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Postoperative epidural analgesia versus systemic analgesia for thoraco-lumbar spine surgery in children (Review)

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[Intervention Review]

Postoperative epidural analgesia versus systemic analgesia for thoraco-lumbar spine surgery in children

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ABSTRACT

Background

Spine surgery may be associated with severe acute postoperative pain. Compared with systemic analgesia alone, epidural analgesia may offer better pain control. However, epidural analgesia has sometimes been associated with rare but serious complications. Therefore, it is critical to quantify the real benefits of epidural analgesia over other modes of pain treatment.

Objectives

To assess the effectiveness and safety of epidural analgesia compared with systemic analgesia for acute postoperative pain control after thoraco-lumbar spine surgery in children.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and Cumulative Index to Nursing and Allied Health Literature on 14 November 2018, together with the references lists of related reviews and retained trials, and two trials registers.

Selection criteria

We included all randomized controlled trials performed in children undergoing any type of thoraco-lumbar spine surgery comparing epidural analgesia with systemic analgesia for postoperative pain. We applied no language or publication status restriction.

Data collection and analysis

We assessed risk of bias of included trials using the Cochrane tool. We analysed data using random-effects models. We rated the quality of the evidence according to the GRADE scale.

Main results

We included 11 trials (559 participants) in the review, and seven trials (249 participants) in the analysis: 140 participants received epidural analgesia and 109 received systemic analgesia.

Most studies included adolescents. Three trials included in the analysis contained some participants older than 18 years. The types of surgery were posterior spinal fusion for idiopathic scoliosis (nine trials), anterior correction for idiopathic scoliosis (one trial), or selective

dorsal rhizotomy in children with cerebral palsy (one trial). The mean numbers of vertebrae operated on were between nine and 14.5 and the mean numbers of spinal levels were between three and four and a half. The length of surgery varied between three and six and a half hours.

Compared with systemic analgesia, epidural analgesia reduced pain at rest at all time points. At six to eight hours, the mean pain score on a 0 to 10 scale with systemic analgesia was 3.1 (standard deviation 0.7) and with epidural analgesia was –1.32 points (95% confidence interval (CI) –1.83 to –0.82; 4 studies, 116 participants; moderate-quality evidence). At 72 hours, the mean pain score with epidural analgesia was equivalent to a –0.8 point reduction on a 0 to 10 scale (standardized mean difference (SMD) –0.65, 95% CI –1.19 to –0.10; 5 studies, 157 participants; moderate-quality evidence).

Return of gastrointestinal function

There was no difference for nausea and vomiting between groups (risk ratio (RR) 0.87, 95% CI 0.58 to 1.30; 6 studies, 215 participants; low-quality evidence). One study found epidural analgesia with local anaesthetics may have increased the number of participants who had their first flatus within 48 hours (RR 1.63, 95% CI 1.08 to 2.47; 30 participants; very low-quality evidence). Two studies found epidural analgesia with local anaesthetics may have increased the number of participants in whom first bowel movement occurred within 48 hours (RR 11.52, 95% CI 2.36 to 56.26; 60 participants; low-quality evidence). It was uncertain whether epidural analgesia reduced the time to first bowel movement (MD 0.09 days, 95% CI –0.32 to 0.50; 1 study, 60 participants; very low-quality evidence) and time to first liquid ingestion following epidural infusion of an opioid alone or a local anaesthetic plus an opioid (mean difference (MD) –5.02 hours, 95% CI –13.15 to 3.10; 2 studies, 56 participants; very low-quality evidence). Epidural analgesia with local anaesthetics may have increased the risk of having first solid food ingestion within 48 hours (RR 7.00, 95% CI 1.91 to 25.62; 1 study, 30 participants; very low-quality evidence).

Secondary outcomes

It was uncertain whether there was a difference in time to ambulate (MD 0.08 days, 95% CI –0.24 to 0.39; 1 study, 60 participants; very low-quality evidence) and hospital length of stay (MD –0.29 days, 95% CI –0.69 to 0.10; 2 studies, 89 participants; very low-quality evidence). Two studies found participants were more satisfied when treated with epidural analgesia (MD 1.62 on a scale from 0 to 10, 95% CI 1.26 to 1.97; 60 participants; very low-quality evidence). It was unclear whether there was a difference in parent satisfaction for epidural analgesia with an opioid alone (MD 0.60, 95% CI –0.81 to 2.01; 1 trial, 27 participants; very low-quality evidence).

Complications

It was uncertain whether there was a difference in the risk of complications such as: respiratory depression (risk difference (RD) –0.05, 95% CI –0.16 to 0.05; 4 studies, 126 participants; very low-quality evidence); wound infection (RD 0.01, 95% CI –0.05 to 0.08; 2 trials, 93 participants; very low-quality evidence); epidural abscess (RD 0, 95% CI –0.05 to 0.05; 3 trials, 120 participants; very low-quality evidence); and neurological complications (RD 0.01, 95% CI –0.04 to 0.06; 4 studies, 151 participants; very low-quality evidence).

Authors' conclusions

There is moderate- and low-quality evidence that there may be a small additional reduction in pain up to 72 hours after surgery with epidural analgesia compared with systemic analgesia. Two very small studies showed epidural analgesia with local anaesthetic alone may accelerate the return of gastrointestinal function. The safety of this technique in children undergoing thoraco-lumbar surgery is uncertain due to the very low-quality of the evidence. The study in 'Studies awaiting classification' may alter the conclusions of the review once assessed.

PLAIN LANGUAGE SUMMARY

Epidural analgesia for postoperative pain after spinal surgery in children

Review question

We tried to determine if epidural analgesia offers some advantages over systemic (vein, skin or muscles) analgesia for treating postoperative pain in children undergoing spine surgery.

Background

Some children need extensive spinal bone surgery. This is a very painful procedure. Traditionally, this pain has mostly been treated with an opioid such as systemic morphine (or morphine like medicine) given via an in injection into the veins, skin or muscles. Epidural analgesia involves giving pain relief medicine into a catheter inserted in the spine to block pain transmission to the brain. The catheter is a small tube usually placed by the surgeon, at the end of the surgery, in the space in the spinal canal known as the epidural space.

Study characteristics

The evidence is current to 14 November 2018. We included 11 trials with 559 participants in the review, and seven trials with 249 participants in the analysis. The trials were funded by departmental resources (five trials), or in part by industry and partly by charity (one trial). Five trials did not mention the source of funding. Three of the trials included in the analysis contained some participants older than 18 years.

Key results

There may be a small additional reduction in pain up to 72 hours after surgery with epidural analgesia compared with systemic analgesia. After an extensive spine surgery, the gut is paralysed for a certain amount of time leading to nausea (feeling sick), vomiting (being sick), inability to ingest liquid or food, and no stools excretion. Two very small studies showed epidural analgesia with local anaesthetic alone may have accelerated the return of gut function. If confirmed, this would mean that children would be able to resume normal liquid and solid food intake faster after extensive spine surgery. Children in two small studies were more satisfied with epidural analgesia compared with children in the systemic analgesia group. However, it was unclear whether their parents were more satisfied with epidural analgesia or systemic analgesia. The safety of this technique in children undergoing spine surgery was uncertain because there was insufficient information to determine whether there was a difference in the rate of complications between epidural analgesia and systemic analgesia and an analysis of small trials might not be the best methodology to evaluate this aspect.

Quality of the evidence

The quality of evidence was moderate, low or very low for reduced pain and low or very low for all other measurements.

Imperfections in the trials and low number of available trials were the main problems leading to rating the quality of evidence as low or very low.

Summary of findings for the main comparison. Epidural analgesia compared to systemic analgesia for postoperative analgesia after thoraco-lumbar spine surgery in children

Epidural analgesia compared to systemic analgesia for postoperative analgesia after thoraco-lumbar spine surgery in children

Patient or population: children having undergone thoraco-lumbar spine surgery. 3 trials included in the analysis contained participants older than 18 years: Blumenthal 2005 (10–30 years; mean age 17 years), Klatt 2013 (10–21 years), and O'Hara 2004 (13–21 years)

Settings: university hospitals in Russia (1 trial), Switzerland (2), and USA (5)

Intervention: epidural analgesia. Local anaesthetic were used alone (2 trials) or in combination with an opioid (8 trials). Opioids alone were infused for one trial

Comparison: systemic analgesia. The comparator was continuous intravenous morphine (2 trials), intravenous patient-controlled analgesia with morphine (4 trials), intravenous patient-controlled analgesia with hydromorphone (2 trials), intravenous patient-controlled analgesia with an opioid (1 trial), intravenous nurse-controlled analgesia with morphine (1 trial), or unspecified (1 trial)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Systemic analgesia	Epidural analgesia				
Pain Assessed with: scale: 0–10 (0 = no pain, 10 = worst pain)	**Pain scores at rest at 6–8 hours after surgery**		—	116 (4 studies)	⊕⊕⊕⊖ **Moderate**[a]	—
	Mean pain score in the control groups was 3.1 ± 0.7 (mean ± SD)	Mean pain score with epidural analgesia was **1.32 lower** (1.83 to 0.82 lower)				
	Pain scores at rest at 20–32 hours after surgery		—	208 (6 studies)	⊕⊕⊕⊖ **Moderate**[a]	—
	Mean pain score in the control groups was 3.5 ± 1.0 (mean ± SD)	Mean pain score with epidural analgesia was **1.06 lower** (1.56 to 0.57 lower)				
	Pain scores on movement at 24 hours after surgery		—	87 (3 studies)	⊕⊕⊖⊖ **Low**[b]	Equivalent to –1.2 on a scale from 0 to 10
	Mean pain score with epidural analgesia was **1.51 SDs lower** (2.27 to 0.76 lower)					
	Pain scores at rest at 48 hours after surgery		—	148 (5 studies)	⊕⊕⊕⊖ **Moderate**[a]	—

	Mean pain score in the control groups was 2.7 ± 0.9 (mean ± SD)	Mean pain score with epidural analgesia was **1.10 lower** (1.62 to 0.58 lower)				
	Pain scores on movement at 48 hours after surgery		—	60 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
	Mean pain score in the control group was 2.9 ± 0.2 (mean ± SD)	Mean pain score with epidural analgesia was **1.35 lower** (1.77 to 0.92 lower)				
	Pain scores at rest at 72 hours after surgery		—	157 (5 studies)	⊕⊕⊕⊖ **Moderate**[a]	Equivalent to –0.8 on a scale from 0 to 10
	Mean pain score with epidural analgesia was **0.65 SDs lower** (1.19 to 0.10 lower)					
	Pain scores on movement at 72 hours after surgery		—	60 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
	Mean pain score in the control group was 2.4 ± 0.5 (mean ± SD)	Mean pain score with epidural analgesia was **1.07 lower** (1.38 to 0.76 lower)				
Vomiting up to 48 hours after surgery	**Study population**		**RR 0.87** (0.58 to 1.30)	215 (6 studies)	⊕⊕⊖⊖ **Low**[b]	—
	510 per 1000	**444 per 1000** (296 to 663)				
Return of gastrointestinal function	**Number of participants with first flatus within 48 hours**		**RR 1.63** (1.08 to 2.47)	30 (1 study)	⊕⊖⊖⊖ **Very low**[c]	—
	600 per 1000	**978 per 1000** (648 to 1000)				
	Number of participants with first bowel movement within 48 hours		**RR 11.52** (2.36 to 56.26)	60 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
	33 per 1000	**384 per 1000** (79 to 1000)				
	Mean time to first bowel movement		—	60 (1 study)	⊕⊖⊖⊖ **Very low**[c]	This trial infused a mixture of a local anaesthetic and an opioid.
	Mean time in the control group was 3.70 ± 0.73 days (mean ± SD)	Mean time with epidural analgesia was **0.09 days longer** (0.32 shorter to 0.50 longer)				

	Mean time to first liquid ingestion		—	56 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	1 trial infused an opioid only and 1 trial infused a mixture of a local anaesthetic and an opioid.
	Mean time in the control groups was 29.55 ± 17.18 hours (mean ± SD)	Mean time with epidural was **5.02 hours shorter** (13.15 hours shorter to 3.10 hours longer)				
	Number of participants with solid food ingestion within 48 hours		**RR 7.00** (1.91 to 25.62)	30 (1 study)	⊕⊖⊖⊖ **Very low**[c]	The trial included in this analysis infused local anaesthetics only without opioids.
	133 per 1000	**933 per 1000** (255 to 1000)				
Time to first mobilization: time ambulate (days)	Mean time in the control group was 2.25 ± 0.55 days (mean ± SD)	Mean time with epidural was **0.08 days longer** (0.24 shorter to 0.39 longer)	—	60 (1 study)	⊕⊖⊖⊖ **Very low**[c]	—
Hospital length of stay (days)	Mean time in the control group was 5.27 ± 0.49 days (mean ± SD)	Mean time with epidural was **0.29 days shorter** (0.69 shorter to 0.10 longer)	—	89 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
Satisfaction with postoperative analgesia regimen Assessed with: scale: 0–10 (0 = not satisfied at all, 10 = very satisfied)	**Participant satisfaction**		—	60 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
	Mean satisfaction score in the control group was 7.10 ± 0.42 (mean ± SD)	Mean satisfaction score with epidural was **1.62 higher** (1.26 to 1.97 higher)				
	Parent satisfaction		—	27 (1 study)	⊕⊖⊖⊖ **Very low**[c]	—
	Mean satisfaction score in the control group was 8.20 ± 2.00 (mean ± SD)	Mean satisfaction score with epidural was **0.60 higher** (0.81 lower to 2.01 higher)				
Complications	**Respiratory depression**		**RD −0.05** (−0.16 to 0.05)	126 (4 studies)	⊕⊖⊖⊖ **Very low**[c]	—
	Study population					
	103 per 1000	**0 per 1000** (0 to 5)				

Wound infection		**RD 0.01** (−0.05 to 0.08)	93 (2 studies)	⊕⊖⊖⊖ **Very low**[c]	—
Study population					
0 per 1000	**18 per 1000** (3 to 93)				
Epidural abscess		**RD 0.00** (−0.05 to 0.05)	120 (3 studies)	⊕⊖⊖⊖ **Very low**[c]	—
Study population					
0 per 1000	**0 per 1000** (0 to 53)				
Neurological complications		**RD 0.01** (−0.04 to 0.06)	151 (4 studies)	⊕⊖⊖⊖ **Very low**[c]	—
Study population					
0 per 1000	**33 per 1000** (11 to 93)				

The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RD:** risk difference; **RR:** risk ratio; **SD:** standard deviation.

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[a]Downgraded by one level for risk of bias.
[b]Downgraded by one level for risk of bias and by one level for imprecision.
[c]Downgraded by one level for risk of bias and by two levels for imprecision.

BACKGROUND

Description of the condition

Idiopathic scoliosis is the most common spinal deformity encountered by general orthopaedic surgeons (Sud 2013). Scoliosis is a disease in which the spine is curved in three dimensions. Although the condition may have various causes (i.e. congenital, neurological, or musculoskeletal disorders), in children (defined as 18 years of age or less for the purpose of this review), idiopathic scoliosis is the most common form (approximately 70% to 80% of all cases) (McNicol 2016; Negrini 2015). The prevalence of idiopathic scoliosis is estimated to be between 0.9% and 12% of the general population, with up to 0.1% at risk of requiring a surgical intervention (Negrini 2015). A severe form is more commonly found in female adolescents (80% to 90%) (Negrini 2015). Problems related to scoliosis include reduced quality of life, disability, pain, cosmetic deformity, functional limitations, and pulmonary problems (Negrini 2015). For idiopathic scoliosis, most surgeons agree that surgical treatment should be considered in skeletally mature people with curves greater than 50° (thoracic Cobb curve angle as measured on x-rays) because of the risk of progression into adulthood (Agabegi 2015). Surgical treatment includes decompression, instrumented fusion, and deformity correction. In children, spinal fusion (with or without thoracotomy) is common and expensive. In the USA, the mean cost of each procedure is USD 28,696, and total annual expenses for spinal fusions in children was estimated to be about USD 600 million in 2013 (Center for Disease Control and Prevention 2015).

Spinal surgery may also be required for treatment of traumatic injuries and infectious, inflammatory, or neoplastic diseases. Around the world, the incidence of traumatic spinal cord injuries varies from 3.6 to 195.4 per million in the general population (Jazayeri 2015). Females are at greatest risk in adolescence (World Health Organization 2013).

Orthopaedic surgeries, including spine surgery, are among the most painful surgical procedures and are frequently associated with severe acute postoperative pain (Borgeat 2008; Gramke 2007). Adequate treatment of acute postoperative pain is considered a human fundamental right (White 2007). Treatment of acute postoperative pain in people undergoing spine surgery may be complicated by the fact that some of these people are experiencing chronic pain and may be opioid tolerant. Modalities that have been proposed to treat acute postoperative pain after spine surgery include systemic opioids, non-steroidal anti-inflammatory drugs, gabapentinoids, N-methyl-D-aspartate (NMDA) antagonists, and neuraxial blocks (Sharma 2012). Systemic opioids for acute postoperative pain may increase postoperative nausea and vomiting and gastrointestinal ileus, and may prolong hospitalization, potentially increasing hospital costs (Guay 2016). Pulmonary function may also be affected in children with scoliosis deformity, particularly among children with non-idiopathic scoliosis or those with idiopathic scoliosis and a thoracic deformity (Chua 2016; Ran 2016), making them more susceptible to respiratory depression from systemic opioids. Non-steroidal anti-inflammatory drugs, gabapentinoids, and NMDA antagonists, although useful, are usually considered as co-analgesic drugs (added to systemic opioids or neuraxial blocks) that are insufficient to be used alone. Neuraxial blocks, including single-injection intrathecal opioids or continuous epidural analgesia with one or two catheters, have been proposed as an alternative.

Description of the intervention

Epidural analgesia, which consists of injection of a solution into the spine outside the dura mater, can be used for surgery as the sole anaesthetic or as a supplement to general anaesthesia for postoperative analgesia (De Rojas 2014). The solution may contain a local anaesthetic alone, an opioid alone, or local anaesthetic plus opioid. Various adjuvants may be added to improve efficacy or prolong duration of the solution. The solution may be administered as a single injection (single shot block) or as a loading dose followed by a continuous infusion (through an epidural catheter) to control postoperative pain for the first few days after surgery, when pain is most intense. For scoliosis surgery, the surgeon usually inserts an epidural catheter at the end of surgery. Injection of a local anaesthetic before surgical incision or at the start of surgery could potentially interfere with the neurological spinal cord monitoring required during this type of surgery (Loughman 1995).

How the intervention might work

When compared with a systemic opioid-based regimen, epidural analgesia with local anaesthetics has been reported to decrease postoperative pain, hasten gastrointestinal transit return, and decrease hospital length of stay for open abdominal surgery (Guay 2016). It has been postulated that faster return of gastrointestinal transit may be due to sympathetic blockade by the epidural, reduced opioid requirements, or local anaesthetics themselves (Guay 2016). Specifically for scoliosis surgery, one non-Cochrane review suggested that epidural analgesia may have improved pain control, hastened gastrointestinal transit return, and improved patient satisfaction (Borgeat 2008).

Why it is important to do this review

It is unknown whether epidural analgesia improves pain control; accelerates return of gastrointestinal transit; or reduces risk of respiratory depression, length of hospitalization, and costs of care among children. Epidural analgesia is more complex to administer than systemic analgesia and is associated with rare but serious adverse events such as epidural haematoma or abscess. it is important to justify epidural use with clear documentation of superiority compared with systemic opioid-based postoperative analgesia. This is the lone Cochrane Review comparing epidural analgesia versus systemic analgesia (opioids or others) for postoperative pain after thoraco-lumbar spine surgery in children.

OBJECTIVES

To assess the effectiveness and safety of epidural analgesia compared with systemic analgesia for acute postoperative pain control after thoraco-lumbar spine surgery in children.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomized controlled trials (RCTs) evaluating epidural analgesia for postoperative pain, and comparing epidural analgesia with any form of systemic analgesia by any route. We excluded observational studies, quasi-randomized trials, cross-over trials, and cluster-randomized trials (Higgins 2011). We

placed no restrictions on the basis of language of publication or publication status.

Types of participants

We included studies performed on children (aged 0 to 18 years) undergoing thoracic, lumbar, or thoraco-lumbar spine surgery for any condition while under general anaesthesia. We included studies using any surgical approach: minimally invasive or not, posterior or anterior or both, and located at the thoracic or lumbar or thoraco-lumbar level.

Types of interventions

We included studies comparing a group of participants with epidural analgesia used for postoperative analgesia versus a group of participants receiving systemic analgesia (opioid based or others) used for postoperative analgesia. We included studies in which investigators administered epidural analgesia as a single shot block or as a continuous infusion for any duration and containing a local anaesthetic alone (extended duration or not) or in combination with an opioid (extended duration or not) or an opioid alone. We included studies in which trialists added an adjuvant to the solution or not. We excluded studies in which investigators added substances directly in the epidural space without the use of an epidural needle/catheter, such as steroids or other substances (gelfoam soaked or microfibrillar collagen or other). We excluded studies in which researchers administered the local anaesthetic or the opioid intrathecally. We excluded trials comparing nerve blocks versus systemic analgesia.

For the comparator, we included all forms of systemic analgesia (opioid-based regimen or other) regardless of the route of administration (intravenous (IV) with or without a proxy- or self-administered patient-controlled device), intramuscular or oral analgesia, or other).

Types of outcome measures

Primary outcomes

1. Pain (at rest and on movement up to 72 hours after surgery). We included pain measured on any ascending or descending scale as provided by study authors.
2. Vomiting up to 48 hours after surgery (number of participants with event). We extracted data on this outcome as the number of participants who experienced vomiting episodes.
3. Return of gastrointestinal function measured as time to first:
   a. flatus (hours);
   b. bowel movement (hours);
   c. liquid ingestion (hours);
   d. solid food ingestion (hours).

Secondary outcomes

1. Time to first mobilization (days).
2. Hospital length of stay (days).
3. Satisfaction with postoperative analgesia regimen (any ascending or descending scale as provided by study authors):
   a. participant satisfaction (any ascending or descending scale as provided by study authors);
   b. parent satisfaction (any ascending or descending scale as provided by study authors).
4. Complications (related to analgesic techniques (epidural or systemic analgesia), including respiratory depression, hospital inpatient falls, and infections (e.g. wound infection, epidural abscess) within 30 days of surgery) and neurological complications.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (2018, Issue 9); MEDLINE Ovid: Epub Ahead of Print, In-Process and Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, and Ovid MEDLINE(R) (from 1946 to 14 November 2018); Embase Ovid (from 1974 to 14 November 2018); and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (from 1981 to 14 November 2018). Our search strategies are displayed in Appendix 1, Appendix 2, Appendix 3, and Appendix 4 (Higgins 2011).

