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The use of ultrasound guidance for perioperative neuraxial and peripheral nerve blocks in children (Review)

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[Intervention Review]

The use of ultrasound guidance for perioperative neuraxial and peripheral nerve blocks in children

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ABSTRACT

Background

The use of ultrasound guidance for regional anaesthesia has become popular over the past two decades. However, it is not recognized by all experts as an essential tool, perhaps because it is unclear whether ultrasound reduces the risk of severe neurological complications, and the cost of an ultrasound machine (USD 22,000) is substantially higher than the cost of other tools. This review was published in 2016 and updated in 2019.

Objectives

To determine whether ultrasound guidance offers any clinical advantage when neuraxial and peripheral nerve blocks are performed in children in terms of decreasing failure rate or the rate of complications.

Search methods

We searched CENTRAL, MEDLINE, Embase, and two trial registers up to March 2018 together with reference checking to identify additional studies and contacted study authors to obtain additional trial information.

Selection criteria

We included all parallel randomized controlled trials that evaluated the effects of ultrasound guidance used when a regional blockade technique was performed in children. We included studies performed in children (≤ 18 years of age) undergoing any type of surgical procedure (open or laparoscopic), for which a neuraxial (spinal, epidural, caudal, or combined spinal and epidural) or peripheral nerve block (any peripheral nerve block including fascial (fascia iliaca, transversus abdominis plane, rectus sheath blocks) or perivascular blocks), for surgical anaesthesia (alone or in combination with general anaesthesia) or for postoperative analgesia, was performed with ultrasound guidance. We excluded studies in which regional blockade was used to treat chronic pain.

We included studies in which ultrasound guidance was used to perform the technique in real time (in-plane or out-of-plane), as pre-scanning before the procedure or to evaluate the spread of the local anaesthetic so the position of the needle could be adjusted or the block complemented. For control groups, any other technique used to perform the block including landmarks, loss of resistance (air or fluid), click, paraesthesia, nerve stimulator, transarterial, or infiltration was accepted.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane. Our primary outcomes were failed blocks, pain scores at one hour after surgery, and block duration. Secondary outcomes included time to perform the block, number of needle passes, and minor and major complications. We used GRADE to assess the quality of evidence for each outcome.

Main results

We included 33 trials with a total of 2293 participants from 0.9 to 12 (mean or median) years of age. Most trials were at low risk of selection, detection, attrition, and reporting bias, however the lack of blinding of participants and personnel caring for participants resulted in 25 trials being judged as at high or unclear risk of bias. We identified five ongoing trials.

Ultrasound guidance probably reduces the risk of failed block (risk difference (RD) −0.16, 95% confidence interval (CI) −0.25 to −0.07; 22 trials; 1789 participants; moderate-quality evidence). When ultrasound guidance was used, there was a small to moderate reduction in pain one hour after surgery, equivalent to a reduction of 1.3 points on the revised Bieri FACES pain scale (scale; 0 = no pain, 10 = maximal pain) (standardized mean difference (SMD) −0.41, 95% CI −0.74 to −0.07 (medium effect size); 15 trials; 982 participants; moderate-quality evidence). Ultrasound guidance increases block duration by the equivalent of 42 minutes (SMD 1.24, 95% CI 0.72 to 1.75; 10 trials; 460 participants; high-quality evidence).

There is probably little or no difference in the time taken to perform the block (SMD −0.46, 95% CI −1.06 to 0.13; 9 trials; 680 participants; moderate-quality evidence). It is uncertain whether the number of needle passes required is reduced with the use of ultrasound guidance (SMD −0.63, 95% CI −1.08 to −0.18; 3 trials; 256 participants; very low-quality evidence).

There were no occurrences of major complications in either the intervention or control arms of the trials (cardiac arrest from local anaesthetic toxicity (22 trials; 1576 participants; moderate-quality evidence); lasting neurological injury (19 trials; 1250 participants; low-quality evidence)).

There may be little of no difference in the risk of bloody puncture (RD −0.02, 95% CI −0.05 to 0.00; 13 trials; 896 participants; low-quality evidence) or transient neurological injury (RD −0.00, 95% CI −0.01 to 0.01; 18 trials; 1230 participants; low-quality evidence). There were no occurrences of seizure from local anaesthetic toxicity (22 trials; 1576 participants; moderate-quality evidence) or block infections without neurological injury (18 trials; 1238 participants; low-quality evidence).

Authors' conclusions

Ultrasound guidance for regional blockade in children probably decreases the risk of failed block. It increases the duration of the block and probably decreases pain scores at one hour after surgery. There may be little or no difference in the risks of some minor complications. The five ongoing studies may alter the conclusions of the review once published and assessed.

PLAIN LANGUAGE SUMMARY

Ultrasound guidance for injecting local anaesthetics in children to block pain transmission

Background

A regional blockade involves injecting a local anaesthetic into the spine or around the nerves to block pain transmission. It can be used to replace general anaesthesia or to treat pain after surgery. Finding an effective alternative to traditional painkillers (pills or injections containing morphine derivatives) is particularly important for children, as they might be more likely to suffer adverse effects from opioid painkillers, and also because pain in early life might do long-term harm (exaggerated response to pain later in life). Traditionally, finding the exact location where the local anaesthetic needs to be injected was done on anatomical landmarks, that is palpation of bones or a pulsatile vessel (artery, using fingers to feel a pulse). Later, an electric needle producing a muscle contraction (nerve stimulator) was advocated as being more precise. Over the past four decades, clinicians have started to use ultrasound to locate nerves. However, ultrasound machines are expensive (USD 22,000 versus USD 1000 for a nerve stimulator).

We wanted to know if ultrasound guidance can improve the success rate and reduce the incidence of complications of regional blockade in children. These complications may include lasting neurological complications, inadvertent needle entry into a blood vessel, and seizure or cardiac arrest from local anaesthetic excess or from inadvertent injection into a blood vessel.

Search date

The evidence is current to March 2018.

Study characteristics

We included 33 well-designed studies with a total of 2293 children in which ultrasound guidance was compared with another method of nerve localization (traditional landmarks techniques or nerve stimulator) for regional blockade in children.

Study funding sources

Sources of funding included a government organization (two studies), a charitable organization (two studies), and an institutional department (13 studies). Two studies declared that they received industry help (equipment loan). The source of funding was unclear for 14 studies.

Key results

Ultrasound guidance for regional blockade in children may decrease the occurrence of failed block. It may also increase duration of the block and reduce pain at one hour after surgery. Ultrasound guidance may decrease the number of needle passes required to perform the block. However, because the vast majority of blocks in children are performed with the child under deep sedation or general anaesthesia, the true value of this finding might be arguable. There were no major complications in the included trials. There may be little or no difference between study groups in risks of minor complications. Altogether, whether or not these findings justify the extra cost of ultrasound guidance should probably also take into account the anaesthesiologist's expertise and local resources. The five ongoing studies may alter the conclusions of the review once published and assessed.

Quality of the evidence

We assessed the quality of the evidence as moderate for decreased occurrence of a failed block and improved pain scores at one hour; high for prolonged block duration; and very low for decreased number of needle passes.

Summary of findings for the main comparison. Ultrasound guidance compared with no ultrasound guidance for children

Ultrasound guidance compared with no ultrasound guidance for children

Patient or population: children (≤ 18 years of age) undergoing any type of surgical procedure (open or laparoscopic) for which a neuraxial (spinal, epidural, caudal, or combined spinal and epidural) or peripheral nerve block (any peripheral nerve block including fascial (fascia iliaca, transversus abdominis plane, rectus sheath blocks) or perivascular blocks) for surgical anaesthesia (alone or in combination with general anaesthesia) or for postoperative analgesia was performed with ultrasound guidance
Settings: data were collected in Austria (N = 1), Belgium (N = 2), Canada (N = 1), China (N = 7), Egypt (N = 2), Greece (N = 1), India (N = 2), Ireland (N = 1), Japan (N = 2), South Africa (N = 4), Turkey (N = 3), and the USA (N = 7)
Intervention: ultrasound guidance
Comparison: no ultrasound guidance

Outcomes	No ultrasound guidance	Ultrasound guidance	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Failed blocks	**Study population**		**RD −0.16** (−0.25 to −0.07)	1789 (22 studies)	⊕⊕⊕⊖ **moderate**[1]	NNTB is 6 (95% CI 5 to 8). The effect was more consistent for peripheral nerve block.
	271 per 1000	**145 per 1000** (124 to 170)				
Pain scores at 1 hour after surgery[6]	Mean pain scores at 1 hour after surgery was **0.41 standard deviation lower** (-0.74 to -0.07).			982 (15 studies)	⊕⊕⊕⊖ **moderate**[1]	The reduction is equivalent to −1.3 on the revised Bieri FACES pain scale (scale: 0 = no pain, 10 = maximal pain).
Block duration (0 to 1 day)	Mean block duration was **1.24 standard deviation higher** (0.72 to 1.75).[7]			460 (10 studies)	⊕⊕⊕⊕ **high**	Prolongation is equivalent to 42 minutes.
Time to perform the block	Mean time to perform the procedure was **0.46 standard deviation lower** (−1.06 to 0.13).			680 (9 studies)	⊕⊕⊕⊖ **moderate**[1]	
Number of needle passes	Mean number of needle passes was **0.63 standard deviation lower** (−1.08 to −0.18).			256 (3 studies)	⊕⊖⊖⊖ **very low**[2]	Reduction is equivalent to 0.4 needle pass less per participant.

