinal anesthesia: Different doses (Bupivacaine 2.5 mg vs. 5mg) for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Mortality 30 days											
1	Cohort	Low	Unknown	Direct	Imprecise	Publication bias: Not investigated	4/121 (3.3%)	4/61 (6.6%)	OR 0.49 (0.12 to 2.02)	32 fewer per 1,000 (from 57 fewer to 59 more)	INSUFFICIENT

Table J-8. Spinal anesthesia: Different doses (Bupivacaine 2.5 mg vs. 5mg) for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Mortality 30 days											
1	Cohort	Low	Unknown	Direct	Imprecise	Publication bias: Not investigated	2/30 (6.7%)	4/30 (13.3%)	OR 0.46 (0.08 to 2.75)	67 fewer per 1,000 (from 1,000 fewer to 164 more)	INSUFFICIENT

Table J-9. Comparative alternative medicine for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) - Acupressure (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	18	20	-	MD 3.01 lower (4.53 to 1.49 lower)	INSUFFICIENT

Table J-9. Comparative alternative medicine for hip fracture (continued)

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) - Relaxation (better indicated by lower values)											
1	RCT	High	Unknown	Direct	Precise	Publication bias: Not investigated	30	30	-	MD 1.1 lower (1.43 to 0.77 lower)	INSUFFICIENT

Table J-10. Multimodal pain management

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Delirium - Protocol #1											
1	Cohort	Medium	Unknown	Direct	Imprecise	Publication bias: Not investigated	12/60 (20%)	14/60 (23.3%)	OR 0.82 (0.34 to 1.96)	34 fewer per 1,000 (from 140 fewer to 140 more)	INSUFFICIENT
Delirium - Protocol #2											
1	Cohort	Medium	Unknown	Direct	Imprecise	Publication bias: Not investigated	1/55 (1.8%)	2/51 (3.9%)	OR 0.45 (0.04 to 5.16)	21 fewer per 1,000 (from 38 fewer to 135 more)	INSUFFICIENT
Mortality 30 days - Protocol #2											
1	Cohort	Medium	Unknown	Direct	Imprecise	Publication bias: Not investigated	5/55 (9.1%)	8/51 (15.7%)	OR 0.54 (0.16 to 1.77)	66 fewer per 1,000 (from 128 fewer to 91 more)	INSUFFICIENT
Myocardial Infarction - Protocol #2											
1	Cohort	Medium	Unknown	Direct	Imprecise	Publication bias: Not investigated	1/55 (1.8%)	2/51 (3.9%)	OR 0.45 (0.04 to 5.16)	21 fewer per 1,000 (from 38 fewer to 135 more)	INSUFFICIENT

Table J-10. Multimodal pain management (continued)

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Stroke - Protocol #2											
1	Cohort	Medium	Unknown	Direct	Imprecise	Publication bias: Not investigated	0/55 (0%)	1/51 (2%)	OR 0.13 (0.00 to 6.32)	17 fewer per 1,000 (from 20 to 93 more)	INSUFFICIENT

Table J-11. Nerve blocks vs. no block for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (better indicated by lower values)											
13	RCTs	High	Consistent	Direct	Precise	Publication bias: Unlikely	508	492	-	Not pooled	MODERATE
Pain on movement (post-treatment) (better indicated by lower values)											
4	RCTs	High	Inconsistent	Direct	Imprecise	Publication bias: Not investigated	128	130	-	Not pooled	LOW
Pain on rest (post-treatment) (better indicated by lower values)											
3	RCTs	High	Inconsistent	Direct	Imprecise	Publication bias: Not investigated	104	104	-	Not pooled	LOW
Day 1 Pain											
1	RCT	High	Unknown	Direct	Precise	Publication bias: Not investigated	7/25 (28%)	20/25 (80%)	OR 0.1 (0.03 to 0.36)	514 fewer per 1,000 (from 210 fewer to 693 fewer)	INSUFFICIENT

Table J-11. Nerve blocks vs. no block for hip fracture (continued)

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Delirium											
6	4 RCTs; 2 Cohorts	Medium	Consistent	Direct	Precise	Publication bias: Not investigated	11/242 (4.5%)	33/219 (7.9%)	OR 0.33 (0.16 to 0.66)	95 fewer per 1,000 (from 46 fewer to 123 fewer)	MODERATE
Mortality 30 days											
4	RCTs	HIGH	Consistent	Direct	Imprecise	Publication bias: Not investigated	2/114 (1.8%)	10/114 (8.8%)	OR 0.28 (0.07 to 1.12)	62 fewer per 1,000 (from 81 fewer to 10 more)	LOW
Myocardial Infarction											
3	2 RCTs; 1 Cohort	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	1/72 (1.4%)	1/73 (1.4%)	OR 1 (0.06 to 16.67)	0 fewer per 1,000 (from 13 fewer to 174 more)	INSUFFICIENT
Stroke											
2	1 RCT; 1 Cohort	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	1/25 (4%)	0/25 (0%)	OR 3.12 (0.12 to 80.39)	0 more per 1,000 (from 0 fewer to 0 more)	INSUFFICIENT

Table J-12. Nerve blocks vs. regional anesthesia for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
3	RCTs	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	55	54	-	MD 0.35 lower (1.1 lower to 0.39 higher)	LOW

Table J-12. Nerve blocks vs. regional anesthesia for hip fracture (continued)

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Delirium											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	6/15 (40%)	5/14 (35.7%)	OR 1.2 (0.27 to 5.4)	43 more per 1,000 (from 227 fewer to 393 more)	INSUFFICIENT

Table J-13. Nerve Blocks: Ropivacaine vs. Bupivacaine for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Delirium											
1	Cohort	Low	Unknown	Direct	Imprecise	Publication bias: Not investigated	2/32 (6.3%)	1/30 (3.3%)	OR 1.93 (0.17 to 22.5)	29 more per 1,000 (from 28 fewer to 404 more)	INSUFFICIENT

Table J-14. Neurostimulation for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
2	RCTs	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	60	63	-	MD 2.79 lower (4.95 to 0.64 lower)	INSUFFICIENT
Pain on movement (post-treatment) (Better indicated by lower values)											
1	RCT	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	30	30	-	MD 3.9 lower (6.22 to 1.58 lower)	INSUFFICIENT

Table J-15. Rehabilitation for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) (Better indicated by lower values)											
1	RCTs	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	18	19	-	MD 1.39 lower (2.27 to 0.51 lower)	INSUFFICIENT

Table J-16. Traction for hip fracture

Quality assessment							Summary of findings				
							No of patients		Effect		Quality
No of studies	Design	Risk of Bias	Consistency	Directness	Precision	Other considerations	Analgesia	control	Relative (95% CI)	Absolute	
Acute pain (post-treatment means) - Skin traction versus no traction (Better indicated by lower values)											
8	RCTs	High	Consistent	Direct	Imprecise	Publication bias: Not investigated	498	594	-	MD 0.20 higher (0.24 lower to 0.65 higher)	MODERATE
Mortality 30 days (traction vs. no traction)											
2	RCTs	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	0/55 (0%)	2/25 (8%)	OR 0.14 (0.01 to 1.44)	65 fewer per 1,000 (from 78 fewer to 35 more)	INSUFFICIENT
Mortality 30 days (skin vs. skeletal) - Skin traction versus skeletal traction											
1	RCTs	High	Unknown	Direct	Imprecise	Publication bias: Not investigated	0/26 (0%)	0/29 (0%)	not pooled	not pooled	INSUFFICIENT