Searching other resources

We searched the World Health Organization International Clinical Trials Registry Platform (www.who.int/trialsearch), and ClinicalTrials.gov (www.clinicaltrials.gov), to identify trials in progress.

We scanned the reference lists and citations of all included trials and of any relevant systematic reviews identified to obtain further references to additional trials. We screened the conference proceedings of anaesthesiology societies from 2012 to 2017, as published in three major anaesthesiology journals: *British Journal of Anaesthesiology*,*European Journal of Anaesthesiology*, and *Regional Anesthesia and Pain Medicine (European Society of Regional Anesthesia (ESRA)* 2012 to 2017 and *American Society of Regional Anesthesia (ASRA)* 2012 to 2016*).* We also looked for abstracts on the websites of the American Society of Anesthesiologists for the same years and of the American Society of Regional Anesthesia 2017. We contacted all trial authors for additional information.

We also searched ProQuest Dissertations and Thesis Global (14 November 2018) as a source of grey literature (Appendix 5).

Data collection and analysis

Selection of studies

Two review authors (JG and RLJ) independently screened the list of all titles and abstracts identified by the search. We retrieved and independently read potential articles to determine their eligibility for inclusion. We resolved discrepancies by discussion, or with the help of a third review author (SK) when required. Two review authors (of JG, RLJ, and SK) examined potential trials found from sources other than electronic databases for classification (included, excluded, or awaiting classification). We documented the selection process in sufficient detail to complete a PRISMA flow diagram (Moher 2009). We listed all reasons for exclusion in the Characteristics of excluded studies table.

Data extraction and management

Two review authors (JG and SK) independently extracted data. When necessary, we sought the help of a third review author (RLJ) to resolve discrepancies. For selected studies, we entered the following parameters onto our data extraction form: risk

of bias as measured with the Cochrane tool; and outcomes and factors chosen a priori for assessment of heterogeneity (Schünemann 2011). We extracted dichotomous data as the number of participants experiencing the event and the total number of participants in each treatment group. We extracted continuous data as means, standard deviations (SDs), and total numbers of participants. When data were not available in these formats, we extracted data as P values, numbers of participants, and direction of effect. We did not consider medians as equivalent to means, and did not estimate SDs from quartiles or ranges. We entered first the site where the study was performed and the date of data collection (to facilitate exclusion of duplicate publications), then whether the study was included in the review or the reason for exclusion. After reaching agreement, one review author entered the data into the comprehensive meta-analysis and moderators for heterogeneity exploration (Comprehensive Meta-Analysis 2007). Also, after reaching agreement, we entered the risk of bias evaluation into Review Manager 5 (Review Manager 2014). We resolved disagreements by discussion or with the help of a third review author (RLJ), and contacted study authors to request additional information when required. We transferred data for analysis to Review Manager 5 in the format required to include the maximal number of studies (events and the total numbers of participants for each group; means, SDs, and numbers of participants included in each group; or generic inverse variance, if necessary). When possible, we entered the data into an intention-to-treat (ITT) analysis.

Assessment of risk of bias in included studies

We assessed the quality of included studies using the Cochrane 'Risk of bias' tool (Schünemann 2011), to examine random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. We resolved disagreements by discussion or with the help of a third review author. We assessed risk of bias on the basis of information presented in the reports, while making no assumptions.

Measures of treatment effect

We reported results as risk ratios (RRs) and 95% confidence intervals (95% CIs) for dichotomous data (vomiting and number of participants with bowel movement within 48 hours) (McColl 1998). Due to the high number of trials with zero cells, we analysed complications (respiratory depression, wound infection, epidural abscess, and neurological complications) as risk differences (RD). We reported results as mean differences (MDs) and 95% CIs for continuous data (pain scores, hospital length of stay, participant or parent satisfaction as much as feasible. If some of the continuous data used different scales (pain scores), or if only P values were extractable, we presented results as standardized mean differences (SMDs) and 95% CIs, and gave equivalence on a clinical scale. For SMDs, we considered 0.2 a small effect, 0.5 a medium effect, and 0.8 a large effect (Pace 2011). For time-to-event data (time to return of gastrointestinal transit, time to first mobilization), we contacted trial authors to try to obtain data as hazard ratios (HRs) for analysis but this proved impossible due to no response from some study authors and unavailability of data in this format for others. As planned in the published protocol (Guay 2017), as an alternative solution, we then analysed these data in the format provided by trial authors in their reports and treated them as other continuous data reported as MDs with 95% CIs. When there was an effect noted, we calculated from the odds ratio a number needed to treat for an additional beneficial outcome (NNTB), or a number needed to treat for an additional harmful outcome (NNTH) (Cates 2016; Deeks 2002). When we were unable to demonstrate an effect, we performed trial sequential analysis to ensure that enough participants were included in the retained studies to justify a conclusion on the absence of effect (Pogue 1998; Thorlund 2018).

Unit of analysis issues

We included only parallel-group trials. If a study contained more than two groups, we fused the two groups (by using the appropriate formula for adding SDs when required), when we thought they were equivalent according to the criteria of our protocol (taking our factors for heterogeneity exploration into account), or we separated them and split the control group in half if we thought they were different (Guay 2017).

Dealing with missing data

We contacted study authors when the published articles did not provide enough information for extraction of data. We made no imputations (Deeks 2011).

Assessment of heterogeneity

We considered clinical heterogeneity before pooling results, and examined statistical heterogeneity before carrying out any meta-analysis. We qualified the amount as low (25% or less), moderate (25% to 74%) or high (75% or greater) depending of the value obtained for the I^2 statistic (see 'Summary of findings' table and GRADE'; Higgins 2003).

Assessment of reporting biases

We assessed publication bias using a funnel plot, followed by Duval and Tweedie's trim and fill technique (Borenstein 2009a; Duval 2000a; Duval 2000b). This technique assessed whether publication bias was likely, and yielded an estimate of effect size after correction for the possibility of publication bias when such bias was suspected.

Data synthesis

We analysed data using Review Manager 5 and Comprehensive Meta-Analysis Version 2.2.044 with random-effects models (Comprehensive Meta-Analysis 2007; Review Manager 2014). For dichotomous data, we provided results as RRs (values best understood by clinicians; McColl 1998), or RDs (trials with zero cells). For continuous data, if some analyses could not be entered in our favoured format (means, SDs, and numbers of participants), we did not consider a median as equivalent to a mean and did not estimate SDs from quartiles. Instead we entered data as P values, numbers of participants, and direction of effect (using the Review Manager 5 calculator; Review Manager 2014). In such cases, MDs cannot be obtained. We then presented our results as SMDs. For results provided as SMDs, we gave clinical equivalents calculated as follows: SMD multiplied by the SD of a study at low risk of bias, and for which a typical SD on a clinical scale was provided (Schünemann 2011). For results in which the intervention produced an effect, we calculated the NNTB or the NNTH using the odds ratio (Cates 2016). We also calculated classical fail-safe numbers (number of missing trials to bring P value greater than 0.05, two-tailed test; Comprehensive Meta-Analysis 2007) for all outcome with a P value less than 0.05 and three studies or more. If an effect could not

be demonstrated, we also calculated optimal information sizes to ensure that enough participants were included in the retained studies to justify a conclusion based on absence of effect (Brant R; Pogue 1998; Thorlund 2018).

Subgroup analysis and investigation of heterogeneity

We explored any amount of heterogeneity greater than 25% using Egger's regression intercept (comprehensive meta-analysis; to eliminate a small-study effect), sensitivity analysis, subgrouping, or meta-regression (comprehensive meta-analysis) as appropriate. Small-study effects relate to the fact that small studies may have different effect size than the larger studies (Rucker 2011). Various explanations have been proposed to explain this effect amongst which is the fact that medical journals may be more inclined to accept small studies when results are positive. Other reasons proposed are: heterogeneity, selective outcome reporting bias, a mathematical artefact, or genuine random variation (Rucker 2011). Egger's regression intercept test that hypothesis. When there is an inverse correlation between the size of the study (number of participants included) and the effect size (the smaller the study, the larger the effect size), then there is a possibility that a small-study effect is present in the results. A small-study effect may introduce heterogeneity in the results and may also increase the overall effect size measured. A priori factors for heterogeneity included the following.

1. Cause of the condition (scoliosis (idiopathic or other) versus traumatic versus other).
2. Elective surgery versus urgent surgery.
3. Surgical approach (open posterior only versus open anterior only versus both versus other techniques).
4. Site of surgery (thoracic versus lumbar versus thoraco-lumbar).
5. Number of fused vertebrae.
6. Epidural technique: number of catheters (one versus two).
7. Solution used in the catheter (local anaesthetics versus local anaesthetics plus opioids versus opioids only versus local anaesthetic plus opioids and other adjuvants).
8. Single shot versus continuous infusion (and duration).
9. Comparator (route, substance used, proxy-patient-controlled device versus continuous infusion versus intermittent administration (mandatory or on request)).
10. Mean age of participants.
11. Sex distribution.

Although we examined forest plots for all outcomes with studies placed in order for all potential heterogeneity factors, to avoid multiple comparisons, we performed analysis (sensitivity, subgrouping, or meta-regression) only when forest plots suggested a statistically significant effect. We analysed subgroup differences using Review Manager 5 (Chi^2) and considered a P value less than 0.05 significant for subgroup differences (Review Manager 2014).

Sensitivity analysis

We performed sensitivity analysis (defined as excluding a study on the basis of its risk of bias (allocation concealment or blinding of outcome assessors, or both) or because it appeared as an outlier on a forest plot).

'Summary of findings' table and GRADE

We judged the quality of the body of evidence according to the GRADE system and presented this assessment in Summary of findings for the main comparison for all outcomes (Schünemann 2013), using the GRADEpro software (GRADEpro GDT). For risk of bias, we judged the quality of evidence as high when we derived most information from studies at low risk of bias, and we downgraded quality by one level when we obtained most information from studies at high or unclear risk of bias (allocation concealment and blinding of outcome assessors), or by two levels when the proportion of information obtained from studies at high risk of bias was sufficient to affect interpretation of results. For inconsistency, we downgraded the quality of evidence by one level when the I^2 statistic was 50% or higher without satisfactory explanation, and by two levels when the I^2 statistic was 75% or higher without explanation. We did not downgrade the quality of evidence for indirectness, because outcomes were based on direct comparisons performed mostly on the population of interest and were not surrogate markers. For imprecision, we downgraded the quality of evidence by one level when the CI around the effect size was large or overlapped an absence of effect and failed to exclude an important benefit or harm, or when the number of participants was fewer than the optimal information size; and we downgraded the quality by two levels when the CI was very wide and included both appreciable benefit and harm. For publication bias, we downgraded the quality of evidence by one level when correcting for the possibility of publication bias as assessed by Duval and Tweedie's trim and fill analysis changed the conclusion. When the quality of the body of evidence is high, further research is very unlikely to change our confidence in the estimate of effect. When quality is moderate, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. When quality is low, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. When the quality is very low, any estimate of effect is very uncertain. The review contains only one comparison as per our protocol: epidural analgesia versus systemic analgesia. Means of control groups and epidural groups provided in the Summary of findings for the main comparison were calculated using the Prism software (Prism 2007).

RESULTS

Description of studies

Results of the search

We identified 1771 records from CENTRAL, 1123 from MEDLINE, 1175 from Embase, 139 from CINAHL, and four from ProQuest Dissertations and Thesis Global. After we removed the duplicates, there were 2734 records left. From these records and from other sources, we retrieved 46 full articles. We excluded 33 trials (see Excluded studies; Characteristics of excluded studies table). Of the 13 other trials, one is an ongoing trial (Characteristics of ongoing studies table), and one is awaiting classification (report not available to date; Characteristics of studies awaiting classification table). Therefore, we included 11 trials in the review (Blumenthal 2005; Blumenthal 2006; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011).

See Figure 1.

Figure 1. Study flow diagram.

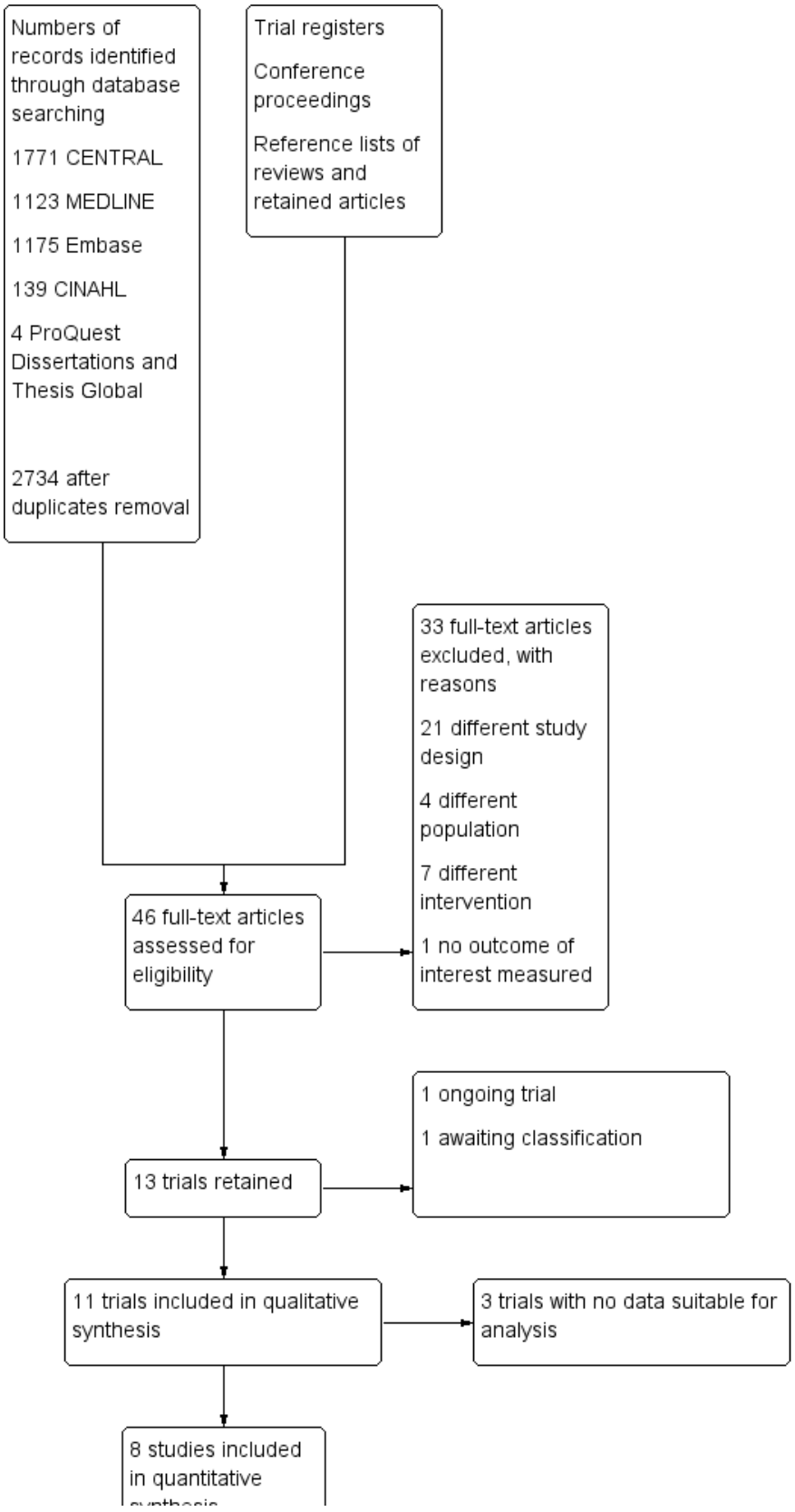
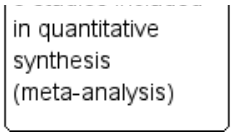


Figure 1. (Continued)



Included studies

We included 11 trials with 559 participants in the review (Blumenthal 2005; Blumenthal 2006; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011). The 11 included trials were published between 1999 and 2015.

Ten trials with 444 participants reported group distribution: 240 participants were in the epidural analgesia group and 204 participants were in the systemic analgesia group (Blumenthal 2005; Blumenthal 2006; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2012a; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011). There were no data suitable for analysis for three trials (Cakar Turhan 2011; Ezhevskaya 2012a; Ozturk Mamik 2011), and one trial did not report the number of participants per group (Ezhevskaya 2015). Therefore, we included seven trials with 249 participants in the analysis (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004): 140 to epidural analgesia and 109 to systemic analgesia (Characteristics of included studies table).

Source of funding

Five of the trials reported funding by departmental resources (Blumenthal 2005; Blumenthal 2006; Klatt 2013; Malviya 1999; O'Hara 2004). One trial reported funding in part by industry and part by a charity (Cassady 2000). Five trials did not specify the source of funding (Cakar Turhan 2011; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Ozturk Mamik 2011).

Setting

Nine trials were conducted in university hospitals (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004). Two trials did not specify the exact setting (Cakar Turhan 2011; Ozturk Mamik 2011).

The trials were conducted in Russia (two: Ezhevskaya 2012a; Ezhevskaya 2015); Switzerland (two; Blumenthal 2005; Blumenthal 2006); Turkey (two: Cakar Turhan 2011; Ozturk Mamik 2011); and the USA (five: Cassady 2000; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004).

Participants

The types of surgery performed were: posterior spinal fusion for idiopathic scoliosis (Blumenthal 2005; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Klatt 2013; O'Hara 2004; Ozturk Mamik 2011); anterior correction for idiopathic scoliosis (Blumenthal 2006); or selective dorsal rhizotomy in children with cerebral palsy (Malviya 1999).

Table 1 provides information on the types of surgeries.

Four trials included participants older than 18 years: Blumenthal 2005 (10 to 30 years; mean age 17 years); Ezhevskaya 2012a (12 to 25 years); Klatt 2013 (10 to 21 years); and O'Hara 2004 (13 to 21 years).

Intervention

In nine trials, the surgeons inserted catheters for continuous infusions at the end of surgery (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011). In one trial, there were additional loading doses administered at two thoracic levels before the surgery (Ezhevskaya 2012a). One trial administered a bolus of solution before surgery and used infiltration for postoperative analgesia (Cakar Turhan 2011). Trials used local anaesthetic alone (Blumenthal 2005; Blumenthal 2006); or in combination with an opioid (Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Gauger 2009; Klatt 2013; O'Hara 2004; Ozturk Mamik 2011). One trial infused an opioid without any local anaesthetic (Malviya 1999). Two trials started the infusion only on postoperative day one, instead of at wound closure (Blumenthal 2005; Blumenthal 2006). Infusions were administered at one level (Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2015; Gauger 2009; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011); or two levels (Blumenthal 2005; Blumenthal 2006; Ezhevskaya 2012a). Klatt 2013 compared one versus two levels versus systemic analgesia.

The types of local anaesthetics used were: ropivacaine (Blumenthal 2005; Blumenthal 2006; Ezhevskaya 2012a; Ezhevskaya 2015); levobupivacaine (Cakar Turhan 2011; Ozturk Mamik 2011); or bupivacaine (Cassady 2000; Gauger 2009; Klatt 2013; O'Hara 2004). Opioids used were: morphine (Cakar Turhan 2011; Malviya 1999; Ozturk Mamik 2011); fentanyl (Cassady 2000; Ezhevskaya 2012a; Ezhevskaya 2015; Klatt 2013; O'Hara 2004); or fentanyl plus hydromorphone (Gauger 2009). Two trials added epinephrine (adrenaline) to the solution (Cassady 2000; Ezhevskaya 2012a). Table 2 shows details of postoperative analgesia.

Comparator

Studies compared epidural analgesia with: continuous IV morphine (Blumenthal 2005; Blumenthal 2006); IV patient-controlled analgesia with morphine (Cakar Turhan 2011; Cassady 2000; O'Hara 2004; Ozturk Mamik 2011); IV patient-controlled analgesia with hydropmorphone (Gauger 2009; Klatt 2013); IV patient-controlled analgesia with an opioid (Ezhevskaya 2012a); or IV nurse-controlled analgesia with morphine (Malviya 1999). One trial did not specify the comparator (Ezhevskaya 2015).

Excluded studies

We excluded 33 trials for the following reasons: different study design (21 trials; Adu-Gyamfi 1995; Aizenberg 2011; Amaranath 1989; Arms 1998; Ekatodramis 2002; Ezhevskaya 2012b; Ezhevskaya 2012c; Khinkover 2006; Lowry 2001; Milbrandt 2009; Nóbrega 2017; Pham 2008; Ravish 2012; Saudan 2008; Shaw 1996; Sparkes 1989; Sucato 2005; Sundarathiti 2010; Tobias 2001; Turner 2000; Van

Boerum 2000); different study population (four trials; Bernard 1995a; Ezhevskaya 2014a; Goodarzi 1993; Sekar 2004); different intervention (seven trials; Akin Takmaz 2011; Cohen 2017; Erdogan 2017; Eshevskaya 2013; Ezhevskaya 2014b; Goodarzi 1999; Lawhorn 1994); and no outcome of interest measured (one trial; Loughnan 1990).

See Characteristics of excluded studies table for more details.

Studies awaiting classification

We have one trial awaiting classification (Kick 1995). This potential trial came from the reference list of a review article (Bernard 1995b). To date, we have been unable to locate this article despite requests at two different university libraries.

See Characteristics of studies awaiting classification table for more details.

Ongoing studies

We found one potential ongoing trial (EUCTR2008-001642-19-SE). This trial aims to compare epidural analgesia with fentanyl, bupivacaine, and epinephrine versus IV analgesia with s-ketamine and morphine. The trial was registered in 2008, and last refreshed in March 2012. There is no contact information provided.

See Characteristics of ongoing studies table for more details.

Risk of bias in included studies

Figure 2 and Figure 3 show the risk of bias of included trials.