Minor complications	**Bloody puncture**		**RD −0.02** (−0.05 to 0.00)	896 (13 studies)	⊕⊕⊖⊖ **low**[3]
	Study population				
	60 per 1000	**16 per 1000** (8 to 32)			
	Transient neurological injury		**RD −0.00** (−0.01 to 0.01)	1230 (18 studies)	⊕⊕⊖⊖ **low**[4]
	Study population				
	7 per 1000	**3 per 1000** (0.9 to 12 per 1000)			
	Seizure from local anaesthetic toxicity		**RD 0.00** (−0.01 to 0.01)	1576 (22 studies)	⊕⊕⊕⊖ **moderate**[5]
	Study population				
	0 per 1000	**0 per 1000** (0 to 5 per 1000)			
	Block infections without neurological injury		**RD 0.00** (−0.01 to 0.01)	1238 (18 studies)	⊕⊕⊖⊖ **low**[4]
	Study population				
	0 per 1000	**0 per 1000** (0 to 6 per 1000)			
Major complications	**Cardiac arrest from local anaesthetic toxicity**		**RD 0.00** (−0.01 to 0.01)	1576 (22 studies)	⊕⊕⊕⊖ **moderate**[5]
	Study population				
	0 per 1000	**0 per 1000** (0 to 5 per 1000)			
	Lasting neurological injury		**RD 0.00** (−0.01 to 0.01)	1250 (19 studies)	⊕⊕⊖⊖ **low**[4]
	Study population				
	0 per 1000	**0 per 1000**			

					(0 to 6 per 1000)

Incidences in study population and their 95% CI were calculated with VassarStat (VassarStats) with no continuity correction.
CI: confidence interval; **NNTB:** number needed to treat for additional beneficial outcome; **RD**: risk difference

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

[1]Downgraded by one level for risk of bias.
[2]Downgraded for risk of bias, imprecision, and the possibility of publication bias.
[3]Downgraded for imprecision and the possibility of publication bias.
[4]Downgraded for risk of bias and imprecision.
[5]Downgraded by one level for imprecision.
[6]Any ascending or descending scale as used by study authors: objective pain scale; Children's and Infants' Postoperative Pain Scale; Wong and Baker FACES pain rating scale; revised Bieri FACES pain scale; Face, Legs, Activity, Cry, Consolability Scale; visual analogue scale; or numerical scale.
[7]Some data had to be extracted as P values. For trials extracted as means and standard deviations (N = 6), mean time was 7.6 hours for ultrasound guidance and 4.0 hours for the comparator.

BACKGROUND

In 2005, in the USA alone, approximately 647,000 children were discharged from a short stay hospital after having undergone a surgical procedure (DeFrances 2007). Anaesthesiologists are involved in these procedures at various steps of the process, amongst which anaesthesia for the procedure itself and treatment of postoperative pain are of the utmost importance. Pain experienced early in life may induce organic brain changes that can make children susceptible to an exaggerated brain response when pain is experienced later in life (Hohmeister 2010). These brain changes are frequently referred to as neuroplasticity. Young children are often unable to understand what is happening to them, and this may increase their distress, leading to an increase in their inability to convey what exactly is making them uncomfortable. In response to this situation, care providers may undertreat or overtreat children experiencing postoperative pain. In one study performed in children, adverse events requiring an intervention (therefore judged as clinically relevant) occurred in 22% and 24% of patients with patient-controlled analgesia (PCA) administered by trained relatives or nurses and by the patients themselves, respectively (Voepel-Lewis 2008). Opioid-based regimens may therefore provide suboptimal treatment for postoperative pain in children.

Description of the condition

Regional blockade interrupts pain transmission to the brain, and may be used during the surgery itself as a replacement for general anaesthesia (regional anaesthesia) or for the treatment of postoperative pain (regional analgesia). In adults, regional analgesic techniques decrease postoperative opioid consumption (Guay 2006), making them a potentially interesting alternative or adjunct to opioid-based regimens for the treatment of children with postoperative pain. It is also possible that regional anaesthesia can reduce persistent, long-term pain after surgery, although there is currently little evidence for this in children (Weinstein 2018). Regional blockade techniques are classified as central neuraxial blocks (spinal, epidural, combined spinal and epidural, or caudal) or as peripheral nerve blocks (Guay 2017). These can be performed with local anaesthetics alone, with opioids or with other adjuncts (Pehora 2017). The use of regional blockade in children is today considered reasonably safe (Long 2014; Walker 2018). A large prospective trial on 104,393 blocks placed in 91,701 children and collected between 1 April 2007 and 30 September 2015 reported no permanent neurologic deficits (95% confidence interval 0 to 0.4 per 10,000) (Walker 2018). The most common adverse events were benign catheter-related failures (4%) (Walker 2018).

Description of the intervention

Ultrasound refers to an oscillating sound pressure wave at a frequency above the upper limit audible to the human ear (approximately 20 kHz). In nature, bats use ultrasounds as a guide for night flights. Ultrasounds emitted by the animal are reflected when they hit an obstacle. The same principle has been applied to develop devices in which ultrasound is used to create two-dimensional (2-D) or even three-dimensional (3-D) pictures (Feinglass 2007). Ultrasound has been used for regional blockade for almost four decades. The pioneers to whom use of ultrasound for regional blockade can be attributed include P La Grange (La Grange 1978), RL Ting (Ting 1989), T-J Wu (Wu 1993), and S Kapral (Kapral 1994). The probe emitting and receiving ultrasounds is placed over the area of the body in which the local anaesthetic will be injected. After appropriate visualization of the target, the needle may be advanced in-plane (parallel to the beam), allowing visualization of the entire needle during its trajectory, or out-of-plane (perpendicular to the beam). The local anaesthetic is then injected under visualization. For neuraxial blocks, ultrasound guidance can be used in real time to observe advancement of the needle within the epidural space or within the intrathecal canal (Niazi 2014), but can also be used as a pre-puncture guide to identify the exact vertebral level needed, to find an appropriate intervertebral space sufficient to allow passage of the needle, to determine the depth to which the needle should be advanced for placement of its tip at the chosen location, and to visualize the spread of the local anaesthetic. For peripheral nerve blocks, ultrasound guidance allows visualization of target nerves, advancement of the needle (in-plane technique), and spread of the local anaesthetic.

How the intervention might work

In children, regional anaesthetic techniques are usually performed with the child under deep sedation or under general anaesthesia. Fortunately, this does not seem to increase the risk of complications associated with regional anaesthesia (Taenzer 2014; Walker 2018). However, as the child cannot express any paraesthesia-related discomfort (with potential needle placement inside a neural structure), visualization might be even more important in this age group. Ultrasound guidance allows adequate visualization of nerves and other structures relevant to the performance of both neuraxial and peripheral nerve blocks, particularly in children, in whom relevant structures are relatively superficial.

Failed block is the most common problem in paediatric regional anaesthesia (Walker 2018). Severe local anaesthetic systemic toxicity is reported in 0.76 per 10,000 blocks (95% confidence interval 0.3 to 1.6 per 10,000 blocks) (Walker 2018). In adults, ultrasound guidance may produce superior peripheral nerve block success rates and decrease inadvertent vascular puncture (Lewis 2015). Ultrasound guidance for regional anaesthesia in children may thus improve the success rate while decreasing the rate of complications.

Why it is important to do this review

The use of ultrasound guidance for regional anaesthesia has become popular over the past two decades. However, ultrasound is not recognized by all experts as an essential tool. Indeed, many authorities believe that "clinical data demonstrating a reduction in neurologic injury with ultrasound guidance are currently lacking" (Neal 2015; Walker 2018). The cost of an ultrasound machine varies, with an average actually estimated at approximately USD 22,000 (Liu 2010; Ponde 2016). The equipment required to use ultrasound guidance is thus substantially more expensive than other tools, such as those used for nerve stimulation, which can be acquired for approximately USD 1000 or less (Liu 2010).

The main findings of a previously published version of our review were a reduction in the risk of failed peripheral nerve block and a longer block duration when ultrasound guidance was used compared with nerve stimulator (Guay 2016a). We undertook this

update to look for new trials and to determine if these claimed advantages still stand.

OBJECTIVES

To determine whether ultrasound guidance offers any clinical advantage when neuraxial and peripheral nerve blocks are performed in children in terms of decreasing failure rate or the rate of complications.

METHODS

Criteria for considering studies for this review

Types of studies

We included all parallel randomized controlled trials that evaluated the effect of ultrasound guidance when a regional blockade technique was performed in children and that included any of our selected outcomes. We excluded observational studies, quasi-randomized trials, cross-over trials, and cluster-randomized trials. We did not exclude studies based on language of publication or publication status.

Types of participants

We included studies performed in children (≤ 18 years of age) undergoing any type of surgical procedure (open or laparoscopic) for which a neuraxial (spinal, epidural, caudal, or combined spinal and epidural) or peripheral nerve block (any peripheral nerve block including fascial (fascia iliaca, transversus abdominis plane, rectus sheath blocks) or perivascular blocks), for surgical anaesthesia (alone or in combination with general anaesthesia) or for postoperative analgesia, was performed with ultrasound guidance. We excluded studies in which regional blockade was used to treat chronic pain.

Types of interventions

We included studies in which ultrasound guidance was used to perform the technique in real time (in-plane or out-of-plane), as pre-scanning before the procedure, or to evaluate the spread of the local anaesthetic so the position of the needle could be adjusted or the block complemented. For control groups, we accepted any other technique used to perform the block including landmarks, loss of resistance (air or fluid), click, paraesthesia, nerve stimulator or transarterial. Infiltration of local anaesthetics was accepted. We excluded no studies based on the specific technique used as the comparator.

Types of outcome measures

We evaluated differences between treatment and control groups based on the following outcomes.

Primary outcomes

1. Success rate (study author's definition).
2. Pain scores at one hour after surgery (any ascendent or descendent pain scale used by study authors).
3. Block duration (study author's definition; 0 to 1 day).

Secondary outcomes

1. Time to perform the block (minutes if available).
2. Number of needle passes.
3. Minor complications: bloody puncture, transient neurological injury, seizure from systemic local anaesthetic toxicity, block infections without neurological injury.
4. Major complications: cardiac arrest from local anaesthetic toxicity, lasting neurological injury (lasting more than three months).