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

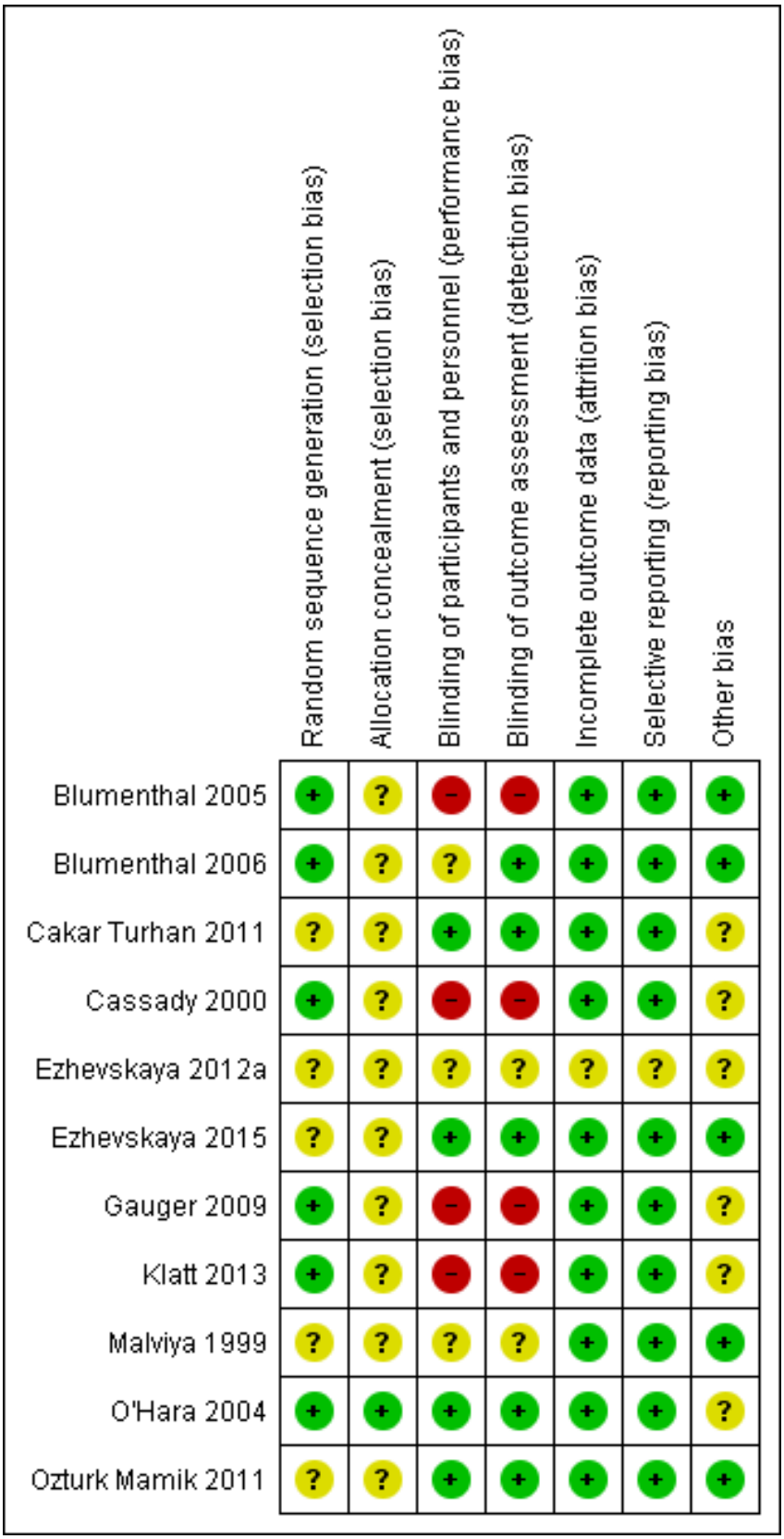
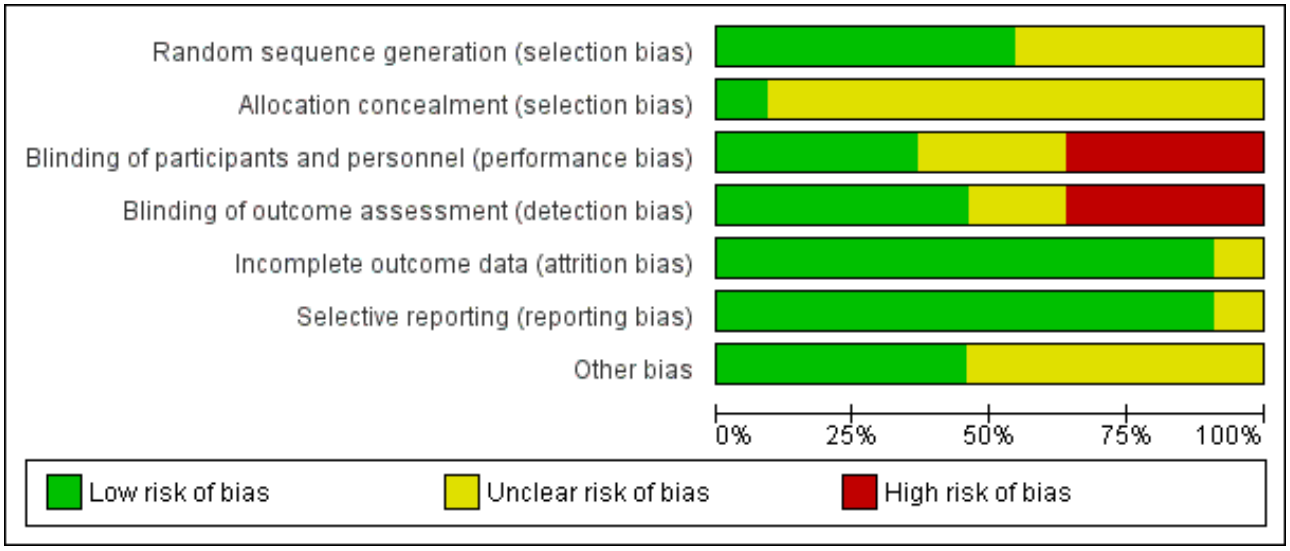


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Random sequence generation was at low risk of bias for six trials (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Gauger 2009; Klatt 2013; O'Hara 2004), and at unclear risk of bias for the other five trials.

Allocation

We judged allocation concealment bias at low risk for one trial (O'Hara 2004), and at unclear risk for the remaining 10 trials.

Blinding

We judged blinding of participants and personnel taking care of participants at low risk of bias for four trials (Cakar Turhan 2011; Ezhevskaya 2015; O'Hara 2004; Ozturk Mamik 2011). We rated this domain at high risk of bias for four trials (Blumenthal 2005; Cassady 2000; Gauger 2009; Klatt 2013). For three trials, there was not enough information in the report to enable us to judge this domain (Blumenthal 2006; Ezhevskaya 2012a; Malviya 1999).

We judged blinding of outcome assessment at low risk of bias for five trials (Blumenthal 2006; Cakar Turhan 2011; Ezhevskaya 2015; O'Hara 2004; Ozturk Mamik 2011). We judged this domain at high risk of bias for four trials (Blumenthal 2005; Cassady 2000; Gauger 2009; Klatt 2013). For two trials, there was not enough information in the report to allow us to judge this domain (Ezhevskaya 2012a; Malviya 1999).

Incomplete outcome data

We judged attrition bias at low risk for 10 trials (Blumenthal 2005; Blumenthal 2006; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011). For Ezhevskaya 2012a, we judged attrition bias at unclear risk. The numbers of participants retained in the analysis by the study authors in one of the conference abstract were 45 and 35 (Ezhevskaya 2012a). There was no explanation provided for apparent loss of 10 participants in the control group. The other conference abstract related to this trial reported that the number of participants retained was 70 and 65 (Ezhevskaya 2012a).

Selective reporting

We judged reporting bias at low risk for 10 trials (Blumenthal 2005; Blumenthal 2006; Cakar Turhan 2011; Cassady 2000; Ezhevskaya 2015; Gauger 2009; Klatt 2013; Malviya 1999; O'Hara 2004; Ozturk Mamik 2011). Ezhevskaya 2012a was reported as conference abstracts only and no data were provided.

Other potential sources of bias

We judged five trials at low risk for other risks of bias (Blumenthal 2005; Blumenthal 2006; Ezhevskaya 2015; Malviya 1999; Ozturk Mamik 2011). We judged the other six trials at unclear risk of other bias. Cakar Turhan 2011 performed wound infiltration in addition to epidural analgesia for one group only, thus generating a potential bias for the present review. Cassady 2000; Gauger 2009; Klatt 2013; and O'Hara 2004 were not analysed by ITT. Ezhevskaya 2012a was published as conference abstracts only and there were no details provided on demographic characteristics.

Effects of interventions

See: **Summary of findings for the main comparison** Epidural analgesia compared to systemic analgesia for postoperative analgesia after thoraco-lumbar spine surgery in children

Primary outcomes

1. Pain (at rest and on movement up to 72 hours after surgery)

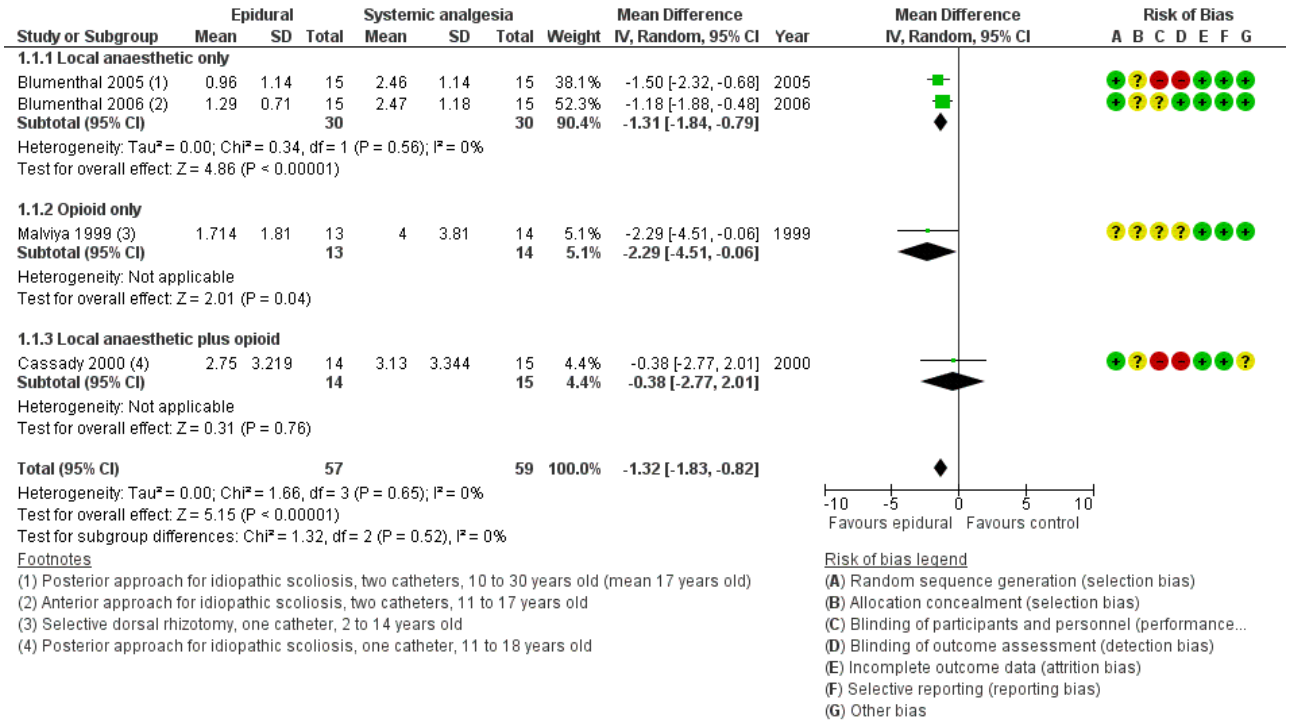
Pain at rest at six to eight hours after surgery

Four trials with 116 participants reported on pain at rest at six to eight hours after surgery (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Malviya 1999). Pain scales were visual analogue pain scale from 0 to 10 or FLACC (Face, Legs, Activity, Cry, Consolability; Malviya 1999; Appendix 6). We judged random sequence generation at low risk of bias for three trials (Blumenthal 2005; Blumenthal 2006; Cassady 2000), and at unclear risk of bias for one trial (Malviya 1999). We judged allocation concealment unclear for the four trials. Blinding of participants and personnel taking care of participants was at high/unclear risk for the four trials. Blinding of outcome

assessment was at unclear/high risk for three trials (Blumenthal 2005; Cassady 2000; Malviya 1999), and at low risk for one trial (Blumenthal 2006). Attrition bias and reporting bias were at low risk for the four trials. We judged other risk of bias at unclear risk for one trial (Cassady 2000), and at low risk for the other three trials.

We found that epidural analgesia reduced pain at rest at six to eight hours after surgery (MD −1.32, 95% CI −1.83 to −0.82; Analysis 1.1; Figure 4; Summary of findings for the main comparison). If data were analysed as SMD to take into account the fact that not all authors used the same pain scale then the SMD was −0.81 (95% CI −1.35 to −0.28).

Figure 4. Forest plot of comparison: 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, outcome: 1.1 Pain at rest at 6 to 8 hours.



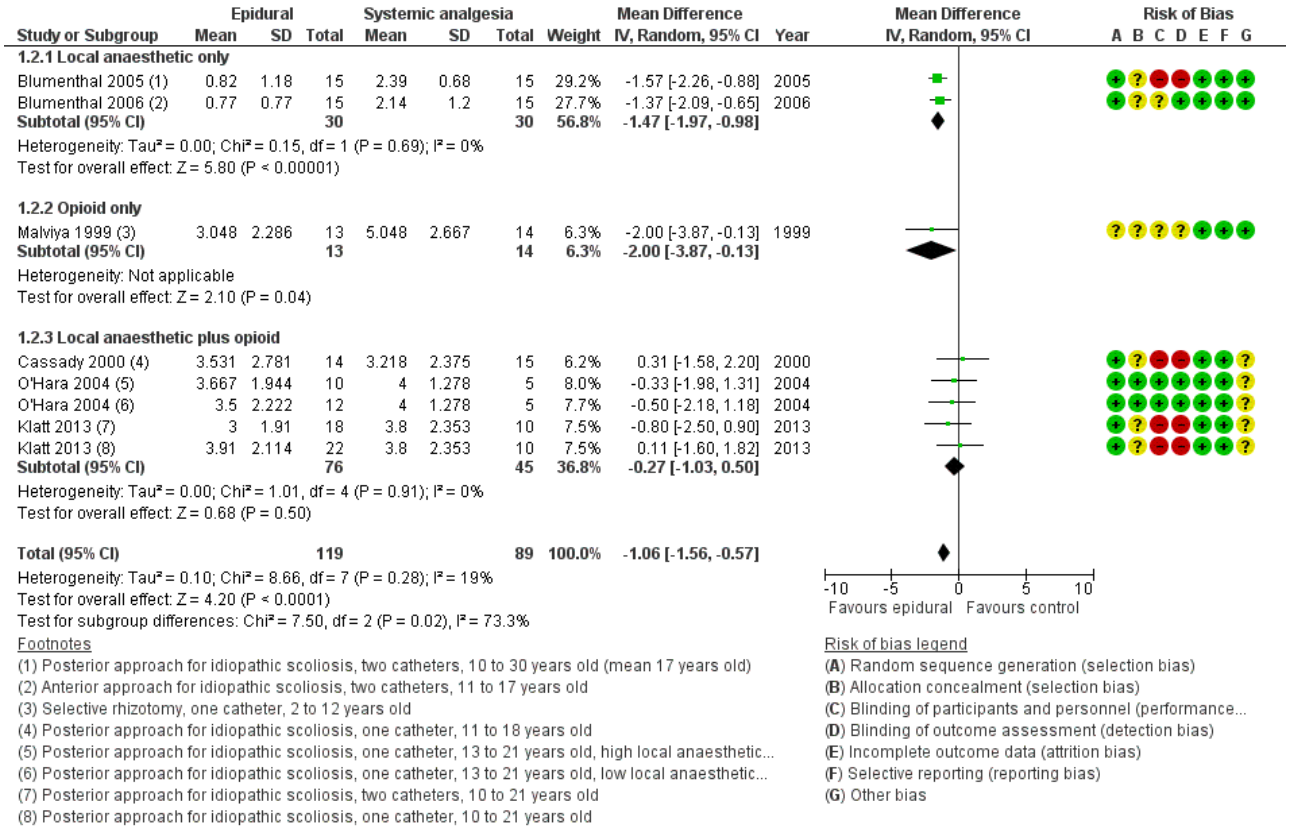
We found no evidence of a small-study effect. The impact of asymmetry in the funnel plot led to a trim and fill estimate MD of −1.28 (95% CI −1.77 to −0.79). The classical fail-safe number was 19. Trial sequential analysis indicated that 60 participants were required to find a 1-point difference in pain (alpha 0.05; power 80%; two-sided test; variance based on studies with blinded assessors; heterogeneity model variance based). We downgraded the quality of evidence by one level for risk of bias and rated it moderate.

Pain at rest at 20 to 32 hours

Six trials with 208 participants reported on pain at rest at 20 to 32 hours (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Klatt 2013; Malviya 1999; O'Hara 2004). Pain scales used were visual analogue pain scale from 0 to 10 or Wong-Baker (Klatt 2013), or FLACC (Malviya 1999; Appendix 6). We judged random sequence generation at unclear risk of bias for one trial (Malviya 1999), and at low risk of bias for the other five trials. We judged allocation concealment at low risk of bias for one trial (O'Hara 2004), and at unclear risk of bias for the other five trials. Blinding of participants and personnel taking care of participants was at low risk for one trial (O'Hara 2004), and at unclear/high risk for the other five trials. Blinding of outcome assessment was at unclear/high risk for four trials (Blumenthal 2005; Cassady 2000; Klatt 2013; Malviya 1999), and at low risk for two trials (Blumenthal 2006; O'Hara 2004).

We found that epidural analgesia reduced pain at rest at 20 to 32 hours (MD −1.06, 95% CI −1.56 to −0.57; Analysis 1.2; Figure 5; Summary of findings for the main comparison). If data were analysed as SMD to take into account the fact that not all authors used the same pain scale then the SMD was −0.54 (95% CI −1.00 to −0.09). We found no evidence of a small-study effect. The impact of asymmetry in the funnel plot led to a trim and fill estimate MD of −1.15 (95% CI −1.74 to −0.56). The classical fail-safe number was 28. Trial sequential analysis indicated that 141 participants were required to find a 1-point difference in pain (alpha 0.05; power 80%; two-sided test; variance based on studies with blinded assessors; heterogeneity model variance based) and that the Z curve crossed the boundary in favour of epidural analgesia. We downgraded the quality of evidence by one level for risk of bias and rated it moderate.

Figure 5. Forest plot of comparison: 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, outcome: 1.2 Pain at rest at 20 to 32 hours.



Pain on movement at 24 hours

Three trials with 87 participants reported on pain on movement at 24 hours (Blumenthal 2005; Blumenthal 2006; Malviya 1999). One trial (Malviya 1999), was at unclear risk of bias for random sequence generation and the two other trials were at low risk of bias for this domain. The three trials were at unclear/high risk of bias for allocation concealment and blinding of participants and personnel taking care of the participants. Blinding of outcome assessment was at low risk for one trial (Blumenthal 2006), and at unclear/high risk for two trials (Blumenthal 2005; Malviya 1999). The three trials were at low risk of bias for attrition bias, reporting bias, and risks of other bias.

Pain on movement at 24 hours was lower for participants treated with epidural analgesia (SMD −1.51, 95% CI −2.27 to −0.76; Analysis 1.3; Summary of findings for the main comparison). There was no evidence of a small-study effect or publication bias. Based on Blumenthal 2005 (SD 0.81), this would be equivalent to 1.22 on a scale from 0 to 10. The classical fail-safe number was 28. We downgraded the quality of evidence by one level for risk of bias and by one level for imprecision, and rated it low.

Pain at rest at 48 hours

Five trials with 148 participants reported on pain at rest at 48 hours (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Malviya 1999; O'Hara 2004). Pain scales used were visual analogue pain scale from 0 to 10 or FLACC (Malviya 1999; Appendix 6). Random sequence generation was at unclear risk of bias for one trial (Malviya 1999), and at low risk of bias for the other four trials. Allocation concealment was at low risk of bias for one trial (O'Hara 2004), and at unclear risk for the other four trials. Blinding of participants and personnel taking care of participants was at low risk of bias for one trial (O'Hara 2004), and at unclear/high risk for the other four trials. Blinding of outcome assessment was at low risk for two trials (Blumenthal 2006; O'Hara 2004), and at unclear/high of bias for the other three trials. The five trials were at low risk of bias for attrition bias and reporting bias. Other risks of bias were at low risk for three trials (Blumenthal 2005; Blumenthal 2006; Malviya 1999), and at unclear risk of bias for the other two trials.

Pain at rest at 48 hours was lower for participants treated with epidural analgesia (MD −1.10, 95% CI −1.62 to −0.58; Analysis 1.4; Summary of findings for the main comparison). If data were analysed as SMD to take into account the fact that not all authors used the same pain scale then the SMD was −0.66 (95% CI −1.22 to −0.10). There was no evidence of a small-study effect. The impact of asymmetry in the funnel plot led to a trim and fill estimate MD of −1.37 (95% CI −2.00 to −0.75). Trial sequential analysis indicated that 163 participants were required to find a 1-point difference in pain (alpha 0.05; power 80%; two-sided test; variance based on studies with blinded assessors; heterogeneity model variance based) but that the Z curve crossed the boundary in favour of epidural analgesia. We downgraded the quality of evidence by one level for risk of bias and rated it moderate.

Pain on movement at 48 hours

Two trials with 60 participants reported on pain on movement at 48 hours (Blumenthal 2005; Blumenthal 2006)

Random sequence generation was at low risk of bias for the two trials. Allocation concealment was at unclear risk of bias for the two trials. Blinding of participants and personnel taking care of the participants was at unclear risk of bias for Blumenthal 2006, and at high risk for Blumenthal 2005. Blinding of outcome assessment was at low risk of bias for Blumenthal 2006, and at high risk of bias for Blumenthal 2005. All other domains were at low risk of bias for the two trials.

Epidural analgesia reduced pain on movement at 48 hours (MD −1.35, 95% CI −1.77 to −0.92; Analysis 1.5; Summary of findings for the main comparison). The classical fail-safe number was 23. Trial sequential analysis indicated that 57 participants were required to find a 1-point difference in pain (alpha 0.05; power 80%; two-sided test; variance based on studies with blinded assessors; heterogeneity model variance based) and that the Z curve crossed the boundary in favour of epidural analgesia. We downgraded the quality of evidence by one level for risk of bias and by two levels for imprecision, and rated it very low.

Pain at rest at 72 hours

Five trials with 157 participants reported on pain at rest at 72 hours (Blumenthal 2005; Blumenthal 2006; Gauger 2009; Malviya 1999; O'Hara 2004). Random sequence generation was at unclear risk for one trial (Malviya 1999), and at low risk of bias for the other four trials. Allocation concealment was at low risk of bias for one trial (O'Hara 2004), and at unclear risk of bias for the other four trials. Blinding of participants and personnel taking care of the participants was at low risk of bias for one trial (O'Hara 2004), and at unclear/high risk of bias for the other four trials. Blinding of outcome assessment was at low risk of bias for two trials (Blumenthal 2006; O'Hara 2004), and at unclear/high risk of bias for the other three trials. The five trials were at low risk of attrition bias and reporting bias. Other risks of bias were at low risk for three trials (Blumenthal 2005; Blumenthal 2006; Malviya 1999), and at unclear/high risk for the other two trials (Gauger 2009; O'Hara 2004).

Epidural analgesia reduced pain at rest at 72 hours (SMD −0.65, 95% CI −1.19 to −0.10; Analysis 1.6; Summary of findings for the main comparison). Heterogeneity was high when all trials were included (I^2 = 61%) but absent (I^2 = 0%) when Blumenthal 2006 was excluded. Blumenthal 2006 studied participants undergoing anterior spinal correction while the other four trials studied participants undergoing posterior spinal correction. Excluding Blumenthal 2006, the SMD was −0.46 (95% CI −0.82 to −0.10). There was no evidence of a small-study effect. The impact of asymmetry in the funnel plot led to a trim and fill estimate SMD of −0.75 (95% CI −1.26 to −0.24). Based on Blumenthal 2006 (SD 1.2) the difference would be equivalent to 0.8 on a scale from 0 to 10. The classical fail-safe number was 17. We downgraded the quality of evidence by one level for risk of bias and rated it moderate.

Pain on movement at 72 hours

Two trials with 60 participants reported on pain on movement at 72 hours (Blumenthal 2005; Blumenthal 2006). Random sequence generation was at low risk of bias for the two trials. Allocation concealment was at unclear risk of bias for the two trials. Blinding of participants and personnel taking care of the participants was at unclear risk of bias for Blumenthal 2006, and at high risk of bias for Blumenthal 2005. Blinding of outcome assessment was at low risk of bias for Blumenthal 2006, and at high risk of bias for Blumenthal 2005. All other domains were at low risk of bias for the two trials.

Epidural analgesia reduced pain on movement at 72 hours (MD −1.07, 95% CI −1.38 to −0.76; Analysis 1.7; Summary of findings for the main comparison). Trial sequential analysis indicated that 57 participants were required to find a 1-point difference in pain (alpha 0.05; power 80%; two-sided test; variance 1.5; heterogeneity model variance based) and that the Z curve crossed the boundary in favour of epidural analgesia. We downgraded the quality of evidence by one level for risk of bias and by two levels for imprecision, and rated it very low.

2. Vomiting up to 48 hours after surgery (number of participants with event)

Six trials with 215 participants reported on nausea and vomiting after surgery (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Gauger 2009; Klatt 2013; Malviya 1999). Available data (closest to 48 hours) suitable for extraction for cumulative number of participants having experienced postoperative nausea and vomiting were found at: six hours (Blumenthal 2005; Blumenthal 2006); around 40 hours (Cassady 2000; during use of epidural or IV patient-controlled analgesia which was discontinued upon successful restoration of oral fluid intake and this occurred at a mean time of 39.3 hours for epidural analgesia and 41.7 hours for systemic analgesia), during the first three postoperative days (Gauger 2009), or at an unspecified time point (emesis; Klatt 2013). One trial was at unclear risk of bias for random sequence generation (Malviya 1999); and all other trials were at low risk of bias for this domain (Blumenthal 2005; Blumenthal 2006; Cassady 2000; Gauger 2009; Klatt 2013). Allocation concealment and blinding of participants or personal taking care of the participants were at unclear/high risk for all six trials. Blinding of outcome assessment was at low risk of bias for Blumenthal 2006, and at unclear/high risk for the other five trials. All six trials were at low risk of attrition bias and selective reporting. Blumenthal 2005; Blumenthal 2006; and Malviya 1999 were rated at low risk of other bias. Cassady 2000; Gauger 2009; and Klatt 2013 were at unclear risk for the possibility of other bias.

We did not find a difference for the risk of nausea and vomiting (RR 0.87, 95% CI 0.58 to 1.30; Analysis 1.8; Summary of findings for the main comparison). There was no evidence of a small-study effect. The impact of asymmetry in the funnel plot led to a trim and fill estimate RR of 1.08 (95% CI 0.70 to 1.67). Trial sequential analysis calculated that 781 participants were required to eliminate a 25% difference (alpha 0.05; power 80%; two-sided test; incidence in the control arm 51%; model based variance) and that the Z curve failed to cross the boundaries. We downgraded the quality of the evidence by one level for risk of bias and by one level for imprecision and rated it low.

3. Return of gastrointestinal function

None of the trials reported gastrointestinal function as time to event. When contacted, some authors did not reply (Cakar Turhan 2011; Ezhevskaya 2012a; Gauger 2009), or gave us results in the format available (mean and SD (Klatt 2013); or number of participants with and without the event at a certain time point (Blumenthal 2006)); or informed us that their data were no longer available (Blumenthal 2005); or sent text of published abstract

(Ezhevskaya 2015). Therefore, we analysed this outcome either as the number of participants with and without the event at a certain time point, or as mean and SD of the time when it occurred.

3a. Time to first flatus (hours)

One trial with 30 participants provided data for first flatus (Blumenthal 2006). Data were available as number of participants who experienced the event within 48 hours. Using a double catheter technique with ropivacaine alone on participants undergoing anterior correction of thoracic scoliosis, Blumenthal and colleagues reported that 15/15 participants with epidural analgesia had their first flatus within 48 hours compared with 9/15 participants for those who had systemic analgesia (RR 1.63, 95% CI 1.08 to 2.47). This trial was at unclear risk of bias for allocation concealment and low risk of bias for all other domains. Trial sequential analysis calculated that 348 participants were required to eliminate a 25% difference (alpha 0.05; power 80%; two-sided test; incidence in the control arm 60%; model-based variance). We downgraded the quality of evidence by one level for risk of bias and by two levels for imprecision, and rated it very low.

3b. Time to first bowel movement (hours)

Two trials infused local anaesthetic alone through two catheters and reported on the number of participants with or without bowel movement within 48 hours (Blumenthal 2005; Blumenthal 2006; Analysis 1.9). Random sequence generation was at low risk of bias for the two trials. Allocation concealment was at unclear risk of bias for the two trials. Blinding of participants and personnel taking care of the participants was at unclear risk of bias for Blumenthal 2006, and at high risk for Blumenthal 2005. Blinding of outcome assessment was at low risk of bias for Blumenthal 2006, and at high risk of bias for Blumenthal 2005. We judged all other domains at low risk of bias for the two trials.

Epidural analgesia increased the possibility of having first bowel movement within 48 hours (RR 11.52, 95% CI 2.36 to 56.26; NNTB 3, 95% CI 2 to 10). Trial sequential analysis calculated that 542 participants were required to eliminate a 25% difference (alpha 0.05; power 80%; two-sided test; incidence in the intervention arm 60%; model-based variance). We downgraded the quality of evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

One trial infused a mixture of local anaesthetic and an opioid, and reported time to first bowel movement (mean ± SD; participants with one catheter: 3.82 ± 0.85 days; 22 participants; participants with two catheters: 3.75 ± 0.68 days; 16 participants; participants with IV patient-controlled analgesia: 3.70 ± 0.73 days; 20 participants; Klatt 2013). This would give an MD of 0.09 days (95% CI −0.32 to 0.50) for epidural analgesia versus systemic analgesia. This trial was at low risk of bias for random sequence generation, attrition bias, and reporting bias. Other domains were at unclear/high risk of bias. Trial sequential analysis calculated that 48 participants were required to eliminate a one-day difference (alpha 0.05; power 80%; empirical variance 1.5; model-based variance). We downgraded the quality of evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

3c. Time to first liquid ingestion (hours)

Two trials with 56 participants reported time to first oral liquid ingestion (Cassady 2000; Malviya 1999). Cassady 2000 infused a mixture of a local anaesthetic and an opioid. Malviya 1999 infused opioids only. Malviya 1999 was at unclear risk of bias for random sequence generation, allocation concealment, blinding of participant and personnel taking care of participant, and for blinding of outcome assessment. Malviya 1999 was at low risk of bias for all other domains. Cassady 2000 was at low risk of bias for random sequence generation, attrition bias, and reporting bias. Cassady 2000 was at unclear/high risk of bias for all other domains.

We did not find a difference in time to first liquid oral intake (MD −5.02 hours, 95% CI −13.15 to 3.10; Analysis 1.10). Trial sequential analysis calculated that 301 participants were required to eliminate a five-day difference (empirical) (alpha 0.05; power 80%; two-sided test; variance empirical; model variance based heterogeneity correction). We downgraded the quality of evidence by one level for risk of bias and two levels for imprecision, and rated quality of evidence for absence of effect as very low.

3d. Time to first solid food ingestion (hours)

One trial with 30 participants provided data for time to ingestion of solid foods (Blumenthal 2006). Using a double catheter technique with ropivacaine alone on participants undergoing anterior correction of thoracic scoliosis, Blumenthal and colleagues reported that participants with epidural analgesia were more likely to have their first solid foods ingested within 48 hours (RR 7.00, 95% CI 1.91 to 25.62). Based on a 13.3% incidence of solid food intake within 48 hours in the control group, the NNTB would be 2 (95% CI 2 to 3). Blumenthal 2006 was at unclear risk of bias for allocation concealment and for blinding of personnel taking care of the participants and at low risk of bias for all other domains. Trial sequential analysis calculated that 150 participants were required to eliminate a 25% difference (alpha 0.05; power 80%; two-sided test; 90% incidence in the intervention arm; model variance based heterogeneity correction). We downgraded the quality of the evidence by one level for risk of bias and by two levels for imprecision and rated it very low.

For Summary of findings for the main comparison for return of gastrointestinal function, we presented all results available. There were no data available as time to event in hours.

Secondary outcomes

1. Time to first mobilization (days)

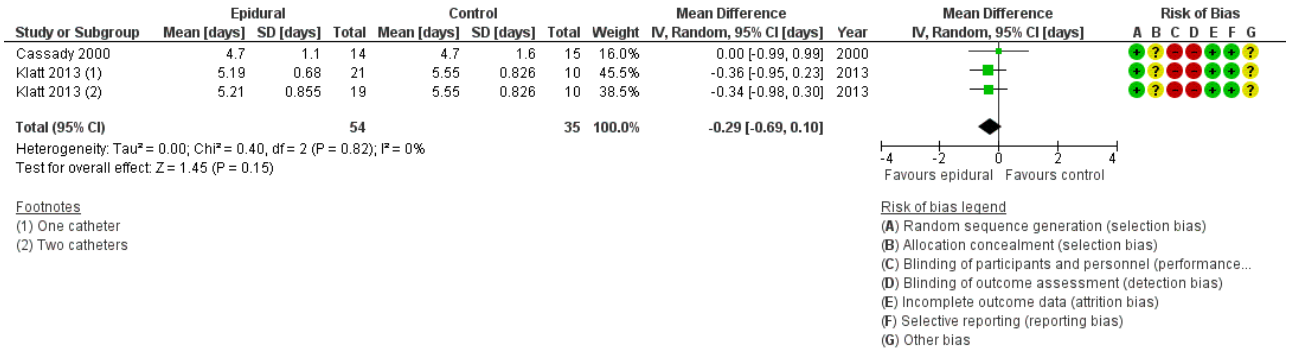
Data related to this outcome were available only for time to ambulate after surgery. One trial with 60 participants gave results for time to ambulate (MD 0.08 days, 95% CI −0.24 to 0.39) (Klatt 2013). Klatt 2013 was at unclear/high risk of bias for allocation concealment, blinding of participants and personnel taking care of the participants, blinding of outcome assessment, and other bias, and at low risk of bias for all other domains. Trial sequential analysis calculated that 48 participants were required to eliminate a one-day difference (alpha 0.05; power 80%; two-sided test; variance 1.5; heterogeneity correction model variance based). We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated absence of effect as very low.

2. Hospital length of stay (days)

We found no data on time to readiness for discharge. Two trials with 89 participants reported on hospital length of stay (Cassady 2000; Klatt 2013). Random sequence generation and attrition bias were at low risk of bias for the two trials. Allocation concealment, blinding of participants and personnel taking care of the participants,

blinding of outcome assessment, and other risk of bias were at unclear/high risk of bias for the two trials. Reporting bias was at low risk for Cassady 2000 and at unclear risk for Klatt 2013. We found no difference in hospital length of stay (MD –0.29 days, 95% CI –0.69 to 010; Analysis 1.11; Figure 6). Trial sequential analysis calculated that 29 participants were required to eliminate a one-day difference (alpha 0.05; power 80%; two-sided test; empirical variance; heterogeneity correction model variance based). We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated absence of effect as very low quality of evidence.

Figure 6. Forest plot of comparison: 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, outcome: 1.11 Hospital length of stay (days).



3. Satisfaction with postoperative analgesia regimen (any ascending or descending scale as provided by study authors)

3a. Participant satisfaction

In their methods section, Gauger 2009 mentioned that participants were asked to rate their level of satisfaction with analgesia treatment as very dissatisfied, somewhat dissatisfied, somewhat satisfied, or very satisfied. Their results were reported as only one participant in each group reported dissatisfaction with their pain management. This trial was at low risk of bias for random sequence generation, attrition bias, and reporting bias. Gauger 2009 was at unclear/high risk of bias for all other domains.

Two trials with 60 participants reported a higher score for participant satisfaction with epidural analgesia (MD 1.62, 95% CI 1.26 to 1.97; Blumenthal 2005; Blumenthal 2006; Analysis 1.12). Random sequence generation, attrition bias, reporting bias, and other bias were at low risk of bias for the two trials. Allocation concealment and blinding of participants and personnel taking care of participants were at unclear/high risk of bias for the two trials. Blinding of outcome assessment was at low risk of bias for Blumenthal 2006 and at high risk of bias for Blumenthal 2005. Trial sequential analysis calculated that 48 participants were required to eliminate a 1-point difference (alpha 0.05; power 80%; two-sided test; variance 1.5; heterogeneity correction model variance based) and that the Z curve crossed the boundary in favour of epidural analgesia. We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

3b. Parent satisfaction

One trial reported on parent satisfaction score (MD 0.60, 95% CI –0.81 to 2.01) (Malviya 1999). Malviya 1999 was at low risk of bias for attrition bias, reporting bias, and other bias, and at unclear risk of bias for all other domains. Trial sequential analysis calculated that 108 participants were required to eliminate a 1-point difference (alpha 0.05; power 80%; two-sided test; variance empirical; heterogeneity correction model variance based). We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

For the 'Summary of findings' table for satisfaction, we presented results available for participant and for parent satisfaction. No trial reported satisfaction at more than one time point.

4. Complications (related to analgesic techniques (epidural or systemic analgesia), including respiratory depression, hospital inpatient falls, and infections (e.g. wound infection, epidural abscess) within 30 days of surgery) and neurological complications

Part of this outcome was reported as a narrative review and we provided additional details in Table 3.

Complications possibly related to epidural analgesia

Technical issues

One trial reported a high rate of primary catheter failure (37%) (Gauger 2009). Gauger 2009 did not confirm the catheter position with an intraoperative radiography. One trial reported 10 cases of epidural leakage (out of 21 participants with a single catheter and 18 participants with two catheters) causing discontinuation for two participants (Klatt 2013). One trial reported one dislodged catheter during utilization. None of these trials mentioned any precautions taken to prevent catheter dislodgment or leakage, or both (Malviya 1999) (Table 3).

Side effects

There was transient partial lower limb motor blockade after the initial loading dose for 4/30 participants (Blumenthal 2005); and for 2/30 participants (Blumenthal 2006), in two trials using ropivacaine alone. Motor strength normalized within 180 minutes for all participants. Three trials noted paraesthesia of the lower limbs: Gauger 2009 (1/19 participants), Klatt 2013 (4/21 for participants with one catheter and 1/18 for participants with two catheters), and O'Hara 2004 (7/22 participants) (Table 3).

One trial reported one participant with hypotension requiring epidural discontinuation (Gauger 2009; Table 3).

Complications

One participant had respiratory depression (oxygen desaturation less than 90%) (Gauger 2009; Table 3; Analysis 1.13). There were no neurological complications attributed to epidural analgesia (see below).

Complications possibly related to systemic analgesia

Two of 19 participants remained intubated and ventilated for several hours (Gauger 2009). Three participants had respiratory depression (oxygen desaturation less than 90%) in Gauger 2009 and one participant had increased partial pressure of carbon dioxide ($PaCO_2$; from 6.5 kPa to 7.8 kPa or 50 mmHg to 60 mmHg) and decreased respiratory rate (6 breaths/minute to 8 breaths/minute) in O'Hara 2004.

4a. Respiratory depression

Four trials with 126 participants reported on the number of participants with respiratory depression for the two modes of treatment (Cassady 2000; Gauger 2009; Malviya 1999; O'Hara 2004). Random sequence generation was at unclear risk of bias for Malviya 1999 and at low risk of bias for the other three trials. Allocation concealment was at low risk of bias for one trial (O'Hara 2004) and at unclear risk of bias for the other three trials. Blinding of participants and personnel taking care of the participants and blinding of outcome assessment were at low risk of bias for O'Hara 2004, and at unclear/high risk of bias for the other three trials. Attrition and reporting bias were at low risk for the four trials. Other risks of bias were at low risk for Malviya 1999, and at unclear risk for the other three trials.

We did not find a difference in the risk of respiratory depression (RD −0.05, 95% CI −0.16 to 0.05; Analysis 1.13). There was no evidence of small-study effect or publication bias. Trial sequential analysis indicated that the information size for a 25% relative risk reduction was 12,200 (alpha 0.05; power 80%; two-sided test; 10.6% incidence in the control arm; RD; random-effects model; model variance based). We downgraded the quality of the evidence by one level for risk of bias and by two levels for imprecision, and rated it very low.

4b. Hospital inpatient falls

No trial reported on hospital inpatient falls.

4c. Infections (e.g. wound infection or epidural abscess) within 30 days of surgery

4c.1. Wound infection

Cassady 2000 reported one wound infection in the epidural group versus none in the systemic analgesia group. Klatt 2013 reported no wound infection in either group. Therefore, based on two trials with 93 participants, we did not find a difference for wound infection (RD 0.01, 95% CI −0.05 to 0.08; I^2 = 0%; Analysis 1.14) (Cassady 2000; Klatt 2013). The two trials were at unclear/high risk of bias for allocation concealment, blinding of participant and personnel taking care of the participant, blinding of outcome assessment, and other risks of bias. The two trials were at low risk of bias for all other domains. Trial sequential analysis calculated that the information size for a 50% relative risk reduction was 15,171 (alpha 0.05; power 80%; two-sided test; 1.8% incidence in the intervention arm; RD; random-effects model; model variance based). We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

4c.2. Epidural abscess

Two trials reported no complication/problem associated with the catheters (Blumenthal 2005; Blumenthal 2006). Ezhevskaya 2015 reported no complications in either group. Klatt 2013 reported that late -onset neurological events were absent in all participants. Random sequence generation was at low risk for three trials (Blumenthal 2005; Blumenthal 2006; Klatt 2013), and at unclear risk for Ezhevskaya 2015. Allocation concealment was at unclear risk of bias for the four trials. Blinding of participant and personnel taking care of the participant and blinding of outcome assessment were at low risk for Ezhevskaya 2015 and at unclear/high risk for the other three trials. Attrition bias and reporting bias were at low risk for the four trials. Other risks of bias were at unclear risk for Klatt 2013 and at low risk for the other three trials. The treatment group distribution was unknown for one trial (Ezhevskaya 2015). Therefore, based on three trials with 120 participants, we did not find a difference in epidural abscess (RD 0.00, 95% CI −0.05 to 0.05; I^2 = 0%; Analysis 1.15) (Blumenthal 2005; Blumenthal 2006; Klatt 2013). Trial sequential analysis indicated that the information size for a 50% relative risk reduction was 2,147,483,647 (alpha 0.05; power 80%; two-sided test; 0.01% incidence in the control arm (Sethna 2010); RD; random-effects model; heterogeneity correction model variance based). We downgraded the quality of the evidence by one level for risk of bias and two levels for imprecision, and rated it very low.

4d. Neurological complications

Blumenthal 2005 and Blumenthal 2006 reported no complications/problems associated with the catheters. Ezhevskaya 2015 reported no complications in either group. Klatt 2013 reported that late-onset neurological events were absent in all participants. O'Hara 2004 reported three participants with lasting neurological problems in the epidural group. Two participants had persistent sensory deficits that resolved at three and six months. Their conclusions were that these problems were secondary to the spinal correction. One participant was excluded from the trial due to lower extremities paralysis on emergence from anaesthesia. According to the protocol, this participant had received a bolus of 3 mL of a solution containing bupivacaine 0.1% and fentanyl 5 µg/mL followed by an infusion at 4 mL/hour started prior to wound closure. Paralysis resolved at eight months and was judged to be secondary to the spinal correction. Therefore, all neurological complications were secondary to the surgical procedure and there was no neurological complication attributed to epidural analgesia. The treatment group distribution was unknown for one trial (Ezhevskaya 2015).

Based on four trials with 151 participants, we did not find a difference in the risk of neurological complications (RD 0.01, 95% CI −0.04 to 0.06; I^2 = 0%). Random sequence generation, attrition bias, and reporting bias were at low risk for the four trials. Allocation concealment was at low risk of bias for one trial (O'Hara 2004), and at unclear risk of bias for the other three trials. Blinding of participant and personnel taking care of the participants was at low risk for one trial (O'Hara 2004), and at unclear/high risk for three trials (Blumenthal 2005; Blumenthal 2006; Klatt 2013). Blinding of outcome assessment was at low risk for two trials

(Blumenthal 2006; O'Hara 2004), and at unclear/high risk for two trials (Blumenthal 2005; Klatt 2013). Other risks of bias were at low risk for two trials (Blumenthal 2005; Blumenthal 2006), and at unclear risk for two trials (Klatt 2013; O'Hara 2004). Trial sequential analysis indicated that the information size for a 50% relative risk increase was 9971 (alpha 0.05; power 80%; two-sided test; 0.033% incidence in the intervention arm; 0.022% incidence in the control arm; random-effects model; heterogeneity correction model variance based). We downgraded the quality of evidence for absence of difference by three levels: one for risk of bias and two for imprecision and rated it very low.

DISCUSSION

Summary of main results

This review demonstrates that epidural analgesia reduces postoperative pain, accelerates return of gastrointestinal function (local anaesthetic alone), and increases patient satisfaction.