Search methods for identification of studies

Electronic searches

We searched for studies with systematic and sensitive search strategies as described in Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). There were no language, publication year, or publication status restrictions. We searched the following databases: Cochrane Central Register of Controlled Trials (CENTRAL) (Appendix 1; 2018, Issue 3), MEDLINE (OvidSP) (from 1946 to 7 March 2018; Appendix 2), and Embase (OvidSP) (from 1974 to 7 March 2018; Appendix 3). The search strategy was done in consultation with the Information Specialist, and run by the Information Specialist.

Searching other resources

We searched the US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; March 2018) and World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/; March 2018) for unpublished and ongoing studies, and the OpenGrey database (www.opengrey.eu; March 2018) for grey literature.

We scanned the reference lists of all studies retained (during data extraction) and recent meta-analysis or reviews on the topic (March 2018). We also scanned conference proceedings of American Society of Regional Anesthesia, European Society of Regional Anaesthesia, European Society of Anaesthesiology, and American Society of Anesthesiology for 2012 to 2017. We contacted trial authors for additional information.

Data collection and analysis

Selection of studies

Two review authors (JG and SK) screened the list of all titles and abstracts identified by the search described above. We retrieved and independently read potential articles for inclusion to determine their eligibility. We resolved discrepancies by discussion without the need for help from the third review author (SS). We recorded 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

We selected studies, extracted data (assessment of risk of bias in included studies; types of outcome measures; assessment of heterogeneity), and entered the data onto our data extraction sheet. We first entered 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 rejection. After we reached agreement, one review author (JG) entered the data and the moderators for heterogeneity exploration into Comprehensive Meta-Analysis (Comprehensive Meta-Analysis 2007), and the same review author (JG) entered the 'Risk of bias' assessment into Review Manager 5 (Review

Manager 2014). Any disagreements were resolved by discussion. We contacted all study authors for additional information. We then transferred data for analysis to Review Manager 5 in the format required to include the maximal number of studies (events and total number of participants for each group; mean, standard deviation, and number of participants included in each group; or generic inverse variance if necessary). When possible, we performed an intention-to-treat analysis.

Assessment of risk of bias in included studies

We assessed the risks of bias of the included studies based on the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, attrition bias, reporting bias, and other risk of bias, using Review Manager 5 (Higgins 2011; Review Manager 2014). Any disagreements were resolved by discussion. We assessed the risk of bias based on information presented in the reports or provided by study authors, with no assumptions made.

Measures of treatment effect

We reported results as risk differences (RDs) and 95% confidence intervals (95% CIs) for dichotomous data (success rate, minor complications) and as mean differences (MDs) and 95% CIs for continuous data (pain scores, block duration, time to perform the procedure) to the degree this was feasible. If continuous data were measured on different scales (pain scores), or if results were provided with P values (number of attempts or needle passes), we presented the results as standardized mean differences (SMDs) and 95% CIs. For SMDs, we considered 0.2 a small effect, 0.5 a medium effect, and 0.8 a large effect (Pace 2011). When an effect was noted, we calculated a number needed to treat for an additional beneficial outcome (NNTB) or a number needed to treat for an additional harmful outcome (NNTH) from the odds ratio (OR). We used the odds ratio for calculation of the number needed to treat for an additional beneficial outcome (NNTB) and number needed to treat for an additional harmful outcome (NNTH) (Cates 2005), as this value is less likely to be affected by the side (benefit or harm) on which data are entered (Cates 2002; Deeks 2002). When we were unable to demonstrate an effect, we calculated the number of participants required in a large trial to ensure that enough participants were included in the retained studies to justify a conclusion on the absence of effect (Pogue 1998).

Unit of analysis issues

We included only parallel-group trials. If a study contained more than two groups, we fused two groups (by using the appropriate formula for adding standard deviations when required) if we thought that they were equivalent according to the criteria of our protocol (taking our factors for heterogeneity exploration into account) (Guay 2014), or we separated them and split the control group in half if we thought that they were different.

Dealing with missing data

We contacted all study authors. We did not consider medians as equivalent to means. Instead, we used the P value and the number of participants included in each group to calculate the effect size. We did not impute results. We entered data as intention-to-treat to the degree this was feasible. If this was not possible, we assessed the study as having unclear risk of bias for other risk of bias and entered the data on a per-protocol basis.

Assessment of heterogeneity

We considered clinical heterogeneity before pooling results and examined statistical heterogeneity before carrying out any meta-analysis. We quantified statistical heterogeneity by using the I^2 statistic. We quantified the amount of heterogeneity as low (< 25%), moderate (50%), or high (75%), depending on the value obtained for the I^2 statistic (Higgins 2003).

Assessment of reporting biases

We examined publication bias by using a funnel plot followed by Duval and Tweedie's trim and fill technique for each outcome. Duval and Tweedie's trim and fill analysis yields an estimate of what would be the effect size (odds ratio, risk ratio, etc.) if no publication bias was present.

Data synthesis

We analysed the data by using Review Manager 5 (Review Manager 2014), and Comprehensive Meta-Analysis (Comprehensive Meta-Analysis 2007), with random-effects models. We presented the characteristics of included and excluded studies in Characteristics of included studies and Characteristics of excluded studies tables. We presented the 'Risk of bias' assessment in a 'Risk of bias' graph. We presented results for each comparison as forests plots.

Subgroup analysis and investigation of heterogeneity

We explored any amount of heterogeneity, but focused more specifically on comparisons with more than a small amount of heterogeneity ($I^2 \geq 25\%$) (Higgins 2003). We explored heterogeneity by applying Egger's regression intercept (to assess the possibility of a small-study effect; Rucker 2011), and by performing visual inspection of the forest plots with studies placed in order according to a specific moderator, subgroupings (categorical moderators), or meta-regressions (continuous moderators). We considered the following factors when exploring heterogeneity: type of block (neuraxial versus peripheral nerve block), type of comparator (nerve stimulator versus other), age and type of guidance (pre-scanning versus real time (in-plane or out-of-plane)), and combined methods (ultrasound plus nerve stimulator compared with other modalities versus ultrasound alone compared with other modalities).

Sensitivity analysis

A sensitivity analysis (based mainly on the 'Risk of bias' assessment (allocation concealment and blinding of outcome assessor) or on an outlier) could also be performed for results with heterogeneity.

'Summary of findings' table and GRADE

We rated the quality of the body of evidence according to the GRADE system (GRADEprofiler; Schünemann 2013). We presented the quality of evidence in a 'Summary of findings' table for all of our outcomes: failed blocks, pain scores at one hour after surgery, block duration, time to perform the block, number of needle passes, and minor and major complications. For risk of bias, we judged the quality of the evidence as high when most information was derived from studies at low risk of bias, and downgraded the quality when most information was derived from studies at high or unclear risk of bias (allocation concealment and blinding of outcome assessors). For inconsistency, we downgraded the quality of evidence when the I^2 statistic was 75% or higher without a

satisfactory explanation. We did not downgrade the quality of evidence for indirectness, because outcomes were based on direct comparisons performed on the population of interest and were not surrogate markers. For imprecision, we downgraded the quality of evidence when the confidence interval 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 less than the one required in a large trial. For publication bias, we downgraded the quality of evidence when correcting for the possibility of publication bias as assessed by Duval and Tweedie's fill and trim analysis changed the conclusion. It should be noted that while factors influencing the quality of evidence are additive - such that the reduction or increase in each individual factor is added together with the other factors to reduce or increase the quality of evidence for an outcome - grading the quality of evidence involves judgements that are not exclusive. GRADE is therefore not a quantitative system for grading the quality of evidence. Each factor for downgrading or upgrading reflects not discrete categories but a continuum within each category and among the categories (Schünemann 2013). When the body of evidence is intermediate with respect to a particular factor, the decision about whether a study falls above or below the threshold for up- or downgrading the quality depends on judgement. Review authors may decide not to downgrade, even if there was some uncertainty around a specific category, when they have already downgraded for another factor, and lowering the quality of evidence further for the outcome would seem inappropriate (Schünemann 2013). 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. Low-quality and very low-quality evidence are considered equivalent to observational studies.

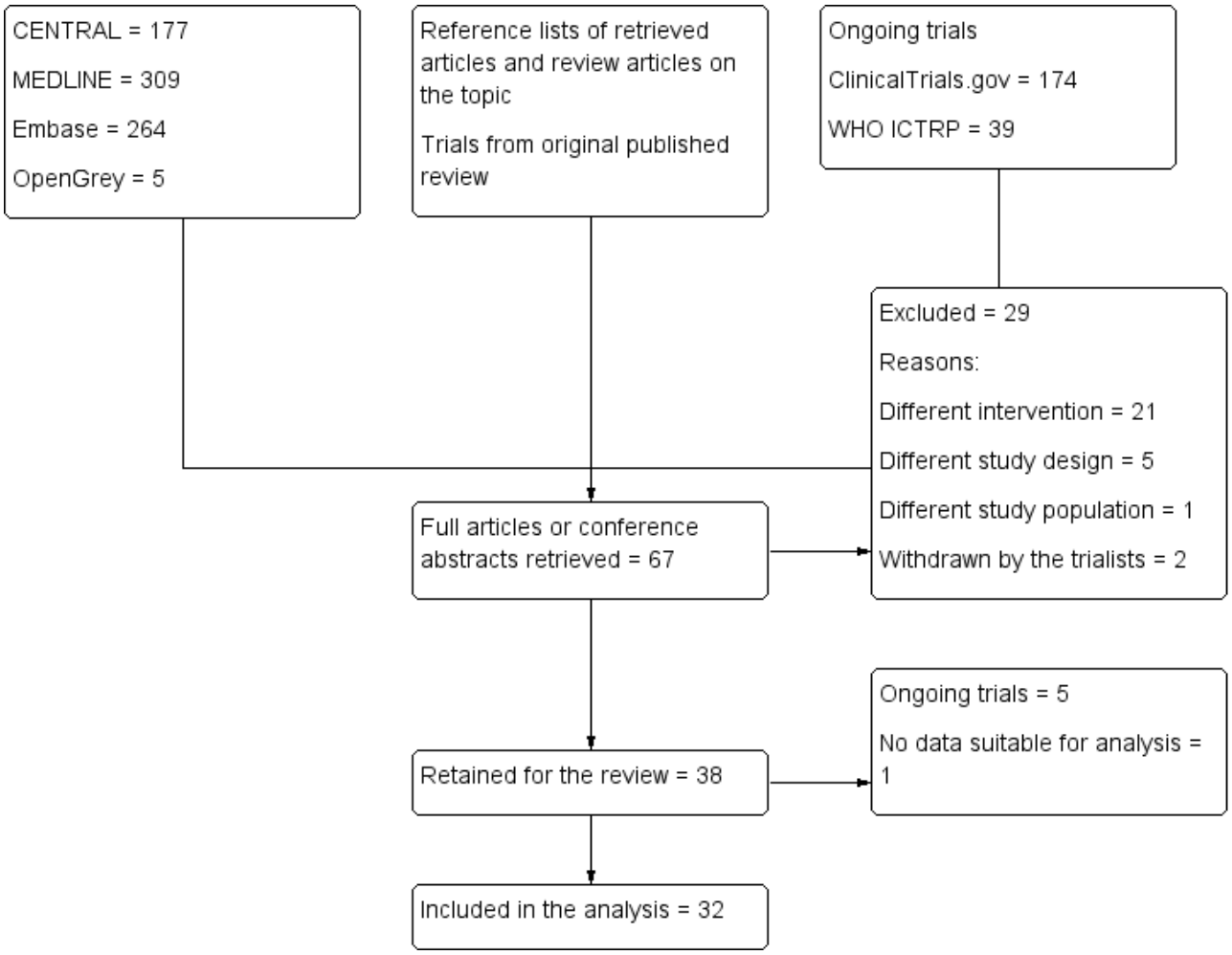
RESULTS

Description of studies

Results of the search

(See Figure 1)

Figure 1. Study flow diagram. Search results for the 2018 update.



Our electronic search identified 755 trials: 177 from CENTRAL, 309 from MEDLINE, 264 from Embase, and 5 from the grey literature. Our search of the trial registries identified a further 213 ongoing trials. After screening the titles/abstracts of trials identified by this search, the reference lists of retained trials and review articles, and conference abstracts, and adding the trials of the previously published version, we retrieved the full texts of 67 trials. We excluded 29 trials, leaving 38 trials in the review, of which 5 are ongoing. We included 33 trials in the review, and 32 in the analysis. One trial did not contain data suitable for analysis (Qiu 2016).

Included studies

We included 33 trials with a total of 2293 participants in the review. Compared with our previously published version (Guay 2016a; 20 trials with 1241 participants), this update contains 13 additional trials with 1052 additional participants. Blocks were performed with ultrasound guidance for 1149 participants, and without ultrasound guidance for 1144 participants. There were no data suitable for analysis for one trial with 100 participants (Qiu 2016), therefore we included 32 trials with 2193 participants in the analysis (Figure 1).

Setting

Trials were performed in Austria (N = 1; Marhofer 2004); Belgium (N = 2; Abasbassi 2017; Faraoni 2010); Canada (N = 1; Lorenzo 2014); China (N = 7; Li 2016; Liu 2012; Liu 2018; Nan 2012; Qiu 2016; Wang 2013; Yang 2015); Egypt (N = 2; Elnour 2009; Shaaban 2014); Greece (N = 1; Gkliatis 2017); India (N = 2; Ponde 2009; Ponde 2013); Ireland (N = 1; O'Sullivan 2011); Japan (N = 2; Tachibana 2012; Uchinami 2017); South Africa (N = 4; Oberndorfer 2007; Weintraud 2009; Willschke 2005; Willschke 2006); Turkey (N = 3; Ahiskalioglu 2018; Kendigelen 2014; Sahin 2013); and the USA (N = 7; Dingeman 2013; Flack 2014; Gurnaney 2011; Hozella 2017; Litz 2017; Relland 2017; Shank 2016). The trials were published between 2004 and 2018.

Funding

The source of funding was a governmental organization (N = 2; Flack 2014; Nan 2012); a charitable organization (N = 2; Dingeman 2013; Shank 2016); departmental/institutional (N = 13; Ahiskalioglu 2018; Faraoni 2010; Kendigelen 2014; Li 2016; Litz 2017; Liu 2018; Lorenzo 2014; O'Sullivan 2011; Ponde 2013; Relland 2017; Uchinami 2017; Wang 2013; Yang 2015); or unspecified (N = 14; Abasbassi 2017; Elnour 2009; Gkliatis 2017; Gurnaney 2011; Hozella 2017; Liu 2012; Marhofer 2004; Oberndorfer 2007; Ponde 2009; Qiu 2016; Sahin 2013; Shaaban 2014; Tachibana 2012; Weintraud 2009). Two studies declared that they received industry help (equipment loan; Willschke 2005; Willschke 2006).

Participants

The mean or median age of participants ranged from 0.9 to 12 years.

The following surgeries were performed: major abdominal or thoracic surgery (Willschke 2006); appendicectomy (Gkliatis 2017; Shaaban 2014); circumcision (Abasbassi 2017; Ahiskalioglu 2018; Faraoni 2010; Li 2016; O'Sullivan 2011); inguinal hernia repair (Kendigelen 2014; Qiu 2016; Sahin 2013; Wang 2013; Weintraud 2009); inguinal hernia repair or hydrocelectomy (Hozella 2017; Yang 2015); inguinal hernia repair or hydrocelectomy or cure of cryptorchidism (Nan 2012; Willschke 2005); lower limb surgery (Oberndorfer 2007; Ponde 2013); laparoscopic surgery (Uchinami 2017); the Nuss procedure for pectus excavatum (Tachibana 2012); open pyeloplasty (Lorenzo 2014); skin grafts (Shank 2016); upper limb surgery (Elnour 2009; Liu 2018; Marhofer 2004; Ponde 2009); umbilical hernia repair (Dingeman 2013; Flack 2014; Gurnaney 2011; Litz 2017; Relland 2017); or urological or perineal surgery (Liu 2012).

The following blocks were performed: brachial plexus block (Elnour 2009; Marhofer 2004; Ponde 2009); a median nerve block (Liu 2018); sciatic and femoral nerve blocks (Oberndorfer 2007; Ponde 2013); a femoral lateral cutaneous nerve block (Shank 2016); ilioinguinal/iliohypogastric nerve blocks (Nan 2012; Weintraud 2009; Willschke 2005; Yang 2015); penile nerve block (Abasbassi 2017; Faraoni 2010; Li 2016; O'Sullivan 2011); rectus sheath block (Dingeman 2013; Flack 2014; Gurnaney 2011; Litz 2017; Qiu 2016; Relland 2017; Uchinami 2017); transversus abdominis plane blocks (Gkliatis 2017; Hozella 2017; Kendigelen 2014; Lorenzo 2014; Sahin 2013; Shaaban 2014); thoracic epidural (Tachibana 2012); thoracic or lumbar epidural (Willschke 2006); and caudal blocks (Ahiskalioglu 2018; Liu 2012; Wang 2013).

Ultrasound guidance

Ultrasound guidance was used in real time with an in-plane (Elnour 2009; Faraoni 2010; Flack 2014; Gurnaney 2011; Hozella 2017; Kendigelen 2014; Li 2016; Liu 2018; Lorenzo 2014; O'Sullivan 2011; Ponde 2009; Ponde 2013; Qiu 2016; Relland 2017; Sahin 2013; Shaaban 2014; Uchinami 2017; Yang 2015); out-of-plane (Abasbassi 2017; Ahiskalioglu 2018; Marhofer 2004; Nan 2012; Oberndorfer 2007; Wang 2013; Weintraud 2009; Willschke 2005; Willschke 2006); or unspecified technique (Dingeman 2013; Gkliatis 2017; Litz 2017; Shank 2016); or as pre-scanning (Liu 2012; Tachibana 2012). (See Table 1)

Comparator

Ultrasound guidance was compared with infiltration (Dingeman 2013; Flack 2014; Gkliatis 2017; Gurnaney 2011; Hozella 2017; Kendigelen 2014; Lorenzo 2014; Relland 2017; Sahin 2013; Shaaban 2014; Shank 2016; Uchinami 2017); landmarks (Abasbassi 2017; Ahiskalioglu 2018; Faraoni 2010; Li 2016; Liu 2012; Liu 2018; Nan 2012; O'Sullivan 2011; Qiu 2016; Tachibana 2012; Wang 2013; Weintraud 2009; Willschke 2005; Willschke 2006; Yang 2015); a surgeon-administered block (Litz 2017); or a nerve stimulator (Elnour 2009; Marhofer 2004; Oberndorfer 2007; Ponde 2009; Ponde 2013).

(See Table 1)

Excluded studies

(See Characteristics of excluded studies)

We excluded 29 trials for the following reasons.

1. Different intervention (Abdellatif 2012; Ahmed 2014; Alsadek 2015; Atta 2008; Aveline 2011; Bryskin 2015; Fiocca 2013; Hamill 2015; Harju 2016; Jagannathan 2009; Matinyan 2015; Micic 2011; Mirjalili 2015; Narasimhan 2017; Oksuz 2017; Sahin 2013; Sethi 2016; Sherif 2011; Shin 2009; Triffterer 2012; Tutuncu 2017).
2. Different study design (Erbuyun 2016; Laserre-Sartre 2009; Lloyd 2016; Ponde 2017; Pérez-Pradilla 2015).
3. Different study population (Fusco 2016).
4. Trial withdrawn by study authors (NCT03427437; Sohn 2010).