An improvement in pain control after surgery with the use of epidural analgesia compared with systemic analgesia such as found in the present review was in accordance with results found in adults for various surgeries including abdominal surgery (Guay 2016). However, it was unclear if better analgesia at rest and on movement for at least 72 hours after surgery would have been significant if all included studies had adhered to aggressive systemic analgesia for all of the included participants.

Likewise, acceleration of return of gastrointestinal function with an epidural containing a local anaesthetic is also consistent with results found on other type of surgeries (Guay 2016). Epidural analgesia may promote a faster return of intestinal transit through various mechanisms including a reduction in opioid administration, a blockade of sympathetic gut innervation (creating a relative parasympathetic predominance), a direct effect of systemic local anaesthetics, or a combination of these (McCarthy 2010). However, as opposed to findings in abdominal surgery, for spine surgery there was a faster return of gastrointestinal function clearly demonstrated only in trials using local anaesthetic without the addition of opioids (Blumenthal 2005; Blumenthal 2006). Although one author reported that bowel sounds were present in a higher percentage of participants on the day of surgery (20% for epidural analgesia versus 0% for systemic analgesia) and at postoperative day one (80% versus 43.75%) while using a mixture of local anaesthetic and an opioid, this did not result in faster resumption of liquid oral intake (Cassady 2000). Likewise, also infusing a mixture of a local anaesthetic and an opioid through one or two catheters, Klatt 2013 reported similar mean times for first bowel movement after surgery.

Thoraco-lumbar spine surgery is associated with risks of neurological damage. Therefore, being able to proceed to a neurological examination after the surgery is critical. Interestingly, our review seemed to suggest that epidural opioids alone would be an acceptable mode of pain control at rest during the first few hours after the surgery (Analysis 1.1). However, it is to note that only one trial used opioids alone (Malviya 1999), and this trial was not performed on children undergoing scoliosis surgery but on children with cerebral palsy undergoing selective dorsal rhizotomy. The latter is a surgery much less extensive than scoliosis surgery consisting in partial or complete laminectomies at six spinal levels only. Therefore, the use of opioids only would need to be studied before applying this solution to children undergoing scoliosis surgery. Also, delaying the introduction of epidural local anaesthetics to postoperative day one such as done in two trials (Blumenthal 2005; Blumenthal 2006), did not seem to impede the beneficial effect of epidural local anaesthetic to influence the accelerative return of gastrointestinal function (Analysis 1.9).

The use of epidural analgesia may be associated with some technical problems. One author noted a high rate of primary catheter failure (Gauger 2009). This was not corroborated by other authors. As the catheter is most often inserted by the surgeon at the end of surgery under direct vision, one would normally expect that most catheters would be placed in an optimal position. However, this might not be the case for surgeons unfamiliar with the technique. Blumenthal and colleagues confirmed all catheter positions with injection of a contrast material and intraoperative radiographies (Blumenthal 2005; Blumenthal 2006). Three trials mentioned that their catheter insertion technique was similar to the one reported by Shaw 1996 (Cassady 2000; Gauger 2009; Klatt 2013). Shaw and colleagues used a Teflon-styletted catheter passed through the paravertebral soft tissue. The exact type of catheter (open-ended versus multiport, soft tip versus firm tip, or wire-reinforced or not) used in the included trials was unclear. One author reported a dislodged catheter (Malviya 1999). None of the trials reported methods of catheter fixation. Finally, one author reported a high rate of catheter leakage causing premature cessation of epidural analgesia in two participants (Klatt 2013). None of the trials mentioned methods to prevent leakage (Auyong 2017).

There were no neurological complications attributed to epidural analgesia in any of the included trials. Our review was clearly underpowered to eliminate an increase in incidence of neurological complications with epidural analgesia in this population. There were three neurological complications attributed to the surgery and they all came from the same trial (O'Hara 2004). This trial included 31 participants. Ten participants received an infusion of bupivacaine 0.1% and fentanyl 5 µg/mL, 12 participants received an infusion of bupivacaine 0.0625% and fentanyl 5 µg/mL, and nine participants received an infusion of 0.9% sodium chloride. They reported three lasting complications (longer than one month). Of the three complications, two were sensory deficits only (no motor loss) and all three complications resolved within one year. The incidence of neurological complications reported by these authors (3/31 participants; 9.7% (95% CI 3.4% to 24.9%) exceeded the incidence expected with actual techniques (less than 1%; de Mendonca 2016).

Haematomas are possible even with epidural catheter placement under direct vision. Some patients may have congenital haemostasis abnormalities contributing or not to increased risk of bleeding. For instance, idiopathic scoliosis is associated with abnormal collagen and platelet function (Floman 1983; Uden 1980). Children with cerebral palsy or muscular dystrophies may have increased bleeding (Brenn 2004; Noordeen 1999). Finally and most of all, dilution of coagulation factors or platelets (or both) or fibrinolysis that may occur (especially with extensive surgeries) not only mandate adequate blood loss/transfusion-sparing strategies but also strict monitoring before considering epidural catheter insertion and withdrawal (Alajmi 2017; Guay 1994; Horlocker 2001; Nakai 2011). It is unclear if laminectomies performed during

surgery would offer any degree of protection against neurological damage due to a compression from haematoma.

Overall completeness and applicability of evidence

We are confident that our review reflects the available literature on epidural analgesia for thoraco-lumbar spine surgery in children.

Quality of the evidence

The quality of evidence was moderate, low, or very low. Despite this imperfect quality of the body of evidence, we are quite confident that epidural analgesia reduces pain at rest and on movement up to 72 hours after surgery. This is supported by the fact that pain was lower in epidural groups at all time points where we measured it. Although the reduction may seem modest, most differences were higher than 1 point. Considering that this is just a mean (some children may have experienced more pain than others) and that this lasted at least 72 hours, we consider that this finding is clinically relevant. Likewise, although some measurements concerning a faster return of gastrointestinal transit were contradictory and present only when local anaesthetics alone were infused, we consider that being able to increase the number of children who tolerate solid food within 48 hours is also highly clinically relevant.

Potential biases in the review process

The quality of the trials, though not optimal, was comparable to other trials published on epidural analgesia (Guay 2016), and probably sufficient enough to allow us to draw valid conclusions. Strikingly, we discovered a low number of published trials on this important issue. Although a well-known unfortunate phenomenon, science on the management of children is often derived from trials published on adults. In this review, three of the trials included in the analysis contained some participants older than 18 years: Blumenthal 2005 (10 to 30 years; mean age 17 years), Klatt 2013 (10 to 21 years), and O'Hara 2004 (13 to 21 years). This causes us to agree with some authorities that specify children as 'therapeutic orphans' within research (Morales-Olivas 2006). Unfortunately, a paucity of evidence to aid clinical practice for children has continued despite efforts such as the Pediatric Research Equity Act (PREA) passed in 2003 (Hudgins 2018). For instance, many drugs commonly used in children are administered without formal paediatric data to support their benefit. A cross-sectional analysis of new drug applications submitted to the US Federal Drug Agency (FDA) from December 2003 to July 2012 revealed that the mean time between approval in adults and availability of paediatric data for drugs approved without paediatric assessments was 6.5 years (Hudgins 2018). Likewise, off-label medications would be prescribed 1.5 times more than FDA-approved medications for children with migraines (Lai 2017). We think that support to encourage more paediatric well-performed trials is still needed. Nevertheless, we do not think that the inclusions of trials that may have contained some participants older than 18 years of age was extensive enough to affect the validity of our findings.

We attempted to conduct a comprehensive search for studies, but the fact that one study has not yet been incorporated may be a source of potential bias.

Study authors used different pain scales. When this happens, analysis should be done as SMD instead of MDs (Borenstein 2009b). Because this is not a 'clinical' unit, we did two things. First, when all scales were scales from 0 to 10, we gave results both as means and SDs and as SMDs (Analysis 1.1; Analysis 1.2; Analysis 1.4). Conclusions drawn were never affected by the type of analysis (MD or SMD). Second, when we could give results only as SMDs, then we gave a clinical equivalence.

Agreements and disagreements with other studies or reviews

Improved postoperative analgesia and acceleration of return of gastrointestinal function with epidural analgesia compared with systemic analgesia is in accordance with the findings reported for other types of surgeries in other populations (Guay 2016). Likewise, one meta-analysis comparing epidural analgesia with IV analgesia in people undergoing major spine surgery reported that epidural analgesia provided significantly superior analgesia, higher patient satisfaction, and decreased overall opioid consumption compared with IV patient-controlled analgesia following major spine surgery (Meng 2017). Review authors found no difference in the adverse effects associated with these two methods of analgesia and conclude that high-quality trials are needed to verify their findings (Meng 2017).

AUTHORS' CONCLUSIONS

Implications for practice

There is moderate- and low-quality evidence that there may be a small additional reduction in pain up to 72 hours after surgery with epidural analgesia compared with systemic analgesia. Two very small studies showed epidural analgesia with local anaesthetic alone may accelerate the return of gastrointestinal function. The safety of this technique in children undergoing thoraco-lumbar surgery is uncertain due to the very low quality of the evidence.

The study in 'Studies awaiting classification' table may alter the conclusions of the review once assessed.

Implications for research

Large randomized trials comparing epidural analgesia with systemic analgesia in the context of maximal co-analgesia and intravenous lidocaine might be useful.

Large prospective trials establishing the safety of epidural analgesia in this specific context might be useful.

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Protocol

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Blumenthal 2005

Methods	Parallel RCT Ethics committee: approval obtained Informed consent: written consents obtained Site: Orthopaedic University Hospital Balgrist, Zurich, Switzerland Setting: university hospital Dates of data collection: over 18-month period Funding: institutional or departmental sources, or both
Participants	30 participants **Inclusion criteria** ASA 1–3, aged 10–30 years (mean age 17 years), body weight 30–90 kg, body height 130–180 cm, elective idiopathic scoliosis correction with a dorsal approach over at least 7 vertebral levels, no participant had iliac crest bone harvest **Exclusion criteria** Any contraindication for epidural catheter placement, known allergy to drugs used in the study, drug abuse, pregnancy, cardiac arrhythmia or myocardial infarction within the previous 6 months, preoperative neurological deficit, inability to use a visual analogue scale with a scaled ruler for assessing adequately postoperative pain, incorrect epidural catheter placement, accidental perforation of the dura while placing the epidural catheter, or occurrence of postoperative neurological deficit No participant had iliac crest bone harvest
Interventions	***Intervention:*** continuous double epidural catheter technique (n = 15) ***Comparator:*** continuous IV morphine (n = 15)
Outcomes	**Relevant to this review** 1. Pain at rest and on movement (coughing) 2. Vomiting (number of participants who experienced vomiting from 0 to 48 hours) 3. Bowel function (time to first flatus) 4. Patient satisfaction **Others** 1. Rescue analgesic 2. Pruritus 3. Pulmonary complications defined as respiratory rate < 8 breaths/minute, oxygen saturation < 92%, or apparent lobar atelectasis on chest radiograph
Notes	Registration: not reported Conflict of interest: none reported DOI: not available

Blumenthal 2005 *(Continued)*

Correspondence: email sent 7 October 2017. Authors replied that their data were no longer available. Additional information requested on 23 February 2018. Authors did not reply.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "prospectively randomized according to a computer randomization list."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "unblinded"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "unblinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants were excluded during the study.
Selective reporting (reporting bias)	Low risk	All measurement reported
Other bias	Low risk	Groups well balanced

Blumenthal 2006

Methods	Parallel RCT Ethics committee: approval obtained Informed consents: written consents obtained Site: Departments of Anesthesiology and Orthopedic Surgery, Balgrist Clinic, and Department of Orthopedics, University of Zurich, Zurich, Switzerland Setting: university hospital Dates of data collection: unspecified Funding: no funds received
Participants	30 adolescents **Inclusion criteria** ASA 1–3, aged 11–17 years (mean age 14 years), body weight 30–90 kg, body height 130–180 cm, thoracic idiopathic scoliosis scheduled for anterior correction through thoracotomy approach with the instrumentation of ≥ 6 vertebral levels **Exclusion criteria**

Blumenthal 2006 *(Continued)*

	Any contraindications for epidural catheter placement, known allergy to the study drugs, drug abuse, preoperative neurological deficit, inability to use a visual analogue scale, incorrect epidural catheter placement including accidental perforation of the dura, and postoperative neurological deficit
Interventions	***Intervention:*** continuous double epidural catheter technique (n = 15) ***Comparator:*** continuous IV morphine (n = 15)
Outcomes	**Relevant to this review** 1. Pain at rest and on movement (coughing) 2. Vomiting (number of participants who experienced vomiting from 0 to 48 hours) 3. Bowel function (time to first flatus) 4. Patient satisfaction **Others** 1. Rescue analgesic 2. Pruritus 3. Pulmonary complications defined as oxygen saturation < 92% or lobar atelectasis on chest radiograph
Notes	Registration: not reported Conflict of interest: no benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript. DOI: N/A Correspondence: Email sent 8 October 2017, reply received 24 October 2017. Additional information requested on 23 February 2018. Authors did not reply.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized to either the IV morphine group or the epidural catheter group using computer randomization program.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Data collection was done by a research nurse not involved in and not aware of the aim of the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Low risk	Groups well balanced

Cakar Turhan 2011

Methods	Parallel RCT Ethics committee: not reported Informed consent: not reported Site: Department of Anesthesiology and Intensive Care Unit, Ankara University, Faculty of Medicine, Ankara, Turkey Setting: university hospital Dates of data collection: unspecified Funding: unspecified
Participants	30 participants **Inclusion criteria** Adolescents with idiopathic scoliosis **Exclusion criteria** Not reported
Interventions	***Intervention:*** preoperative segmental epidural analgesia (single injection) plus wound infiltration plus IV PCA with morphine (n = 15) ***Comparator:*** IV PCA with morphine (n = 15)
Outcomes	**Relevant to this review** 1. Pain scores at rest and on movement 2. Patient satisfaction **Others** 1. Rescue analgesia 2. Sleep quality
Notes	Registration: not reported Conflict of interest: not reported DOI: N/A Conference abstract only Correspondence: email sent 9 October 2017, no reply received. Additional information requested on 23 February 2018. Authors did not reply.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized;" no details
Allocation concealment (selection bias)	Unclear risk	Not reported

Cakar Turhan 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double blind study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported
Selective reporting (reporting bias)	Low risk	Results reported in the method section were reported in the results section
Other bias	Unclear risk	Few details available, conference abstract. Wound infiltration at the end of surgery for the epidural group only.

Cassady 2000

Methods	Parallel RCT Ethics committee: approved by the Nemours Children's Clinic Clinical Research Review Committee and the Baptist Medical Center Institutional Review Board. Informed consent: each participant gave written assent for participation in the investigation. Written informed consent was obtained from each patient's parent or legal guardian. Site: Wolfson Children's Hospital, Jacksonville, FL Setting: university hospital Dates of data collection: unspecified Funding: supported by the Nemours Foundation. One study author was working for Ancile Pharmaceuticals (DDC), San Diego, CA, USA
Participants	33 participants **Inclusion criteria** ASA 1 or 2, aged 11–18 years with idiopathic scoliosis scheduled for elective posterior spinal fusion **Exclusion criteria** Coexisting haematological, cardiac, gastrointestinal, neurological, psychiatric, or pulmonary diseases; or a history of allergy to any of the study medications
Interventions	***Intervention:*** epidural analgesia (n = 17) ***Comparator:*** IV PCA with morphine (n = 16) Premedication: midazolam, either 0.5 mg/kg orally or 0.1–0.2 mg/kg IV, before entering the operating room Induction: sodium thiopental 4–5 mg/kg or propofol 2–3 mg/kg and a non-depolarizing muscle relaxant, i.e. either vecuronium 0.1 mg/kg or pancuronium 0.1 mg/kg

Cassady 2000 *(Continued)*

	Maintenance: nitrous oxide, isoflurane, and fentanyl
Outcomes	**Relevant to this review** 1. Pain scores (a 0 score was attributed when the participant was asleep; values taken at rest) 2. Vomiting 3. Return of gastrointestinal function 4. Respiratory depression (airway obstruction or respiratory rate < 10 breaths/minute or pulse oximetry ≤ 94% despite oxygen administration at 2 L/minute) **Others** 1. Analgesic requirement 2. Transfusion requirement
Notes	Registration: not reported Conflict of interest: not reported DOI: 10.1053/xr.2000.5661 Correspondence: Joseph R Cassady Jr, MD, Department of Anesthesiology and Critical Care Medicine, Nemours Children's Clinic, 807 Nra St, Jacksonville, FL 32207. E-mail: jcassady@nemours.org. Additional information requested on 23 February 2018. Invalid email address. Letter sent on 23 February 2018. Authors did not reply.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized by use of random numbers table"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "nonblinded"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "nonblinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 participants assigned to receive epidural analgesia and 1 participant receiving IV PCA were withdrawn from the study. Among the epidural group, 1 participant was judged by a member of the medical staff as too somnolent for safe initiation of the epidural bupivacaine-fentanyl infusion until approximately 2 hours after the required time, thus prohibiting initial data collection and introducing a major protocol violation. The second participant refused to comply with data collection postoperatively by rejecting the pain scale. The third participant had the epidural catheter removed in the postanaesthesia care unit at the request of her surgeon for a transient unilateral upper extremity neurological deficit that subsequently proved unrelated to analgesic therapy. The participant in the IV PCA group withdrew because of postoperative noncompliance with patient-controlled instructions.

Cassady 2000 *(Continued)*

Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Unclear risk	Not by intention-to-treat Number of fused vertebrae was 12.1 for epidural group and 10.4 for systemic analgesia

Ezhevskaya 2012a

Methods	Parallel RCT Ethics committee: not reported Informed consent: not reported Site: not reported Setting: university hospital Dates of data collection: not reported Funding: unspecified
Participants	135 participants aged 12–25 years with idiopathic scoliosis undergoing posterior spinal fusion and instrumentation **Inclusion criteria** Deformities Grade III or IV **Exclusion criteria** Not reported
Interventions	***Intervention:*** epidural analgesia (n = 70) ***Comparator:*** IV PCA with opioids (n = 65) Maintenance: sevoflurane and fentanyl
Outcomes	**Relevant to this review** 1. Pain scores 2. Return of gastrointestinal function 3. Satisfaction **Others** 1. Blood loss 2. Haemodynamic parameters
Notes	Registration: unspecified Conflict of interest: not reported DOI: not reported Correspondence: Anna A Ezhevskaya, MD, Department of Anesthesiology and Reanimation, Nizhny Novgorod Research Institute of Traumatology and Orthopedics, 18 Verhne-Voljskaya naberejnaya, Nizhny Novgorod, Russia, 603155; E-mail: annaezhe@yandex.ru

Ezhevskaya 2012a *(Continued)*

	Email sent 22 January 2018, no reply received. Additional information requested on 23 February 2018. Authors did not reply

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "prospectively randomized", no details
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear; groups unequal (45 vs 35), no explanation provided
Selective reporting (reporting bias)	Unclear risk	Conference abstract; no numbers provided
Other bias	Unclear risk	No details on group characteristics

Ezhevskaya 2015

Methods	Parallel RCT Ethics committee: not reported Informed consent: not reported Site: not reported Setting: university hospital Dates of data collection Funding: unspecified
Participants	115 participants, aged 15–18 years undergoing scoliosis surgery **Inclusion criteria** Not reported **Exclusion criteria** Not reported
Interventions	***Intervention:*** epidural analgesia with (n = unspecified) or without tranexamic acid (n = unspecified)

Ezhevskaya 2015 *(Continued)*

	Comparator: systemic analgesia with (n = unspecified) or without tranexamic acid (n = unspecified) General anaesthesia with sevoflurane
Outcomes	**Relevant to this review** 1. Complications **Others** 1. Blood loss
Notes	Registration: unspecified Conflict of interest: not reported DOI: N/A Correspondence: Anna A Ezhevskaya, MD, Department of Anesthesiology and Reanimation, Nizhny Novgorod Research Institute of Traumatology and Orthopedics, 18 Verhne-Voljskaya naberejnaya, Nizhny Novgorod, Russia, 603155; E-mail: annaezhe@yandex.ru Email sent to authors 22 January 2018. Text of abstract received from authors. Additional information requested 23 February 2018. Authors did not reply

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized," no details
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blind study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported
Selective reporting (reporting bias)	Low risk	Conference abstract reporting on blood loss
Other bias	Low risk	No failed epidural reported No details on demographic data provided

Gauger 2009

Methods	Parallel RCT

Gauger 2009 *(Continued)*

	Ethics committee: approved by Institutional Review Board Informed consent: written informed consent obtained from parents or guardians, and oral assent obtained from participant Site: University of Michigan Health Systems, Ann Arbor, MI, USA Setting: university hospital Dates of data collection: between August 2003 and June 2006 Funding: unspecified
Participants	38 participants **Inclusion criteria** ASA 1 or 2, aged 8–18 years undergoing posterior spinal fusion for idiopathic scoliosis **Exclusion criteria** Unspecified
Interventions	***Intervention:*** epidural analgesia (n = 19) ***Comparator:*** IV PCA (n = 19) Premedication: oral acetaminophen (paracetamol; 15 mg/kg; maximum 650 mg) plus midazolam at the discretion of the attending physician Induction: sevoflurane Maintenance: nitrous oxide, isoflurane, propofol, and sufentanil Aprotinin
Outcomes	**Relevant to this review** 1. Pain scores 2. Vomiting 3. Satisfaction (number of participants satisfied with the technique) **Others** 1. Analgesic requirements 2. Muscle spasms (8% of participants who received epidural analgesia experienced moderate-to-severe spasms through postoperative day 3 compared with 35% of participants in the IV group (P > 0.05). 7 (58%) participants in the epidural analgesia group and 17 (100%) participants in the systemic analgesia group required diazepam (P = 0.007).
Notes	Registration: not reported Conflict of interest: not reported DOI: 10.1097/BPO.0b013e3181b2ba08 Correspondence: Michelle S Caird, MD, Department of Orthopaedic Surgery, Pediatric Orthopaedics Service, 1500 E. Medical Center Dr Ann Arbor, MI 48109; E-mail: sugiyama@med.umich.edu. Email sent 13 January 2018, no reply received. Additional information requested 23 February 2018. Authors did not reply
Risk of bias	

Gauger 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random numbers table"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "findings from this study may have been limited by our inability to blind patients or care providers to the study group assignment."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Self-reported pain score of unblinded participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	43 participants enrolled in this study. However, 2 participants with neuromuscular scoliosis were inadvertently recruited and 3 in the epidural group never had an epidural catheter placed (1 due to intraoperative bleeding, 1 due to intraoperative hypotension, and 1 where the catheter could not be advanced). These participants were excluded from the study, leaving 19 participants each in the epidural and IV groups. 7 participants in the epidural analgesia group (37%) experienced early epidural failure, and 2 in the IV PCA group remained intubated, sedated, and ventilated for several hours postoperatively; these participants were included in the intention-to-treat analysis.
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Unclear risk	Not by intention-to-treat Quote: "all data are presented as "per protocol" unless otherwise specified."