Ongoing studies

We found five ongoing trials that could fit our inclusion criteria (ACTRN12608000488303; CTRI/2014/09/005023; CTRI/2018/01/011534; NCT02321787; NCT02352519). (See Characteristics of ongoing studies)

Awaiting classification

There are no trials awaiting classification.

Risk of bias in included studies

We have included a summary of our 'Risk of bias' assessment in Figure 2 and Figure 3.

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

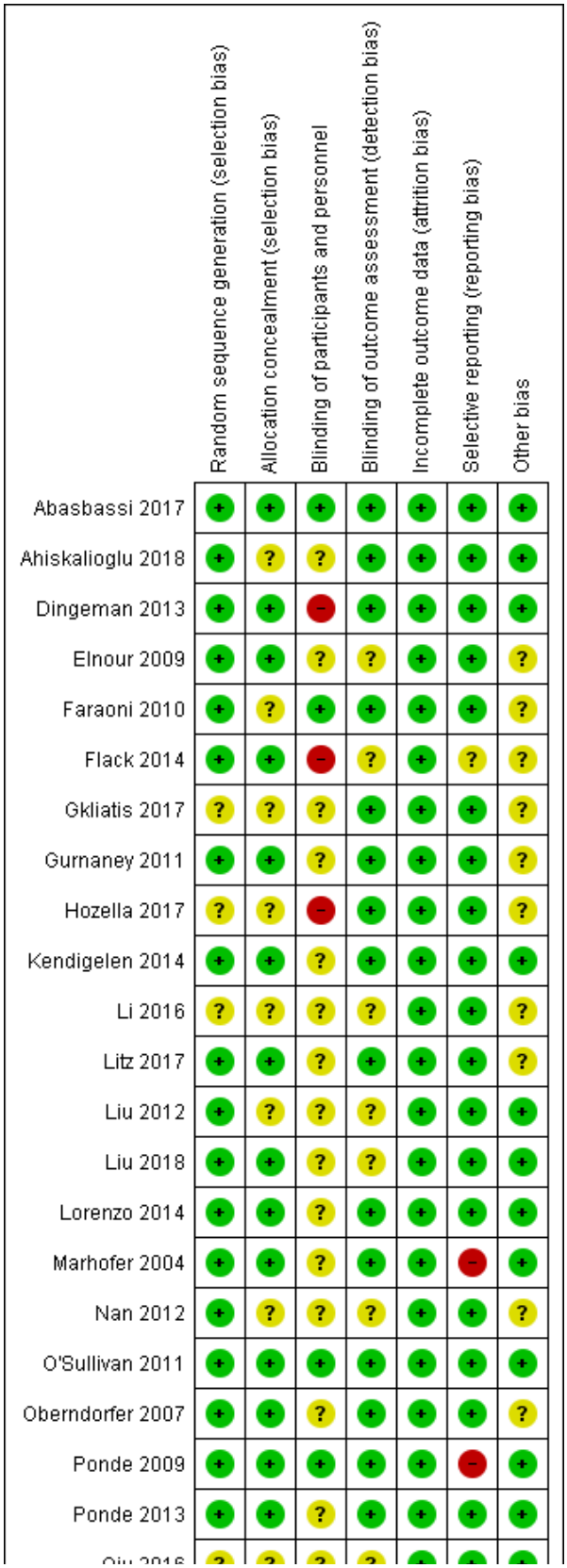


Figure 2. (Continued)

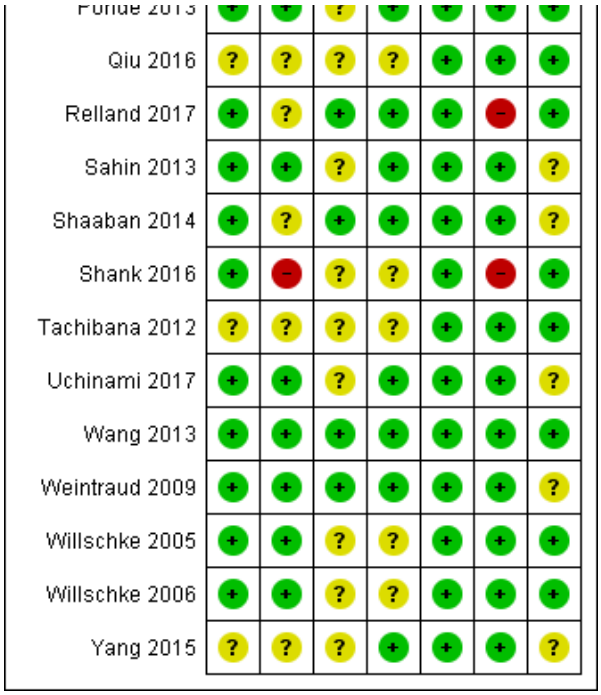
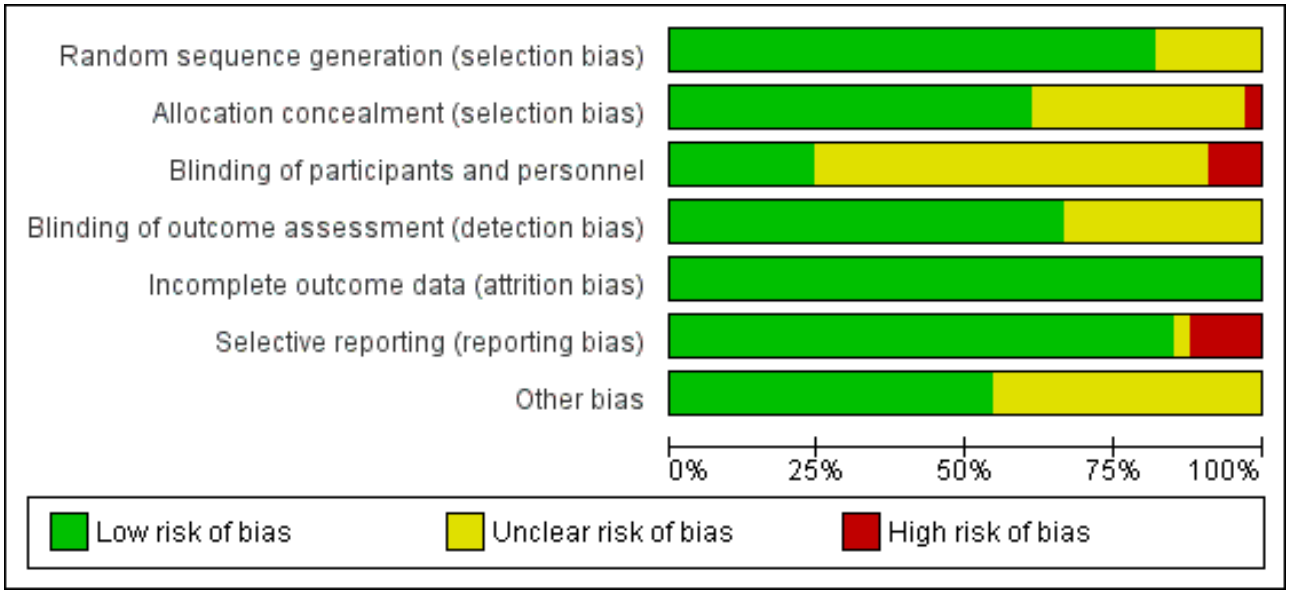


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



We judged random sequence generation as at low risk of bias for 27 trials (Abasbassi 2017; Ahiskalioglu 2018; Dingeman 2013; Elnour 2009; Faraoni 2010; Flack 2014; Gurnaney 2011; Kendigelen 2014; Litz 2017; Liu 2012; Liu 2018; Lorenzo 2014; Marhofer 2004; Nan 2012; O'Sullivan 2011; Oberndorfer 2007; Ponde 2009; Ponde 2013; Relland 2017; Sahin 2013; Shaaban 2014; Shank 2016; Uchinami 2017; Wang 2013; Weintraud 2009; Willschke 2005; Willschke 2006), and as at
unclear risk of bias for the other six trials.

Allocation

We judged allocation concealment as at low risk of bias for 20 trials (Abasbassi 2017; Dingeman 2013; Elnour 2009; Flack 2014; Gurnaney 2011; Kendigelen 2014; Litz 2017; Liu 2018; Lorenzo 2014; Marhofer 2004; O'Sullivan 2011; Oberndorfer 2007; Ponde 2009; Ponde 2013; Sahin 2013; Uchinami 2017; Wang 2013; Weintraud 2009; Willschke 2005; Willschke 2006). We judged it as at unclear/ high risk of bias for the remaining 13 trials.

Blinding

We judged blinding of participants and personnel caring for the participants as at low risk of bias for eight trials (Abasbassi 2017; Faraoni 2010; O'Sullivan 2011; Ponde 2009; Relland 2017; Shaaban 2014; Wang 2013; Weintraud 2009). We judged it as at unclear/high risk of bias for the remaining 25 trials.

We judged blinding of outcome assessment as at low risk of bias for 22 trials (Abasbassi 2017; Ahiskalioglu 2018; Dingeman 2013; Faraoni 2010; Gkliatis 2017; Gurnaney 2011; Hozella 2017; Kendigelen 2014; Litz 2017; Lorenzo 2014; Marhofer 2004; O'Sullivan 2011; Oberndorfer 2007; Ponde 2009; Ponde 2013; Relland 2017; Sahin 2013; Shaaban 2014; Uchinami 2017; Wang 2013; Weintraud 2009; Yang 2015). We judged it as at unclear/high risk of bias for the remaining 11 trials.

Incomplete outcome data

We judged all 33 included trials as at low risk of bias for this domain.