Klatt 2013

Methods	Parallel RCT Ethics committee: approval obtained Informed consent: informed consents obtained Site: Primary Children's Medical Center, Salt Lake City, University of Utah School of Medicine, Salt Lake City, UT, USA Setting: university hospital Dates of data collection: 2009–2011 Funding: departmental "no funds were received in support of this work."
Participants	60 participants **Inclusion criteria** Aged 10–21 years; body weight 30–90 kg

Klatt 2013 *(Continued)*

	Exclusion criteria Contraindications to epidural catheter placement, known allergy to study drugs, history of drug abuse, pregnancy, cardiac arrhythmia, or neurological deficit
Interventions	***Intervention:*** single catheter epidural analgesia (n = 21) or double catheter technique (n = 18) ***Comparator:*** IV analgesia (n = 21) Premedication: participants who required preoperative anxiolysis received midazolam 0.5 mg/kg (up to a maximum of 15 mg) orally or 2 mg IV Induction: propofol, lidocaine, fentanyl, and rocuronium Maintenance: desflurane or propofol and fentanyl Nausea and vomiting prophylaxis with dexamethasone 4 mg and ondansetron 4 mg
Outcomes	**Relevant to this review** 1. Pain scores 2. Vomiting 3. Return of gastrointestinal function 4. Time to first mobilization 5. Hospital length of stay **Others** 1. Analgesic requirements
Notes	Registration: not registered Conflict of interest: "relevant financial activities outside the submitted work: board membership, consultancy, royalties" DOI: 10.1097/BRS.0b013e31829cab0b Correspondence: Joshua WB Klatt, MD, Department of Orthopaedic Surgery, University of Utah School of Medicine, Primary Children's Medical Center, 100 N Mario Capecchi Dr, Ste 4550, Salt Lake City, UT 84113; E-mail: joshua.klatt@hsc.utah.edu Email sent 20 January 2018, additional information received 22 and 28 January 2018. Additional information requested 23 February 2018, response received 23 February 2018

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized using a random number generator"
Allocation concealment (selection bias)	Unclear risk	Quote: "randomized using a random number generator"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "unblinded"
Blinding of outcome assessment (detection bias)	High risk	Quote: "unblinded"

Klatt 2013 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants were withdrawn due to the inability to maintain the pain management protocol (n = 4) or epidural leak (n = 2)
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Unclear risk	Not in intention-to-treat: 3 of the withdrawn participants mistakenly received alternate modes of pain management, whereas 1 (withdrawn due to a protocol deviation) continued on the same mode; however, the protocol regimen was modified.

Malviya 1999

Methods	Parallel RCT Ethics committee: approved by the University of Michigan Institutional Review Board Informed consent: written informed consents obtained from parents Site: CS Mott Children's Hospital, Ann Harbor, MI, USA Setting: university hospital Dates of data collection Funding: departmental
Participants	27 participants **Inclusion criteria** Aged 2–14 years with spastic cerebral palsy scheduled for posterior selective rhizotomy **Exclusion criteria** Scheduled for multiple procedures
Interventions	***Intervention:*** epidural analgesia (n = 13) ***Comparator:*** IV analgesia (n =14) Induction and maintenance: halothane Maintenance: nitrous oxide and isoflurane Rectal acetaminophen (paracetamol)
Outcomes	**Relevant to this review** 1. Pain scores 2. Vomiting 3. Return of gastrointestinal function measured as: time to first liquid ingestion (hours) and time to first solid food ingestion (hours) 4. Parent satisfaction **Others**

Malviya 1999 *(Continued)*

1. Respiratory depression
2. Muscles spasms
3. Activity tolerance

Notes	Registration: unspecified Conflict of interest: unspecified DOI: N/A Correspondence: Shobha Malviya, MD, Department of Anesthesiology, CS Mott Children's Hospital, F3900/Box 0211, 1500 E Medical Center Drive, Ann Arbor, MI 48109-0211, USA. Email: smalviya@u-mich.edu. Additional information requested 23 February 2018. Authors did not reply

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned," no details
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	These nurses, blinded to the method of analgesia and to the bedside nurses' assessments, scored the child's pain during each segment using the FLACC behavioural tool. scores were later correlated with the bedside nurse's FLACC scores to determine the reliability of the bedside assessment of pain.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 participants in the epidural group excluded because 1 had received intraoperative IV opioids and in 1, the epidural catheter became dislodged on the first postoperative day
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Low risk	No failed epidural reported Groups well balanced

O'Hara 2004

Methods	Parallel RCT Ethics committee: institutional research board approval obtained Informed consent: written informed consents obtained Site: The Cleveland Clinic Foundation, Cleveland, OH, USA Setting: university hospital Dates of data collection: approximately 1998–2002

O'Hara 2004 *(Continued)*

	Funding: departmental resources
Participants	31 ASA 1 or 2 adolescents/young adults aged 13–21 years scheduled for elective posterior spinal fusion for idiopathic scoliosis **Inclusion criteria** Able to participate in visual analogue scale evaluations **Exclusion criteria** Anaesthetic or opioid allergy; history of chemical dependency; non-ambulatory status; participants with coexisting haematological, cardiac, gastrointestinal, neurological, psychiatric, or pulmonary disease
Interventions	***Intervention:*** epidural analgesia with 2 different concentrations (n = 22) ***Comparator:*** epidural saline infusion (n = 9) Premedication: midazolam ≤ 2 mg IV Induction: thiopental, sufentanil and a neuromuscular blocking agent (atracurium or vecuronium) Maintenance: nitrous oxide, isoflurane, sufentanil
Outcomes	**Relevant to this review** 1. Pain scores 2. Return of gastrointestinal function measured as: time to first liquid ingestion (hours) and time to first solid food ingestion (hours) 3. Time to first mobilization 4. Hospital length of stay (days) **Others** 1. Time ambulate
Notes	Registration: not registered outside the institution Conflict of interest: none DOI: 10.1111/j.1460-9592.2004.01387.x Correspondence: Jerome F O'Hara, Department of General Anesthesiology/E31, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA (email: oharaj@ccf.org). Additional information requested on 23 February 2018. Response received 1 March 2018

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random numbers table, patients were assigned to one of the three groups."
Allocation concealment (selection bias)	Low risk	Quote: "was blinded"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blinded"

O'Hara 2004 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	36 participants enrolled: epidural catheter could not be inserted for 2 participants; 1 participant had severe respiratory depression postoperatively; 1 participant emerged from anaesthesia with lower extremity paralysis, and 1 participant had incomplete data collection.
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Unclear risk	Not in intention-to-treat Groups comparable for demographic characteristics

Ozturk Mamik 2011

Methods	Parallel RCT Ethics committee: not reported Informed consent: not reported Site: not reported Setting: unspecified Dates of data collection: unspecified Funding: unspecified
Participants	30 participants **Inclusion criteria** Adolescents with idiopathic scoliosis undergoing posterior spinal fusion **Exclusion criteria** Not reported
Interventions	***Intervention:*** epidural analgesia (n = 15) ***Comparator:*** IV PCA (n = 15)
Outcomes	**Relevant to this review** 1. Pain scores **Others** 1. Analgesic requirements 2. Haemodynamic parameters
Notes	Registration: unspecified Conflict of interest: not reported DOI: not reported

Ozturk Mamik 2011 *(Continued)*

Correspondence: contact information not provided in the conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized: no details"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double blind study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All results reported
Other bias	Low risk	No failed epidural reported Groups were comparable for demographic data.

ASA: American Society of Anesthesiologists, DOI: Digital Object Identifier, FLACC: Faces, Legs, Activity, Cry, Consolability pain scores, IV: intravenous, n: number of participants; N/A: not available, PCA: patient-controlled analgesia; RCT: randomized controlled trial.

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

Study	Reason for exclusion
Adu-Gyamfi 1995	Different study design: not randomized
Aizenberg 2011	Different study design: not randomized
Akin Takmaz 2011	Different intervention. Compared continuous infusion vs patient-controlled analgesia in people with epidural analgesia with 2 catheters
Amaranath 1989	Different study design: not randomized
Arms 1998	Different study design. All participants had epidural analgesia
Bernard 1995a	Different population. Study on "young adults"
Cohen 2017	Different intervention. Comparison of intrathecal morphine vs epidural morphine
Ekatodramis 2002	Different study design. All participants had epidural analgesia

Study	Reason for exclusion
Erdogan 2017	Different intervention. Compared patient-controlled intermittent bolus epidural analgesia and patient-controlled continuous epidural analgesia for postoperative pain control in adolescent idiopathic scoliosis
Eshevskaya 2013	Different intervention. All participants had epidural analgesia after surgery
Ezhevskaya 2012b	Different study design. Possibly a retrospective study
Ezhevskaya 2012c	Different study design. Not randomized. Quote: "all patients were divided into two groups. Group E (N = 105) had epidural analgesia (ropivacaine, fentanyl, and epinephrine) and endotracheal anaesthesia with sevoflurane during surgery and continuous epidural analgesia with ropivacaine, fentanyl and epinephrine after surgery; Group G (N = 60) had general anaesthesia with sevoflurane and fentanyl and systemic administration of opioids after surgery."
Ezhevskaya 2014a	Different study population: 350 participants aged 15–65 years
Ezhevskaya 2014b	Different intervention: comparison of analgesic and opioid-sparing effects of a single-injection ultrasound-guided subcostal transversus abdominal plane block with continuous thoracic epidural analgesia
Goodarzi 1993	Different study population: no back surgery
Goodarzi 1999	Different intervention: comparison of epidural morphine, hydromorphone, and fentanyl for postoperative pain control in children undergoing various types of orthopaedic surgery
Khinkover 2006	Different study design. Not an RCT
Lawhorn 1994	Different intervention. Authors reported a randomized double-blind prospective study comparing epidural morphine 80 µg/kg to epidural morphine 80 µg/kg plus butorphanol 40 µg/kg in children undergoing rhizotomy.
Loughnan 1990	No outcome of interest measured
Lowry 2001	Different study design. Not an RCT, did not contain a control group without epidural analgesia
Milbrandt 2009	Different study design. Retrospective cohort study
Nóbrega 2017	Different study design. Retrospective study
Pham 2008	Different study design. No control group. All participants received epidural analgesia with either ropivacaine or bupivacaine
Ravish 2012	Different study design. Retrospective study
Saudan 2008	Different study design. Observational study. All participants received epidural analgesia
Sekar 2004	Different population. Only 1 of the 2 groups contained participants under 18 years of age
Shaw 1996	Different study design. Descriptive clinical study
Sparkes 1989	Different study design. Not an RCT
Sucato 2005	Different study design. Retrospective study
Sundarathiti 2010	Different study design. Descriptive clinical study

Study	Reason for exclusion
Tobias 2001	Different study design. Not an RCT, did not contain a control group without epidural analgesia
Turner 2000	Different study design. Not an RCT
Van Boerum 2000	Different study design. Retrospective study

RCT: randomized controlled trial.

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

Kick 1995

Methods	N/A
Participants	N/A
Interventions	N/A
Outcomes	N/A
Notes	This reference came from the list of reference of a review article (Bernard JM et al. Analgésie après chirurgie du rachis chez l'adulte et l'adolescent. Cahiers d'Anesthésiologie 1995; 43:6: 557-64) and no details were available. We have not been able to obtain a copy of this article despite requests to 2 university libraries

N/A: not available.

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

EUCTR2008-001642-19-SE

Trial name or title	Perioperative pain management in children and adolescents undergoing scoliosis surgery. Intravenous analgesia with s-ketamine and morphine versus epidural analgesia with fentanyl-bupivacaine-epinephrine. Pain, nausea and psychological impact
Methods	Parallel single-blind RCT
Participants	Consecutive children/adolescents scheduled for correctional surgery for idiopathic scoliosis. Aged 12–18 years
Interventions	**Intervention group:** epidural analgesia with fentanyl-bupivacaine-epinephrine **Comparator group:** intravenous analgesia with s-ketamine and morphine
Outcomes	Primary end points: pain at hospital and at home, intensity and duration, measured by VAS (0–100 mm) Secondary objectives: nausea, gastrointestinal function, amount of and time to first rescue analgesia, global rating of patient satisfaction, pruritus, postoperative psychological impact
Starting date	Registered 27 June 2008
Contact information	No contact author listed, no contact address

EUCTR2008-001642-19-SE *(Continued)*

Notes	Last refreshed on 19 March 2012

RCT: randomized controlled trial; VAS: visual/verbal analogue scale.

DATA AND ANALYSES

Comparison 1. Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children

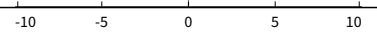
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain at rest at 6–8 hours	4	116	Mean Difference (IV, Random, 95% CI)	-1.32 [-1.83, -0.82]
1.1 Local anaesthetic only	2	60	Mean Difference (IV, Random, 95% CI)	-1.31 [-1.84, -0.79]
1.2 Opioid only	1	27	Mean Difference (IV, Random, 95% CI)	-2.29 [-4.51, -0.06]
1.3 Local anaesthetic plus opioid	1	29	Mean Difference (IV, Random, 95% CI)	-0.38 [-2.77, 2.01]
2 Pain at rest at 20–32 hours	6	208	Mean Difference (IV, Random, 95% CI)	-1.06 [-1.56, -0.57]
2.1 Local anaesthetic only	2	60	Mean Difference (IV, Random, 95% CI)	-1.47 [-1.97, -0.98]
2.2 Opioid only	1	27	Mean Difference (IV, Random, 95% CI)	-2.0 [-3.87, -0.13]
2.3 Local anaesthetic plus opioid	3	121	Mean Difference (IV, Random, 95% CI)	-0.27 [-1.03, 0.50]
3 Pain on movement at 24 hours	3	87	Std. Mean Difference (Random, 95% CI)	-1.51 [-2.27, -0.76]
3.1 Local anaesthetic only	2	60	Std. Mean Difference (Random, 95% CI)	-1.81 [-2.74, -0.89]
3.2 Opioid only	1	27	Std. Mean Difference (Random, 95% CI)	-0.95 [-1.76, -0.15]
4 Pain at rest at 48 hours	5	148	Mean Difference (IV, Random, 95% CI)	-1.10 [-1.62, -0.58]
4.1 Local anaesthetic only	2	60	Mean Difference (IV, Random, 95% CI)	-1.48 [-1.97, -0.99]
4.2 Opioid only	1	27	Mean Difference (IV, Random, 95% CI)	0.0 [-1.22, 1.22]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.3 Local anaesthetic plus opioid	2	61	Mean Difference (IV, Random, 95% CI)	-0.74 [-1.80, 0.31]
5 Pain on movement at 48 hours	2	60	Mean Difference (IV, Random, 95% CI)	-1.35 [-1.77, -0.92]
6 Pain at rest at 72 hours	5	157	Std. Mean Difference (Random, 95% CI)	-0.65 [-1.19, -0.10]
6.1 Local anaesthetic only	2	60	Std. Mean Difference (Random, 95% CI)	-1.36 [-2.40, -0.33]
6.2 Opioid only	1	27	Std. Mean Difference (Random, 95% CI)	-0.27 [-1.03, 0.49]
6.3 Local anaesthetic plus opioid	2	70	Std. Mean Difference (Random, 95% CI)	-0.37 [-0.87, 0.12]
7 Pain on movement at 72 hours	2	60	Mean Difference (IV, Random, 95% CI)	-1.07 [-1.38, -0.76]
8 Vomiting up to 48 hours after surgery	6	215	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.58, 1.30]
8.1 Local anaesthetic only	2	60	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.14, 1.90]
8.2 Opioids only	1	27	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.73, 1.96]
8.3 Local anaesthetic and opioid	3	128	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.46, 1.53]
9 Return of gastrointestinal function: number of participants with bowel movement at 48 hours	2	60	Risk Ratio (M-H, Random, 95% CI)	11.52 [2.36, 56.26]
10 Return of gastrointestinal function: time to first liquid ingestion	2	56	Mean Difference (IV, Random, 95% CI)	-5.02 [-13.15, 3.10]
10.1 Opioid only	1	27	Mean Difference (IV, Random, 95% CI)	-6.70 [-17.10, 3.70]
10.2 Local anaesthetic and opioid	1	29	Mean Difference (IV, Random, 95% CI)	-2.40 [-15.42, 10.62]
11 Hospital length of stay	2	89	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.69, 0.10]
12 Participant satisfaction	2	60	Mean Difference (IV, Random, 95% CI)	1.62 [1.26, 1.97]
13 Respiratory depression	4	126	Risk Difference (M-H, Random, 95% CI)	-0.05 [-0.16, 0.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14 Wound infection	2	93	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.05, 0.08]
15 Epidural abscess	3	120	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.05, 0.05]
16 Neurological complications	4	151	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.04, 0.06]

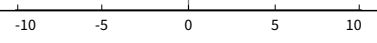
Analysis 1.1. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 1 Pain at rest at 6–8 hours.

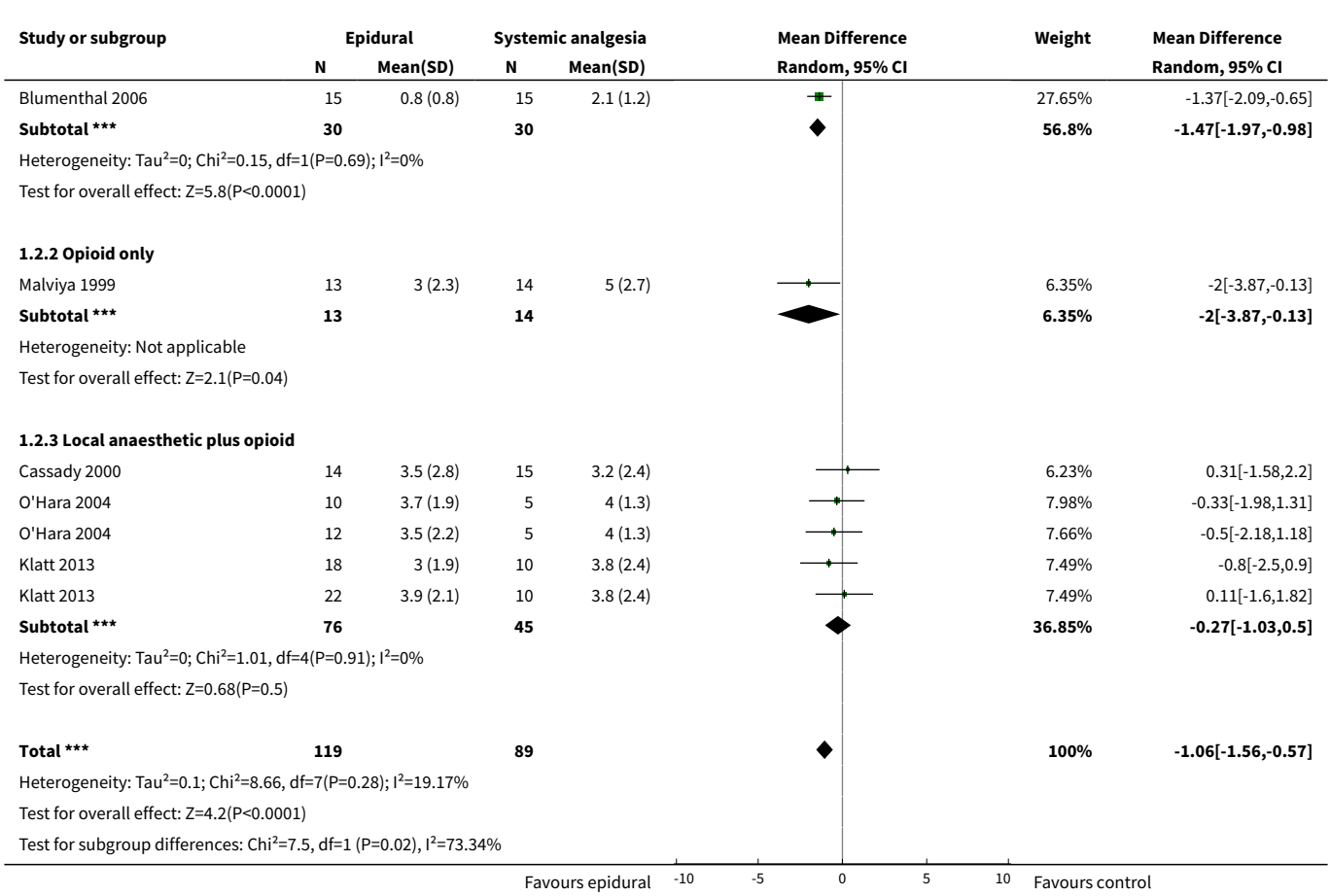
Study or subgroup	Epidural N	Epidural Mean(SD)	Systemic analgesia N	Systemic analgesia Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Local anaesthetic only							
Blumenthal 2005	15	1 (1.1)	15	2.5 (1.1)		38.14%	-1.5[-2.32,-0.68]
Blumenthal 2006	15	1.3 (0.7)	15	2.5 (1.2)		52.28%	-1.18[-1.88,-0.48]
Subtotal ***	**30**		**30**			**90.42%**	**-1.31[-1.84,-0.79]**
Heterogeneity: Tau^2=0; Chi^2=0.34, df=1(P=0.56); I^2=0%							
Test for overall effect: Z=4.86(P<0.0001)							
1.1.2 Opioid only							
Malviya 1999	13	1.7 (1.8)	14	4 (3.8)		5.13%	-2.29[-4.51,-0.06]
Subtotal ***	**13**		**14**			**5.13%**	**-2.29[-4.51,-0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.01(P=0.04)							
1.1.3 Local anaesthetic plus opioid							
Cassady 2000	14	2.8 (3.2)	15	3.1 (3.3)		4.45%	-0.38[-2.77,2.01]
Subtotal ***	**14**		**15**			**4.45%**	**-0.38[-2.77,2.01]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.31(P=0.76)							
Total ***	**57**		**59**			**100%**	**-1.32[-1.83,-0.82]**
Heterogeneity: Tau^2=0; Chi^2=1.66, df=3(P=0.65); I^2=0%							
Test for overall effect: Z=5.15(P<0.0001)							
Test for subgroup differences: Chi^2=1.32, df=1 (P=0.52), I^2=0%							



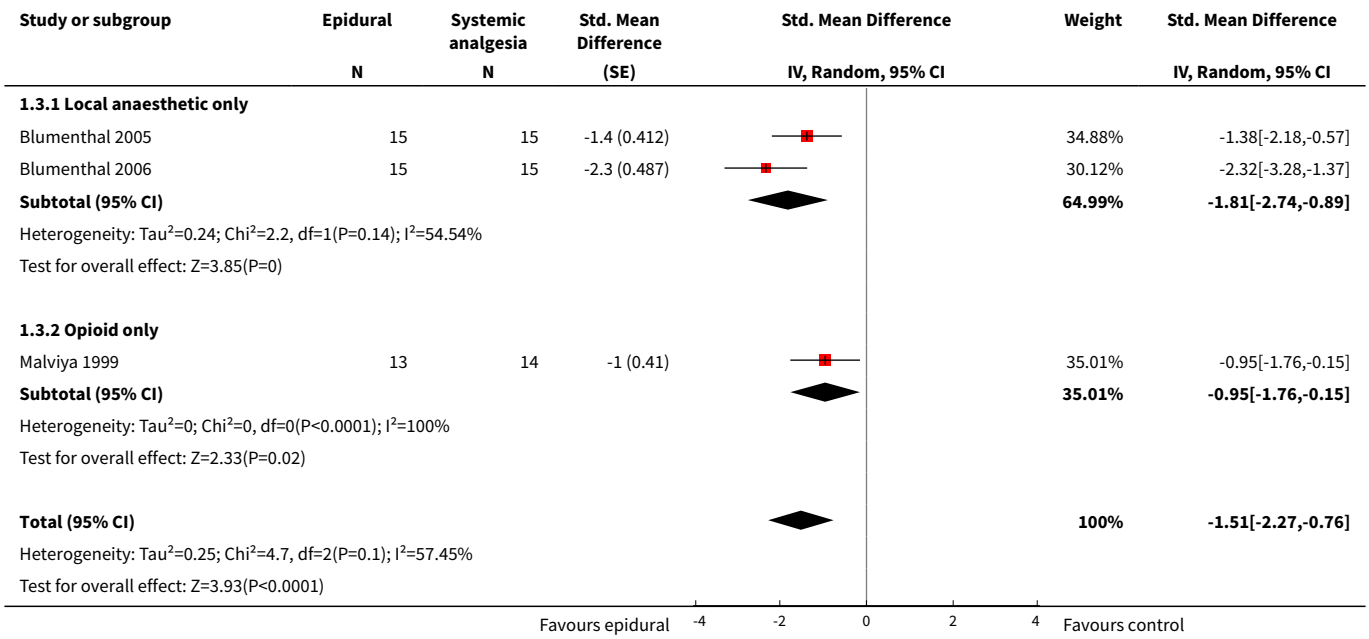
Analysis 1.2. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 2 Pain at rest at 20–32 hours.