Selective reporting

We judged 28 trials as at low risk of reporting bias (Abasbassi 2017; Ahiskalioglu 2018; Dingeman 2013; Elnour 2009; Faraoni 2010; Gkliatis 2017; Gurnaney 2011; Hozella 2017; Kendigelen 2014; Li 2016; Litz 2017; Liu 2012; Liu 2018; Lorenzo 2014; Nan 2012; O'Sullivan 2011; Oberndorfer 2007; Ponde 2013; Qiu 2016; Sahin 2013; Shaaban 2014; Tachibana 2012; Uchinami 2017; Wang 2013; Weintraud 2009; Willschke 2005; Willschke 2006; Yang 2015). We judged the remaining five trials as at unclear/high risk of bias.

Other potential sources of bias

We judged 18 trials as exempt from other risk of bias (Abasbassi 2017; Ahiskalioglu 2018; Dingeman 2013; Kendigelen 2014; Liu 2012; Liu 2018; Lorenzo 2014; Marhofer 2004; O'Sullivan 2011; Ponde 2009; Ponde 2013; Qiu 2016; Relland 2017; Shank 2016; Tachibana 2012; Wang 2013; Willschke 2005; Willschke 2006). We judged the remaining 15 trials as at unclear risk of bias for this domain.

Effects of interventions

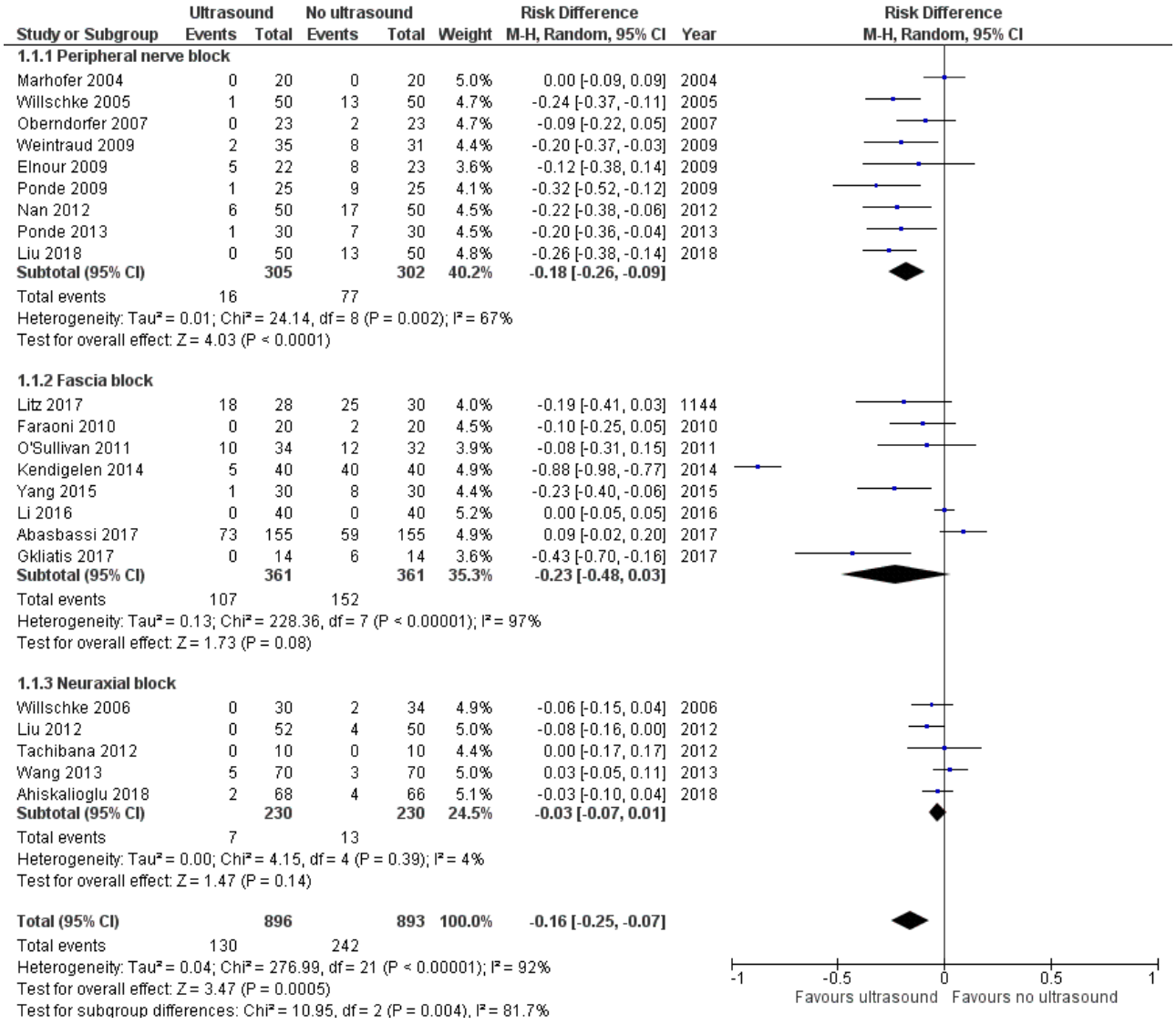
See: **Summary of findings for the main comparison** Ultrasound guidance compared with no ultrasound guidance for children

Primary outcomes

1. Success rate (study authors' definition)

Twenty-two trials with 1789 participants provided results for failure rate for peripheral nerve blocks (N = 9), fascia blocks (N = 8), or neuraxial blocks (N = 5) (Figure 4; Analysis 1.1). As per our previously published version (Guay 2016a), we did not include data from Lorenzo and colleagues in this analysis because failure reported by these authors was considered a failure of one specific regional anaesthetic for this specific indication and not a failure of ultrasound guidance (Lorenzo 2014). The definitions used by study authors can be found in Table 2. We obtained data from the reports.

Figure 4. Forest plot of comparison: 1 Ultrasound versus no ultrasound, outcome: 1.1 Success (event = failed block).



As per our previous version, we have presented data as failure rate. Ultrasound guidance reduces the risk of failed blocks (risk difference (RD) −0.16, 95% confidence interval (CI) −0.25 to −0.07; Figure 4; Summary of findings for the main comparison). The effect was more consistent for peripheral nerve blocks (RD −0.18, 95% CI −0.26 to −0.09; P = 0.004 for subgroups difference). There was no statistically significant evidence of small-study effect. The asymmetry of the funnel plot leads to a trim and fill estimate (RD −0.24, 95% CI −0.34 to −0.15). Based on a failure rate of 27%, 238 participants (119 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; one-sided test). The number needed to treat for an additional beneficial outcome (NNTB) is 6 (95% CI 5 to 8). We downgraded the quality of the evidence once for risk of bias, rating the quality as moderate.

2. Pain scores at one hour after surgery

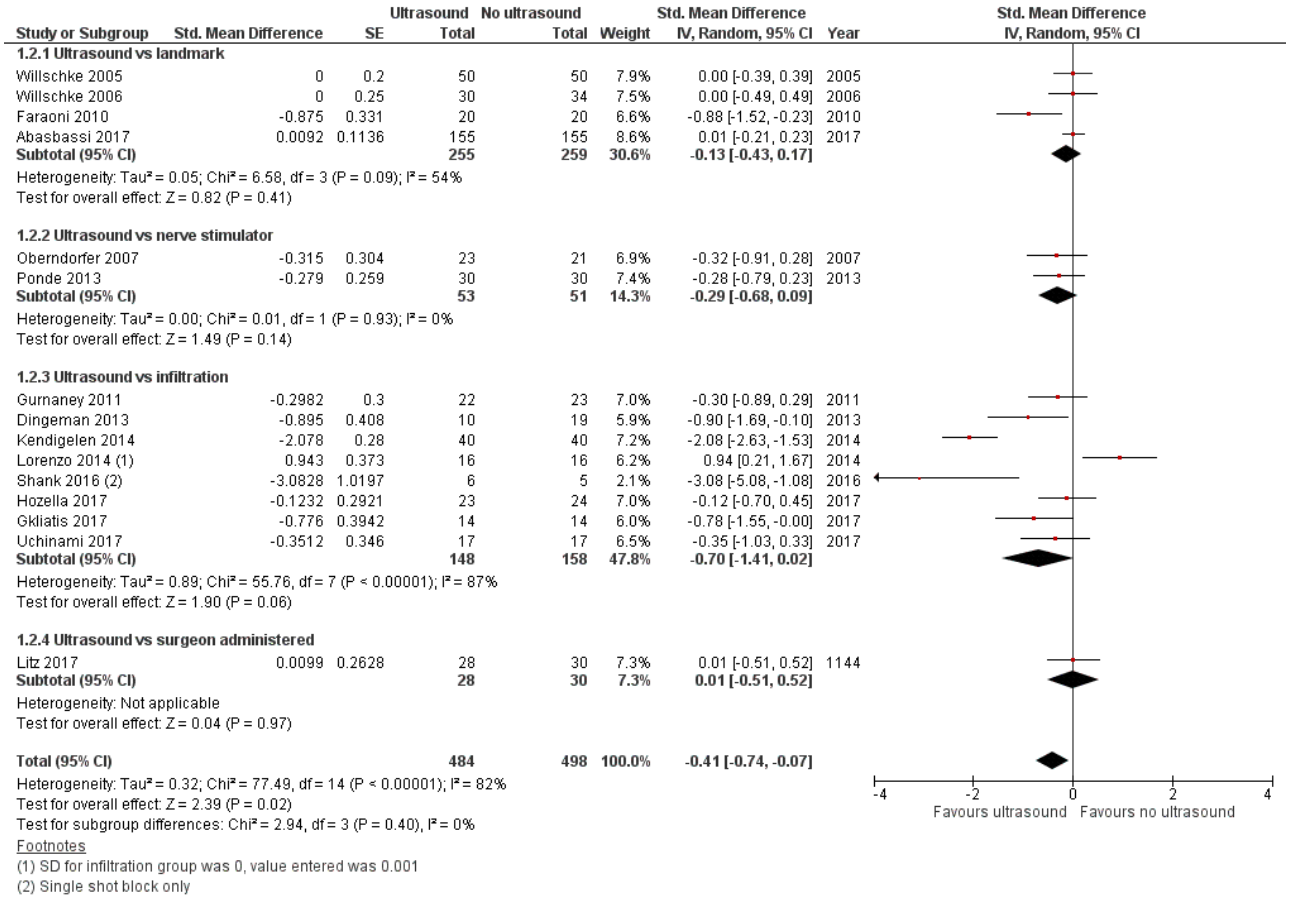
Fifteen trials with 982 participants provided results for pain at 1 hour after surgery (Analysis 1.2). The trials compared ultrasound guidance with landmarks (N = 4), a nerve stimulator (N = 2), wound infiltration (N = 8) or a surgeon-administered block (Litz 2017). We obtained data from the reports or from study authors (N = 8).