Study or subgroup	Epidural N	Epidural Mean(SD)	Systemic analgesia N	Systemic analgesia Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.2.1 Local anaesthetic only							
Blumenthal 2005	15	0.8 (1.2)	15	2.4 (0.7)		29.15%	-1.57[-2.26,-0.88]

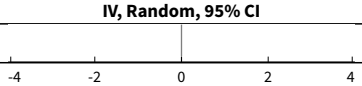




Analysis 1.3. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 3 Pain on movement at 24 hours.

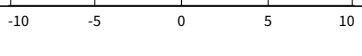


Study or subgroup	Epidural	Systemic analgesia	Std. Mean Difference	Std. Mean Difference	Weight	Std. Mean Difference
	N	N	(SE)	IV, Random, 95% CI		IV, Random, 95% CI
Test for subgroup differences: Chi²=1.89, df=1 (P=0.17), I²=47.17%						



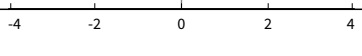
Analysis 1.4. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 4 Pain at rest at 48 hours.

Study or subgroup	Epidural		Systemic analgesia		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
1.4.1 Local anaesthetic only							
Blumenthal 2005	15	0.8 (1.1)	15	2.4 (0.7)		34.77%	-1.64[-2.29,-0.99]
Blumenthal 2006	15	0.5 (0.6)	15	1.8 (1.4)		29.19%	-1.27[-2.02,-0.52]
Subtotal ***	**30**		**30**			**63.97%**	**-1.48[-1.97,-0.99]**
Heterogeneity: Tau²=0; Chi²=0.53, df=1(P=0.47); I²=0%							
Test for overall effect: Z=5.9(P<0.0001)							
1.4.2 Opioid only							
Malviya 1999	13	2 (1.6)	14	2 (1.6)		14.48%	0[-1.22,1.22]
Subtotal ***	**13**		**14**			**14.48%**	**0[-1.22,1.22]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.4.3 Local anaesthetic plus opioid							
Cassady 2000	14	2.7 (2.5)	15	3.5 (2.5)		7.35%	-0.75[-2.56,1.06]
O'Hara 2004	12	3 (1.7)	5	3.9 (1.5)		8.8%	-0.94[-2.58,0.69]
O'Hara 2004	10	3.6 (2.7)	5	3.9 (1.5)		5.41%	-0.39[-2.53,1.75]
Subtotal ***	**36**		**25**			**21.55%**	**-0.74[-1.8,0.31]**
Heterogeneity: Tau²=0; Chi²=0.16, df=2(P=0.92); I²=0%							
Test for overall effect: Z=1.38(P=0.17)							
Total ***	**79**		**69**			**100%**	**-1.1[-1.62,-0.58]**
Heterogeneity: Tau²=0.09; Chi²=6.38, df=5(P=0.27); I²=21.64%							
Test for overall effect: Z=4.18(P<0.0001)							
Test for subgroup differences: Chi²=5.69, df=1 (P=0.06), I²=64.83%							

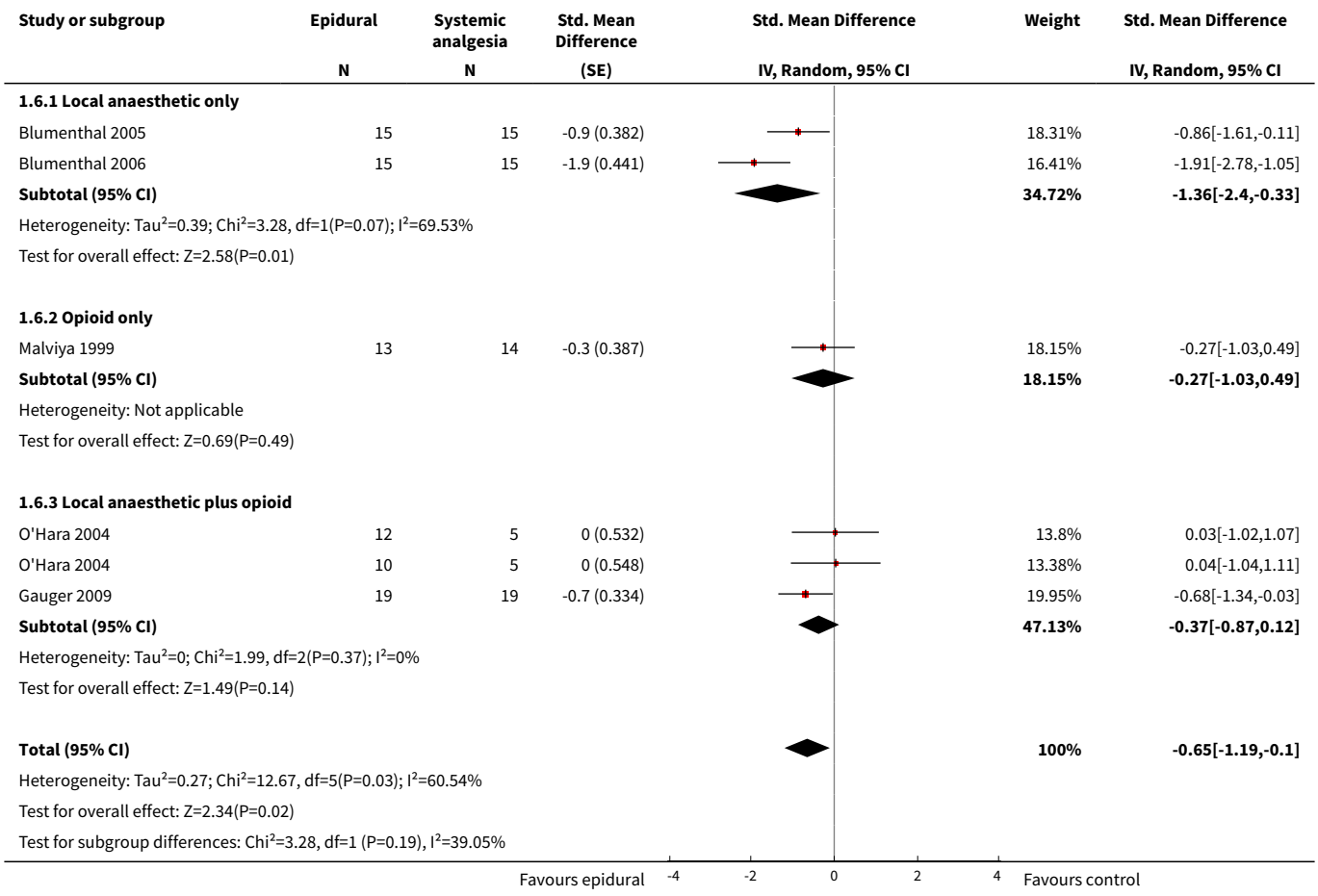


Analysis 1.5. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 5 Pain on movement at 48 hours.

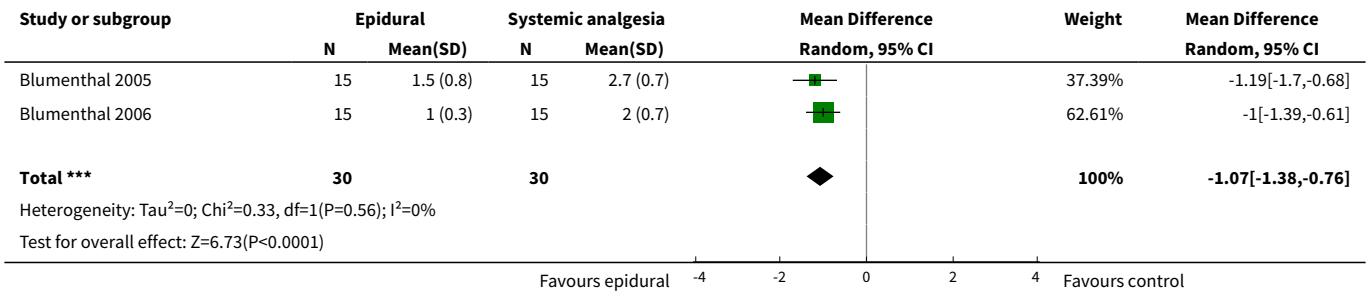
Study or subgroup	Epidural		Systemic analgesia		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Blumenthal 2005	15	1.6 (0.8)	15	3.1 (0.7)		61.53%	-1.5[-2.04,-0.96]
Blumenthal 2006	15	1.7 (0.8)	15	2.8 (1.1)		38.47%	-1.1[-1.78,-0.42]
Total ***	**30**		**30**			**100%**	**-1.35[-1.77,-0.92]**
Heterogeneity: Tau²=0; Chi²=0.82, df=1(P=0.37); I²=0%							
Test for overall effect: Z=6.26(P<0.0001)							



Analysis 1.6. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 6 Pain at rest at 72 hours.

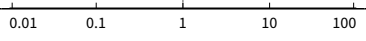


Analysis 1.7. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 7 Pain on movement at 72 hours.



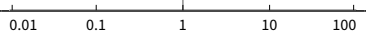
Analysis 1.8. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 8 Vomiting up to 48 hours after surgery.

Study or subgroup	Epidural n/N	Systemic analgesia n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Local anaesthetic only					
Blumenthal 2005	4/15	5/15		9.78%	0.8[0.27,2.41]
Blumenthal 2006	1/15	5/15		3.59%	0.2[0.03,1.51]
Subtotal (95% CI)	**30**	**30**		**13.37%**	**0.52[0.14,1.9]**
Total events: 5 (Epidural), 10 (Systemic analgesia)					
Heterogeneity: Tau^2=0.34; Chi^2=1.48, df=1(P=0.22); I^2=32.65%					
Test for overall effect: Z=0.99(P=0.32)					
1.8.2 Opioids only					
Malviya 1999	10/13	9/14		23.42%	1.2[0.73,1.96]
Subtotal (95% CI)	**13**	**14**		**23.42%**	**1.2[0.73,1.96]**
Total events: 10 (Epidural), 9 (Systemic analgesia)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.72(P=0.47)					
1.8.3 Local anaesthetic and opioid					
Cassady 2000	12/14	12/15		28.84%	1.07[0.77,1.49]
Gauger 2009	6/19	14/19		16.91%	0.43[0.21,0.88]
Klatt 2013	8/18	3/11		9.89%	1.63[0.55,4.87]
Klatt 2013	4/21	3/11		7.56%	0.7[0.19,2.58]
Subtotal (95% CI)	**72**	**56**		**63.2%**	**0.84[0.46,1.53]**
Total events: 30 (Epidural), 32 (Systemic analgesia)					
Heterogeneity: Tau^2=0.2; Chi^2=7.26, df=3(P=0.06); I^2=58.66%					
Test for overall effect: Z=0.56(P=0.58)					
Total (95% CI)	**115**	**100**		**100%**	**0.87[0.58,1.3]**
Total events: 45 (Epidural), 51 (Systemic analgesia)					
Heterogeneity: Tau^2=0.12; Chi^2=11.37, df=6(P=0.08); I^2=47.23%					
Test for overall effect: Z=0.68(P=0.5)					
Test for subgroup differences: Chi^2=1.8, df=1 (P=0.41), I^2=0%					



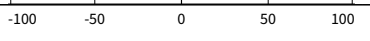
Analysis 1.9. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 9 Return of gastrointestinal function: number of participants with bowel movement at 48 hours.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Blumenthal 2005	9/15	1/15		66.95%	9[1.3,62.51]
Blumenthal 2006	9/15	0/15		33.05%	19[1.2,299.63]
Total (95% CI)	**30**	**30**		**100%**	**11.52[2.36,56.26]**
Total events: 18 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.2, df=1(P=0.66); I^2=0%					
Test for overall effect: Z=3.02(P=0)					



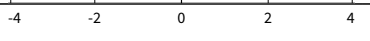
Analysis 1.10. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 10 Return of gastrointestinal function: time to first liquid ingestion.

Study or subgroup	Epidural N	Epidural Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.10.1 Opioid only							
Malviya 1999	13	10.7 (9.9)	14	17.4 (17)		61.04%	-6.7[-17.1,3.7]
Subtotal ***	**13**		**14**			**61.04%**	**-6.7[-17.1,3.7]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.26(P=0.21)							
1.10.2 Local anaesthetic and opioid							
Cassady 2000	14	39.3 (14.9)	15	41.7 (20.6)		38.96%	-2.4[-15.42,10.62]
Subtotal ***	**14**		**15**			**38.96%**	**-2.4[-15.42,10.62]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.36(P=0.72)							
Total ***	**27**		**29**			**100%**	**-5.02[-13.15,3.1]**
Heterogeneity: Tau^2=0; Chi^2=0.26, df=1(P=0.61); I^2=0%							
Test for overall effect: Z=1.21(P=0.23)							
Test for subgroup differences: Chi^2=0.26, df=1 (P=0.61), I^2=0%							



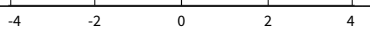
Analysis 1.11. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 11 Hospital length of stay.

Study or subgroup	Epidural N	Epidural Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Cassady 2000	14	4.7 (1.1)	15	4.7 (1.6)		15.98%	0[-0.99,0.99]
Klatt 2013	21	5.2 (0.7)	10	5.6 (0.8)		45.52%	-0.36[-0.95,0.23]
Klatt 2013	19	5.2 (0.9)	10	5.6 (0.8)		38.5%	-0.34[-0.98,0.3]
Total ***	**54**		**35**			**100%**	**-0.29[-0.69,0.1]**
Heterogeneity: Tau^2=0; Chi^2=0.4, df=2(P=0.82); I^2=0%							
Test for overall effect: Z=1.45(P=0.15)							



Analysis 1.12. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 12 Participant satisfaction.

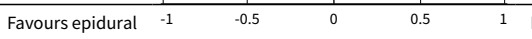
Study or subgroup	Epidural N	Epidural Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Blumenthal 2005	15	8.3 (0.9)	15	6.8 (0.6)		42.08%	1.5[0.95,2.05]
Blumenthal 2006	15	9.1 (0.6)	15	7.4 (0.7)		57.92%	1.7[1.23,2.17]
Total ***	**30**		**30**			**100%**	**1.62[1.26,1.97]**
Heterogeneity: Tau^2=0; Chi^2=0.3, df=1(P=0.59); I^2=0%							



Study or subgroup	Epidural N	Epidural Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Test for overall effect: Z=8.92(P<0.0001)							

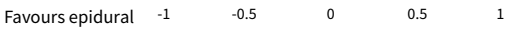
Analysis 1.13. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 13 Respiratory depression.

Study or subgroup	Epidural n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Malviya 1999	0/13	0/14		31.84%	0[-0.13,0.13]
Cassady 2000	0/14	0/15		34.04%	0[-0.12,0.12]
O'Hara 2004	0/22	1/10		17.69%	-0.1[-0.31,0.11]
Gauger 2009	1/19	5/19		16.44%	-0.21[-0.43,0.01]
Total (95% CI)	**68**	**58**		**100%**	**-0.05[-0.16,0.05]**
Total events: 1 (Epidural), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.81, df=3(P=0.19); I^2=37.66%					
Test for overall effect: Z=0.99(P=0.32)					



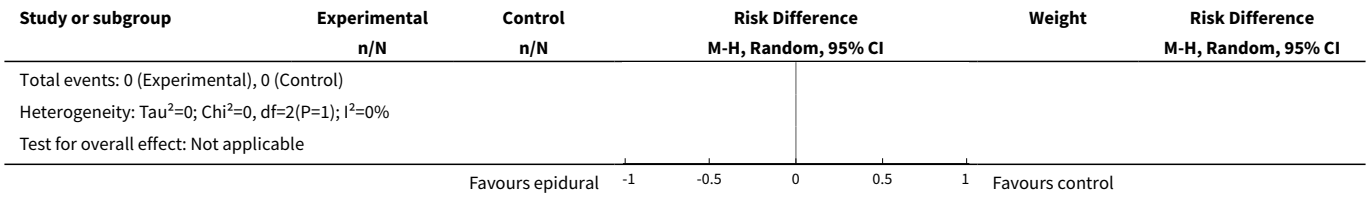
Analysis 1.14. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 14 Wound infection.

Study or subgroup	Epidural n/N	Systemic analgesia n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Cassady 2000	1/17	0/16		19.12%	0.06[-0.09,0.21]
Klatt 2013	0/40	0/20		80.88%	0[-0.07,0.07]
Total (95% CI)	**57**	**36**		**100%**	**0.01[-0.05,0.08]**
Total events: 1 (Epidural), 0 (Systemic analgesia)					
Heterogeneity: Tau^2=0; Chi^2=0.58, df=1(P=0.44); I^2=0%					
Test for overall effect: Z=0.33(P=0.74)					

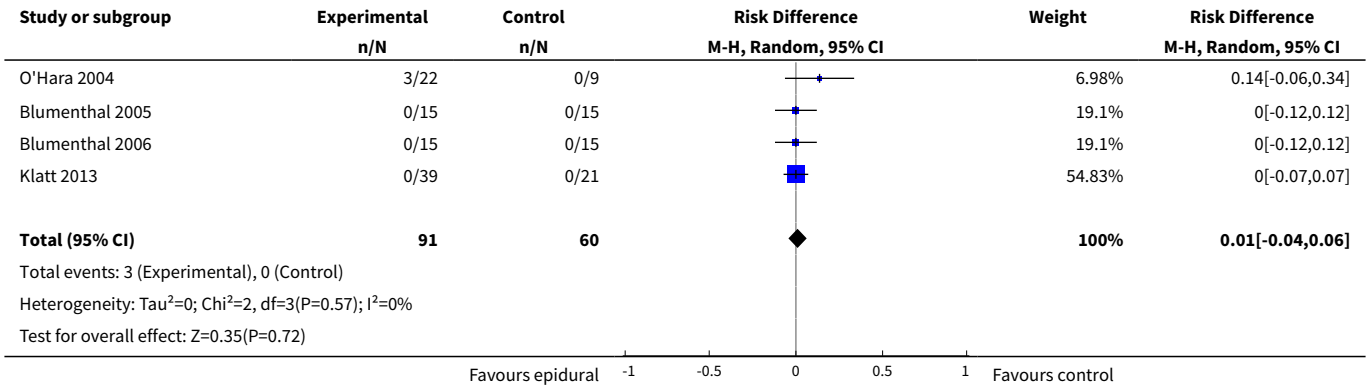


Analysis 1.15. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 15 Epidural abscess.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Blumenthal 2005	0/15	0/15		20.53%	0[-0.12,0.12]
Blumenthal 2006	0/15	0/15		20.53%	0[-0.12,0.12]
Klatt 2013	0/39	0/21		58.94%	0[-0.07,0.07]
Total (95% CI)	**69**	**51**		**100%**	**0[-0.05,0.05]**



Analysis 1.16. Comparison 1 Epidural analgesia versus systemic analgesia for postoperative pain after back surgery in children, Outcome 16 Neurological complications.



ADDITIONAL TABLES

Table 1. Surgical technique

Trial	Surgical technique
Blumenthal 2005	The posterior instrumentation of the spine was done with pedicle screws in the thoracic and lumbar spine using universal spine system (USS, Stratec, Oberdorf, Lucerne, Switzerland). The procedures were performed over 7 to 11 vertebral levels. No surgical complications occurred.
Blumenthal 2006	The thoracotomy was done on the convex side through a single skin incision with subperiosteal resection of 1 rib. The anterior instrumentation of the spine was done with vertebral screws and single 6-mm rod titanium implants. The resected rib was used as autologous bone graft. The length of the instrumentation was 6 or 7 vertebrae No surgical complication occurred
Cakar Turhan 2011	Posterior instrumentation or fusion
Cassady 2000	Posterior thoraco-lumbar spinal fusion using 1 of 3 standard types of surgical instrumentation, i.e. Cotrel-Doubosett (CD; n = 10), Texas Scottish Rite Children's Hospital (TSRH; n = 5), or Synthes (n = 20).

Table 1. Surgical technique *(Continued)*

	No excessive intraoperative blood loss was observed during this investigation. 1 participant had the epidural catheter removed in the postanaesthesia care unit at the request of her surgeon for a transient unilateral upper extremity neurological deficit that subsequently proved unrelated to analgesic therapy.
Ezhevskaya 2012a	Posterior spinal fusion and segmental spinal instrumentation
Ezhevskaya 2015	Scoliosis surgery
Gauger 2009	Posterior spinal fusion procedures involved segmental instrumentation with hybrid constructs including pedicle screws, sublaminar wires, and hooks. 8% of participants who received patient-controlled epidural analgesia experienced moderate-to-severe spasms through postoperative day 3 compared with 35% of participants in the IV patient-controlled analgesia group (P = not significant). 7 (58%) participants in the patient-controlled epidural analgesia group and 17 (100%) in the intravenous patient-controlled analgesia group required diazepam (P = 0.007).
Klatt 2013	Posterior spinal fusion was performed using segmental instrumentation with pedicle screws and bilateral transverse process hooks at the most cranial level of the construct. There were no instances of spinal cord monitoring changes during surgery. Late-onset neurological events were absent in all participants.
Malviya 1999	Complete laminectomy at L3 to L5 and partial laminectomies at L2 and S1 The incidence of muscle spasms was lower in the epidural group compared with the nurse-controlled analgesia group through postoperative day 3 and statistical significance for the difference was reached on the evening of surgery (P = 0.005), the morning of postoperative day 1 (P = 0.01), and evening of postoperative day 2 (P = 0.04). Although fewer children in the epidural group required diazepam for muscle spasms through postoperative day 3, this was not statistically significant.
O'Hara 2004	Posterior thoraco-lumbar segmental instrumentation. 2/9 (22%) participants had paraesthesia likely secondary to spinal correction. 1 participant had a persistent partial sensory block which resolved after 3 months and the other participant after 6 months. 1 participant in the high-dose epidural group was also excluded after emerging from anaesthesia with lower extremity paralysis secondary to surgical correction. Paralysis resolved by 8 months.
Ozturk Mamik 2011	Posterior fusion for scoliosis

n: number of participants; NR: not reported.

Table 2. Analgesic techniques

Trial	Epidural analgesia	Systemic analgesia
Blumenthal 2005	Double catheter technique inserted by the surgeon (T1–T4 and L1–L4) (placement confirmed radiologically) with ropivacaine 0.3% started the morning after surgery for 1 group: 4–8 mL boluses through each catheter according to the height of	Remifentanil target-controlled infusion for all participants for the first night after surgery.

Table 2. Analgesic techniques *(Continued)*

	the participants, followed by infusions of 4–10 mL/hour in each catheter to obtain a sensory blockade from T2 to T12.	Continuous intravenous analgesia with morphine at 0.05 mg/kg/hour thereafter for 1 group. All participants received oral rofecoxib once a day (25 mg when < 50 kg body weight or 50 mg when > 50 kg body weight) and intravenous acetaminophen (paracetamol) 1 g every 6 hours was provided for participants weighing > 40 kg and 25 mg/kg every 6 hours for participants weighing < 40 kg. As a rescue analgesic, intravenous morphine 0.025 mg/kg was administered if VAS was greater than 30 and titrated to keep a respiratory rate > 8 breaths/minute.
Blumenthal 2006	Double catheter technique inserted by the surgeon (T1–T4 and L1–L4) (placement confirmed radiologically) with ropivacaine 0.3% started the morning after surgery for 1 group: 4–8 mL boluses through each catheter according to the height of the participants, followed by infusions of 4–10 mL/hour in each catheter to obtain a sensory blockade from T2 to T12.	Remifentanil target-controlled infusion for all participants for the first night after surgery. Continuous intravenous analgesia with morphine at 0.05 mg/kg/hour thereafter for 1 group. All participants received oral rofecoxib once a day (25 mg when < 50 kg or 50 mg when > 50 kg) and intravenous acetaminophen (1 g for participants > 40 kg body weight and 25 mg/kg for participants < 40 kg) every 6 hours. Intravenous morphine 0.025 mg/kg was administered as a rescue analgesic if VAS exceeded 30.
Cakar Turhan 2011	Solution of morphine 20 µg/kg plus 15 mL of 0.5% levobupivacaine plus 15 mL of sodium chloride 0.9% was prepared. 2 mL of the above solution per level of fused vertebrae was administered before surgery. At the end of operation, wound infiltration was done with 20 mL of levobupivacaine 0.25%.	IV PCA with morphine for all participants.
Cassady 2000	Epidural catheter (T6–T7, inserted 4–5 cm into the epidural space) was placed by the surgeon under direct visualization of the spine before surgical closure of the back, as described by Shaw 1996. 10 mL bolus of bupivacaine 0.25% with epinephrine (adrenaline) 1:200,000. Bupivacaine 0.125% and fentanyl 0.0025 mg/mL was begun at a rate of 0.35 mg/kg/hour (up to 0.4 mg/kg/hour) of bupivacaine (0.28–0.32 mL/kg/hour) started within 30 minutes of arrival in postanaesthesia care unit continued an adequate oral fluid intake.	IV PCA with morphine (up to 0.03 mg/kg/dose or 0.3 mg/kg/4 hours). Rescue analgesia with ketorolac 0.5 mg/kg (maximum single dose 30 mg) every 6 hours as required for the first 72 hours.

Table 2. Analgesic techniques *(Continued)*

Ezhevskaya 2012a	Preoperative epidural puncture at 2 levels (T4–T5 and T10–T11) with injection of 0.75% ropivacaine (15–25 mL) plus fentanyl 200 µg. Postoperative infusion of ropivacaine 0.2% plus fentanyl and epinephrine (adrenaline),	IV PCA with opioids.
Ezhevskaya 2015	Thoracic epidural anaesthesia with 0.75% ropivacaine and fentanyl	Not reported.
Gauger 2009	Epidural catheter was inserted by the surgeon under direct visualization at the midpoint of the incision (T9–T12) and advanced 3–5 cm cephalad as described by Shaw 1996. Loaded with fentanyl 1 µg/kg (maximum 50 µg) and 5 µg/kg hydromorphone (maximum 0.2 mg) diluted in 0.3 mL/kg preservative-free saline (maximum 10 mL). Patient-controlled epidural analgesia. Bupivacaine 0.1% plus hydromorphone 10 µg/mL at 8 mL/hour plus bolus dosing of 2 mL every 30 minutes Adjusted for pain score < 4 without oversedation.	IV PCA. Hydromorphone 2 µg/kg/hour continuous infusion; 2 µg/kg bolus dose. All participants received oral acetaminophen (paracetamol; 15 mg/kg; maximum 650 mg) every 4–6 hours for adjuvant analgesia, diazepam (0.05–0.1 mg/kg IV; maximum 5 mg) every 6 hours as needed for muscle spasms, diphenhydramine (0.5 mg/kg IV; maximum 25 mg) and dolasetron (0.35 mg/kg, maximum 12.5 mg) for pruritus and postoperative nausea and vomiting as required. Adjusted for pain score < 4 without oversedation.
Klatt 2013	1 (T10–T11 advanced 5 cm cephalad; Shaw 1996) or 2 (T7T8 and T12-L1) epidural catheters placed under direct visualization after instrumentation of the spine was complete. A rongeur was used to make a hole in the ligamentum flavum large enough for placement of the catheter. The distal end of the catheter was tunnelled through the paraspinal muscles at separate entry-site in the skin. Bupivacaine 0.1% plus fentanyl 2 µg/mL 0.2 mL/kg (divided in 2 for participants with 2 catheters) (maximum 12 mL). Bupivacaine 01% plus fentanyl 2 µg/mL at 12 mL/hour plus 0.1 mL/kg (lockout period 1 hour). Rate, bolus dose, and fentanyl concentrations adjusted on pain scores.	IV PCA with hydromorphone.
Malviya 1999	1 catheter placed by the surgeon at the cephalad end of the incision. Preservative-free morphine (Duramorph) 30 µg/kg (saline added for a volume of 0.15 mL/kg) followed by 3 µg/kg/hour (adjusted on FLACC pain scores ≤ 3; maximal dose 5 µg/kg/hour) for 3 days.	IV morphine 0.05–0.1 mg/kg followed by 0.02 mg/kg dose via a nurse-controlled analgesia device. Diazepam for muscle spasms.
O'Hara 2004	Directly placed midthoracic epidural catheter advanced 3–5 cm cephaladly.	IV PCA with morphine adjusted on pain scores.

Table 2. Analgesic techniques *(Continued)*

	3 mL bolus followed by 4 mL/hour of 0.1% bupivacaine plus fentanyl 5 µg/mL (n = 10) or 0.065% bupivacaine plus fentanyl 5 µg/mL (n = 12). Bolus allowed.	
Ozturk Mamik 2011	Catheter inserted before surgery. 15 mL levobupivacaine 0.5% plus morphine 20 µg/kg and saline 15 mL: 2 mL of solution per segment operated on administered before surgery. Catheter removed after injection.	IV PCA with morphine.

FLACC: Faces, Legs, Activity, Cry, Consolability pain scores; IV: intravenous; L: lumbar vertebrae; PCA: patient-controlled analgesia; T: thoracic vertebrae; VAS: verbal/visual analogue scale for pain.

Table 3. Complications possibly related to the analgesic technique

Trial	Epidural analgesia	Systemic analgesia
Blumenthal 2005	No complications related to the epidural catheter occurred. Postoperative clinical neurological assessment was uneventful. After the initial epidural ropivacaine bolus, 4 participants showed a transient motor blockade of > 1 (1 participant had Bromage 2, 3 participants had Bromage 3) on the modified Bromage scale, which spontaneously resolved within 180 minutes and did not recur during the continuous epidural infusion until the end of the study. The occurrence of postoperative pruritus was significantly decreased in the epidural group.	The occurrence of postoperative pruritus was significantly decreased in the epidural group
Blumenthal 2006	No technical problem occurred with the epidural catheters. No neurological complications observed. 2 participants had a transient motor blockade. (Bromage 1 and 2) after epidural bolus injections, which normalized within 120 minutes. Postoperative pruritus occurred significantly lower in the epidural group.	Postoperative pruritus occurred significantly lower in the epidural group
Cakar Turhan 2011	No adverse effects related to morphine and local anaesthetic consumption seen	No adverse effects related to morphine seen.
Cassady 2000	1/14 participants receiving epidural analgesia developed a wound infection. There were no incidents of clinically significant hypotension noted in either group. There were no incidents of clinically significant respiratory depression noted in either group. 6/14 (42.9%) participants receiving epidural analgesia experienced pruritus, with a mean of 1.3 ± 1.9 episodes.	No participants receiving PCA experienced an infection. There were no incidents of clinically significant respiratory depression noted in either group. There were no incidents of clinically significant hypotension noted in either group.

Table 3. Complications possibly related to the analgesic technique *(Continued)*

		There were no incidents of clinically significant respiratory depression noted in either group. 7/15 (46.7%) participants receiving patient-controlled analgesia experienced pruritus, with a mean of 0.7 ± 1.7 episodes
Ezhevskaya 2012a	Non-invasive haemodynamic monitoring showed that epidural does not lead to life-threatening disorders in myocardial contractility, cardiac output, systemic vascular resistance, and critical increase of the content of extravascular lung water.	The incidence of adverse effects was significantly higher in the group without epidural (no details provided).
Ezhevskaya 2015	There were no complications.	There were no complications.
Gauger 2009	7 (37%) participants experienced early epidural failure. 1 participant experienced respiratory depression (i.e. decreased respiratory rate and oxygen desaturation < 90%) treated with supplemental oxygen and lowering or discontinuation of the opioid infusion. 1 participant had hypotension requiring discontinuation of the epidural. 1 participant complained of paraesthesia. 1 participant required readmission for an ileus. 1 participant developed a pneumothorax requiring chest tube placement.	2 participants in the IV group remained intubated, sedated, and ventilated for several hours postoperatively. 3 participants experienced respiratory depression (i.e. decreased respiratory rate and oxygen desaturation < 90%) treated with supplemental oxygen and lowering or discontinuation of the opioid infusion. 1 participant developed a pneumothorax. 1 participant developed a fever.
Klatt 2013	Paraesthesia: 4 participants with 1 catheter and 1 participant with 2 catheters. 10 participants had epidural leakage causing discontinuation for 2 participants. No respiratory distress. No cases of clinically significant hypotension that were thought to be directly related to the epidural infusions to the extent that the infusions were changed. No alterations to the epidurals were necessary so that a better neurological examination could be obtained. No episodes of wound infection. No readmission. Late-onset neurological events were absent in all participants. All adverse effects were minor in nature and required routine nursing and medical care.	Paraesthesia: 2 participants. No episodes of wound infection. No readmission. Late-onset neurological events were absent in all participants. All adverse effects were minor in nature and required routine nursing and medical care.
Malviya 1999	1 dislodged catheter. No respiratory depression. The incidence of pruritus that required treatment was similar between groups during the postoperative period.	No respiratory depression. The incidence of pruritus that required treatment was similar between groups during the postoperative period.

Table 3. Complications possibly related to the analgesic technique *(Continued)*

		1 participant required catheterization for urinary retention after initial removal of the bladder catheter.
O'Hara 2004	9/22 (41%) participants with the active epidural infusions vs 0/9 participants with placebo had a lower extremity paraesthesia. Within 24 hours after epidural catheter was discontinued, sensory examination returned to normal in 7/9 (78%) of these participants who had a paraesthesia postoperatively. In 2/9 (22%) participants, the paraesthesia was likely secondary to spinal correction. 1 participant had a persistent partial sensory block which resolved after 3 months and the other participant after 6 months. 1 participant in the high-dose epidural group was also excluded after emerging from anaesthesia with lower extremity paralysis secondary to surgical correction. Paralysis resolved by 8 months. No significant difference detected among the groups regarding the incidence of sedation (P = 0.10) or pruritus (P = 0.32).	1 participant in the placebo group was excluded secondary to severe respiratory depression demonstrated by increased $PaCO_2$ (6.5–7.8 kPa; 50–60 mmHg) and a decreased respiratory rate (6–8 breaths/minute). This was felt to be secondary to IV patient-controlled analgesia morphine dosing. No significant difference detected among the groups regarding the incidence of sedation (P = 0.10) or pruritus (P = 0.32).
Ozturk Mamik 2011	Not reported	Not reported

IV: intravenous; $PaCO_2$: partial pressure of carbon dioxide.

APPENDICES

Appendix 1. Search terms for CENTRAL

September 2017

Cochrane Central Register of Controlled Trials : Issue 8 of 12, August 2017
#1 MeSH descriptor: [Spinal Diseases] explode all trees and with qualifier(s): [Surgery - SU] 1169
#2 MeSH descriptor: [Spinal Fusion] explode all trees 1078
#3 MeSH descriptor: [Scoliosis] explode all trees 293
#4 ((Spine* or spinal or lumbar) near/3 surg*) or scolios* or thoracolumbar or (thoraco* near/3 lumbar) or (thoracic near/3 (lumbar or spine)) 6192
#5 #1 or #2 or #3 or #4 6638
#6 MeSH descriptor: [Analgesia, Epidural] explode all trees 1960
#7 MeSH descriptor: [Anesthetics, Local] explode all trees 7115
#8 MeSH descriptor: [Analgesics, Opioid] explode all trees 6247
#9 ((local or systemic) near/4 an?esth*) or opioid* or epidural* or analg* 54236
#10 #6 or #7 or #8 or #9 56615
#11 MeSH descriptor: [Postoperative Period] explode all trees 5354
#12 MeSH descriptor: [Pain, Postoperative] explode all trees 11672
#13 MeSH descriptor: [Postoperative Care] explode all trees 4406
#14 postoperative or post operative 82797
#15 #11 or #10 or #12 or #14 118395
#16 #5 and #10 and #15 1954
#17 #16 in Trials **1697**

14 November 2018 (September 2017 to December 2018)

(spine surgery OR spinal surgery) AND (epidural analgesia OR epidural anesthesia) AND (postoperative pain OR postoperative care) **74**

Total CENTRAL 1771

Appendix 2. Search terms for MEDLINE

September 2017

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) < 1946 to Present>

1 ((Spine* or spinal or lumbar) adj3 surg*).mp. or exp Spinal Diseases/su or Spinal Fusion/ or scoliosis/ or scolios*.mp. or thoracolumbar.mp. or (thoraco* adj3 lumbar).mp. or (thoracic adj3 (lumbar or spine)).mp. (83497)

2 Analgesia, Epidural/ or Anesthetics, Local/ or Analgesics, Opioid/ or ((local or systemic) adj4 an?esth*).mp. or opioid*.mp. or epidural*.mp. or analg*.mp. (306319)

3 exp Postoperative Period/ or exp Pain, Postoperative/ or Postoperative Care/ or post?operative.mp. or post operative.mp. (751418)

4 ((randomized controlled trial or controlled clinical trial).pt. or randomi?ed.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) (3698955)

5 1 and 2 and 3 and 4 **(1116)**

14 November 2018 (2017 to 2018)

1 (spine and (epidural anesthesia or epidural analgesia) and (postoperative pain or postoperative period)).af. (41)

2 limit 1 to yr="2017 - 2018" (**7**)

Total MEDLINE = **1123**

Appendix 3. Search terms for Embase

Database: Embase < 1974 to 2017 Week 38>
1 ((Spine* or spinal or lumbar) adj3 surg*).mp. or exp spine disease/su or exp spine fusion/ or exp scoliosis/ or scolios*.mp. or thoracolumbar.mp. or (thoraco* adj3 lumbar).mp. or (thoracic adj3 (lumbar or spine)).mp. (115650)

2 epidural analgesia/ or local anesthetic agent/ or narcotic analgesic agent/ or ((local or systemic) adj4 an?esth*).mp. or opioid*.mp. or epidural*.mp. or analg*.mp. (430622)

3 exp postoperative period/ or postoperative pain/ or post?operative.mp. or post operative.mp. (1072155)

4 ((crossover procedure or double blind procedure or single blind procedure).sh. or (crossover* or cross over*).ti,ab. or placebo*.ti,ab,sh. or (doubl* adj blind*).ti,ab. or (controlled adj3 (study or design or trial)).ti,ab. or allocat*.ti,ab. or trial*.ti,ab. or randomized controlled trial.sh. or random*.ti,ab.) not ((exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)) (2015360)

5 1 and 2 and 3 and 4 **(1156)**

14 November 2018

spine AND 'epidural anesthesia' AND ('postoperative period' OR 'postoperative pain') AND [2017-2018]/py = 19

Total Embase = 1175

Appendix 4. Search terms for CINAHL

September 2017		
S1	((Spine* or spinal or lumbar) N3 surg*) or (MH "Spinal Diseases+") or (MH "Spinal Fusion") or (MH "Scoliosis+") or scolios* or thoracolumbar or (thoraco* N3 lumbar) or (thoracic N3 (lumbar or spine))	20,243
S2	(MH "Analgesia, Epidural") or (MH "Anesthetics, Local+") or (MH "Analgesics, Opioid+") or ((local or systemic) N4 an?esth*) or opioid* or epidural* or analg*	58,832

(Continued)

S3	(MH "Postoperative Period") or (MH "Postoperative Pain") or (MH "Postoperative Care+") or postoperative or post operative	66,564
S4	S1 AND S2 AND S3	403
S5	((MM "Randomized Controlled Trials") OR (MM "Random Assignment") OR (MM "Prospective Studies+") OR (MM "Clinical Trial Registry") OR (MM "Double-Blind Studies") OR (MM "Single-Blind Studies") OR (MM "Triple-Blind Studies") OR (MM "Multicenter Studies") OR (MM "Placebos")) OR (random* or placebo* or trial*)	297,938
S6	S4 AND S5	**123**
14 November 2018 (2017-2018)		
(spine surgery or spinal surgery) AND (epidural analgesia or epidural anesthesia) AND (postoperative pain)		**16**
Total CINAHL		**139**

Appendix 5. Search terms for ProQuest Dissertations and Theses Global 2 September 2018

Spine surgery AND epidural = **4**

14 November 2018

Spine surgery AND epidural 2018 = **0**

Total ProQuest Dissertations and Thesis Global = 4

Appendix 6. Pain scales used in included trials

Blumenthal 2005; visual analogue scale from 0 to 10

Blumenthal 2006; visual analogue scale from 0 to 10

Cakar Turhan 2011; visual analogue scale from 0 to 10

Cassady 2000; visual analogue scale from 0 to 10

Ezhevskaya 2012a; pain scores not included

Ezhevskaya 2015; pain scores not included

Gauger 2009; pain scale from 0 to 10

Klatt 2013; Wong-Baker system scale from 0 to 10

Malviya 1999; FLACC (Face, Legs, Activity, Cry, Consolability) scale from 0 to 10

O'Hara 2004; visual analogue scale from 0 to 10

Ozturk Mamik 2011: visual analogue scale from 0 to 10

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Co-ordinating the review: JG.

Undertaking manual searches: JG and RLJ.

Screening search results: JG and RLJ.

Organizing retrieval of papers: JG.

Screening retrieved papers against inclusion criteria: JG and RLJ.

Appraising quality of papers: JG and SK.

Abstracting data from papers: JG and SK.

Writing to authors of papers for additional information: JG.

Obtaining and screening data on unpublished studies: JG and RLJ.

Managing data for the review: JG.

Entering data into Review Manager : JG.

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DECLARATIONS OF INTEREST

JG: none.

SS: none.

SK: none.

RLJ: none.

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Internal sources

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- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following changes to the published protocol (Guay 2017).

1. The study population was specified as being up to 18 years of age in the protocol. Due to the low number of trials available, we included four trials with participants older than 18 years: Blumenthal 2005 (10 to 30 years; mean age 17 years), Ezhevskaya 2012a (12 to 25 years), Klatt 2013 (10 to 21 years) and O'Hara 2004 (13 to 21 years).
2. Due to the high number of trials with zero cells, we analysed complications (respiratory depression, wound infection, epidural abscess and neurological complications) as RDs.
3. For three of the analysis (Analysis 1.1; Analysis 1.2; Analysis 1.4), data included pain measured on different pain scales, although all on scales from 0 to 10. For these three analyses, we gave results both as MDs and SMDs. Analysis in SMD were performed because this is the recommended way to analysis such data (Borenstein 2009b). Analysis in MDs were done to help the readers to interpret our results.

INDEX TERMS

Medical Subject Headings (MeSH)

*Analgesia, Epidural [adverse effects]; Analgesia [adverse effects] [*methods]; Early Ambulation [statistics & numerical data]; Lumbar Vertebrae [*surgery]; Operative Time; Pain Measurement; Pain, Postoperative [*drug therapy]; Patient Satisfaction; Randomized Controlled Trials as Topic; Thoracic Vertebrae [*surgery]; Vomiting [chemically induced]

MeSH check words

Humans