The study authors measured pain scores on various scales (Appendix 4). We extracted data as means and standard deviations (SDs) or as P values due to non-normal distribution (Kolmogorov-Smirov test; N = 4) or because they were not available as means and SDs (N = 4).

Ultrasound guidance reduces pain at one hour after surgery (standardized mean difference (SMD) −0.41, 95% CI −0.74 to −0.07; Figure 5; Summary of findings for the main comparison). There was no statistically significant evidence of a small-study effect or evidence of publication bias. Taking Gurnaney 2011 (SD in the control group 3.1), the difference would be equivalent to −1.3 on the revised Bieri FACES pain scale (scale: 0 = no pain, 10 = maximal pain; Chambers 1999; Hicks 2001). On the basis of Gurnaney 2011 (mean value 4.35; SD 3.1 for the control group), 238 (119 per group) would be required for a large trial to eliminate a difference of 1 on a score from 0 to 10 (alpha 0.05; beta 0.2; one-sided test). We downgraded

the quality of the evidence once for risk of bias, rating the quality as moderate.

Figure 5. Forest plot of comparison: 1 Ultrasound versus no ultrasound, outcome: 1.2 Pain at one hour after surgery.

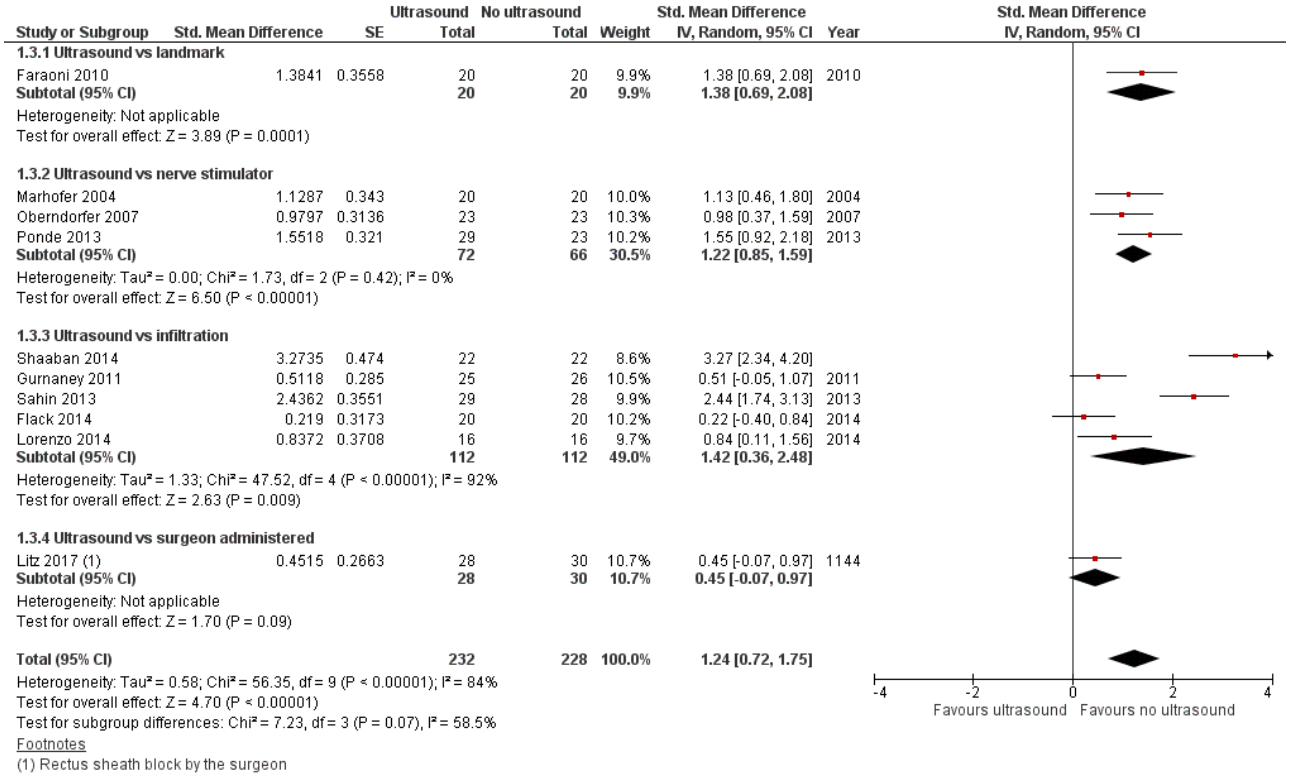


3. Block duration (study authors' definition; 0 to 1 day)

Ten trials with 460 participants provided results for duration of analgesia when ultrasound guidance was compared with landmarks (N = 1), a nerve stimulator (N = 3), wound infiltration (N = 5), or surgeon-administered block (Analysis 1.3) (Litz 2017). We obtained data from reports or from study authors (N = 2). We extracted data as means and SDs or as P value (non-normality distribution, Kolmogorov-Smirov test; N = 1) (not available as means and SDs: N = 3).

Ultrasound guidance prolongs block duration (SMD 1.24, 95% CI 0.72 to 1.75; Figure 6; Summary of findings for the main comparison). Egger's regression intercept showed that a small-study effect might be present (P = 0.005; two-sided test). Correcting the asymmetry of the funnel plot leads to an estimate (SMD 1.38, 95% CI 0.88 to 1.87). Based on Ponde 2013 (SD of the control group 0.57 hour), this would be equivalent to 0.71 hour or 42 minutes. For the six trials where we extracted the data as means and SDs, the mean time was 7.6 hours (SD 6.3 hours) for ultrasound guidance and 4.0 hours (SD 3.0 hours) for the comparators (Appendix 5). We did not downgrade the quality of the evidence and rated it as high.

Figure 6. Forest plot of comparison: 1 Ultrasound versus no ultrasound, outcome: 1.3 Block duration.



Secondary outcomes

1. Time to perform the block

Nine trials with 680 participants provided results for time to perform the block (Analysis 1.4). Ultrasound guidance was used in real-time in-plane (N = 4), real-time out-of-plane (N = 3), or as pre-scanning (N = 2). We obtained data from reports and extracted data as mean and SDs or as P value (not available as means and SDs: N = 2).

We did not find a difference a difference in time to perform the block (SMD −0.46, 95% CI −1.06 to 0.13). There was no evidence of small-study effect. Correcting the asymmetry of the funnel plot leads to an estimate (SMD −0.09, 95% CI −0.77 to 0.58). For the seven trials for which data were extracted as means and SDs, means and SDs were 4.6 minutes ± 4.6 minutes for ultrasound guidance and 5.2 minutes ± 5.0 minutes for the comparators (Appendix 6). We downgraded the quality of the evidence by one level for risk of bias, rating the quality as moderate.

2. Number of needle passes

Three trials with 256 participants provided results for number of needle passes for a neuraxial block (Analysis 1.5) (Ahiskalioglu 2018; Liu 2012; Tachibana 2012). We obtained data from the reports and extracted data as means and SDs or as P value (Tachibana 2012). Ultrasound guidance reduces the number of needle passes required to perform the block (SMD −0.63, 95% CI −1.08 to −0.18). There was no evidence of small-study effect. Correcting for the asymmetry of the funnel plot would lead to an estimate (SMD −0.32, 95% CI −0.82 to 0.17). From Liu 2012 (SD of the control group 0.6), the difference would be equivalent to 0.4 needle pass less per participant. For trials extracted as means and SDs, means and SDs were 1.2 ± 0.2 for ultrasound guidance and 1.5 ± 0.1 for the comparator (Appendix 7). We downgraded the quality of the evidence for risk of bias, imprecision and, and the possibility of publication bias, rating the quality as very low.

3. Minor complications

3a. Bloody puncture

Thirteen trials with 896 participants provided results for bloody punctures for peripheral nerve blocks (N = 5), fascia blocks (N = 5), or neuraxial blocks (N = 3) (Analysis 1.6). We obtained data from reports or from study authors (N = 4).

We did not find a difference in the risk of bloody puncture (RD −0.02, 95% CI −0.05 to 0.00). There was no evidence of small-study effect. Correcting for the asymmetry of the funnel plot would lead to an estimate (RD −0.02, 95% CI −0.04 to −0.01). Based on a rate of 5.3%, 1404 participants (702 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; one-sided test). We downgraded the quality of the evidence for imprecision and risk of publication bias, rating the quality as low.

3b. Transient neurological injury

Eighteen trials with 1230 participants provided results for transient neurological injury (paraesthesia) (RD −0.00, 95% CI −0.01 to 0.01; Analysis 1.7). We obtained data from reports or from study authors (N = 2). We downgraded the quality of the evidence by one level for risk of bias due to lack of clarity on specific methods and time points of assessment and by one level for imprecision, rating the quality as low.

3c. Seizures from local anaesthetic toxicity

Twenty-two trials with 1576 participants provided results for seizures from systemic local anaesthetic toxicity (RD 0.00, 95% CI −0.01 to 0.01; Analysis 1.8). We obtained data from reports or from study authors (N = 2). Based on an incidence of 0.05% (Walker 2018), 148,324 participants (74,162 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; one-sided test). We downgraded the quality of the evidence by one level for imprecision, rating the quality as moderate.

3d. Block infections without neurological injury

Eighteen trials with 1238 participants provided results for infection without neurological injury (RD 0.00, 95% CI −0.01 to 0.01; Analysis 1.9). We obtained data from reports or from study authors (N = 2). Based on an incidence of 0.5% of cutaneous infections with catheter insertions (Walker 2018), 18,766 participants (9383 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; two-sided test). We downgraded the quality of the evidence by one level for risk of bias (uncertainty about follow-up) and by one level for imprecision, rating the quality as low.

4. Major complications

No major complications were reported in any of the included studies (see Table 3).

4a. Cardiac arrest from local anaesthetic toxicity

Twenty-two trials with 1576 participants provided results for cardiac arrest from systemic local anaesthetic toxicity (RD 0.00, 95% CI −0.01 to 0.01; Analysis 1.10). We obtained data from reports or from study authors (N = 2). Based on an incidence of 0.05% (Walker 2018), 148,324 participants (74,162 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; one-sided test). We downgraded the quality of the evidence by one level for imprecision, rating the quality as moderate.

4b. Lasting neurological injury (lasting more than three months)

Nineteen trials with 1250 participants provided results for lasting neurological injury (RD 0.00, 95% CI −0.01 to 0.01; Analysis 1.11). We obtained data from reports or from study authors (N = 2). Based on a maximal incidence of 0.004% (Walker 2018), 1,854,710 participants (927,355 per group) would be required in a large trial to eliminate a 50% difference (alpha 0.05; beta 0.2; one-sided test). We downgraded the quality of the evidence by one level for risk of bias (uncertainty about follow-up) and by one level for imprecision, rating the quality as low.

DISCUSSION

Summary of main results

Failed block is the most common problem encountered in paediatric regional anaesthesia (Walker 2018). Our meta-analysis showed that ultrasound guidance may decrease the risk of failed blocks (Summary of findings for the main comparison). However, results for this outcome revealed some heterogeneity when all studies were included. The increased success rate was most evident for peripheral nerve block (Analysis 1.1).

Pain scores at one hour after surgery were reduced when ultrasound guidance was used; the difference was equivalent to −1.3 on a scale from 0 to 10 (Analysis 1.2). Ultrasound guidance may also significantly prolong block duration (Analysis 1.3).

We could not demonstrate a difference in minor complications (bloody punctures), and the difference between subgroups (neuraxial blocks versus peripheral nerve blocks versus fascia blocks) was not statistically different (Analysis 1.6). Reducing bloody punctures may be interesting for some patients (Suresh 2015), particularly those undergoing surgery requiring full heparinization (e.g. cardiac surgery) (Monahan 2019). For cardiac surgery, official societies suggest delaying surgery for 24 hours in case of traumatic attempt of neuraxial or deep block (Horlocker 2018). Postponing surgery may have an emotional and economical impact. Additional data are required before firm conclusions can be drawn regarding this.

None of the included studies reported major complications (Analysis 1.10; Analysis 1.11; Table 3). Walker and colleagues reported no lasting neurological complications in 104,393 blocks placed in 91,701 children (95% CI 0 to 0.4 per 10,000 blocks) (Walker 2018). It is therefore not surprising than none of these complications were reported in any of the randomized controlled trials included in our review. As a result of the extremely low incidence of major complications associated with paediatric regional anaesthesia, the incidence of these very rare events is probably best evaluated by large prospective studies. For adults, the risk of long-term neurological injury is estimated at 2 to 4 per 10,000 procedures, and there is no data demonstrating that any given technique would reduce the risk of major postoperative neurological complications (Neal 2015).

Although some bloody punctures were reported in our review (Analysis 1.6), there was no case of systemic local anaesthetic toxicity reported in any the trials included in the present review (seizure or cardiac arrest; Analysis 1.8; Analysis 1.10). In their large prospective trial, Walker and colleagues reported seven cases of severe local anaesthetic toxicity (seizures or cardiac arrest), for an incidence of 0.76 per 10,000 (95% CI 0.3 to 1.6 per 10,000) (Walker 2018). All cases of severe local anaesthetic systemic toxicity involved bolus dosing. This suggests that local anaesthetic toxicity (seizures or cardiac arrests) may have occurred due to either increased individual susceptibility, relative overdose, or inadvertent intravascular injection (Walker 2018). A possible reduction of bloody punctures in neuraxial blocks (RD −0.08, 95% CI −0.15 to −0.02; Analysis 1.6), eventually possibly leading to a decreased risk of inadvertent intravascular injection, might thus be interesting. In adults, a retrospective analysis of regional anaesthesia registries indicated that ultrasound guidance may have reduced the risk of local anaesthetic toxicity, actual risk 8.7 per 10,000 peripheral nerve blocks (95% CI 5.4 to 1.3 per 10,000 procedures) (Barrington 2013).

Infections after a single shot block are rarely observed if at all in immunocompetent individuals (Walker 2018). However, infections are reported with catheters (neuraxial or peripheral nerve blocks). Walker and colleagues reported 92 local cutaneous infections out of 18,065 continuous catheters, for an incidence of 53 per 10,000 catheters (95% CI 43 to 64 per 10,000) (Walker 2018). Antibiotics were prescribed in 29 of the 92 cases (Walker 2018). One child had a deep infection, epidural abscess requiring laminectomy (Walker 2018). The child made a full recovery (Walker 2018). None of these complications were reported in any of the trials included in our review (Analysis 1.9).

The overall incidence of transient postblock paraesthesia (less than 1%) found in the present review is in agreement with numbers reported in adults and children (Analysis 1.7). While reviewing 1614 axillary blocks performed on 607 adults with a nerve stimulator, paraesthesia technique, or transarterial technique, Horlocker and colleagues found seven neurological complications related to the anaesthetic technique, for an incidence of 43 per 10,000 procedures (95% CI 21 to 89 per 10,000 procedures) (Horlocker 1999). Symptoms had a median duration of four weeks (Horlocker 1999). In children, Walker and colleagues reported 25 neurological complications, for an incidence of 2.4 per 10,000 blocks (95% CI 1.6 to 3.6 per 10,000) (Walker 2018). Neurologic complications were more common in children more than 10 years of age, primarily sensory in nature and all resolved over a period of weeks to months, with only 2 cases demonstrating a sensory deficit beyond 3 months (Walker 2018). All events reported in the present review were from one small trial (Elnour 2009), on axillary brachial plexus block. Elnour and colleagues reported 6 postblock paraesthesia out of 50 participants: 4 when axillary brachial plexus blocks were performed with a nerve stimulator (distal motor response at 0.5 mA or less and 0.3 milliseconds, Locoplex needle, Vygon, Ecouen, France), and 2 with ultrasound guidance (in-plane technique, selective injections to target each nerve, unspecified type of needle). All paraesthesia were classified as transient and resolved within five days after surgery (Elnour 2009). In adults, ultrasound guidance may reduce the risk of procedural paraesthesia (Lewis 2015). In children, performing regional blockade under general anaesthesia or deep sedation is considered standard of care (Ivani 2015), therefore reducing procedural paraesthesia in children with ultrasound guidance may not be as relevant as it is for adults. It is unclear if reducing procedural paraesthesia would have any beneficial effect on the risk of postoperative transient paraesthesia in children.

Overall completeness and applicability of evidence

Our review included both peripheral and neuraxial blocks in children from birth to 18 years of age undergoing a wide variety of surgeries. For this reason, we had to subgroup the studies according to predefined criteria in our exploration of heterogeneity. We are confident that the evidence obtained is sufficient to allow us to draw valid conclusions for failed blocks. Due to their extremely low incidence, major complications might be best evaluated with large prospective trials. More data may be useful regarding the possibility of decreased bloody puncture when ultrasound guidance is used for neuraxial blocks.

Quality of the evidence

Details of our reasons for upgrading or downgrading the quality of the evidence are provided in the Effects of interventions section. We rated the quality of evidence as high for block duration, moderate for success rate and pain at one hour after surgery, and very low for number of needle passes required to perform the block (Summary of findings for the main comparison). Risk of bias and imprecision were the major reasons for downgrading the quality of the evidence. For neurological injury (transient or lasting), lack of clarity on follow-up was also considered to be an issue.

Potential biases in the review process

We are confident that given our extensive search we have included the available literature on this topic. The included studies were all relatively recent (from 2004 to 2018) and therefore likely well reflect actual medical practice and technology. Although doses and volumes of injected solutions varied, they seemed appropriate for the surgical indications for which they were used in most studies.

Agreements and disagreements with other studies or reviews

Unlike the Cochrane Review on ultrasound guidance for peripheral nerve block in adults (Lewis 2015), we could not demonstrate a reduction in the risk of bloody punctures. However, we believe that additional paediatric data are required before firm conclusions can be drawn on a possible decreased incidence of bloody punctures when ultrasound guidance is used for caudal blocks. Indeed, bloody punctures may be decreased with ultrasound guidance for caudal blocks (Analysis 1.6). Our finding on decreased failed blocks is in agreement with Lewis and colleagues, Lewis 2015, and with the previous version of the present review (Guay 2016a).

AUTHORS' CONCLUSIONS

Implications for practice

Ultrasound guidance for regional blockade in children probably reduces the risk of failed block. It also increases duration of the block and produces a small to moderate reduction in pain scores at one hour after surgery. There is probably little or no difference in the time taken to perform the block, and it is uncertain whether the use of ultrasound guidance reduces the number of needle passes required. There were no occurrences of major complications in either the intervention or control arms of the trials. There may be little or no difference between groups in the risk of bloody puncture. There were no occurrences of seizure from local anaesthetic toxicity or block infections without neurological injury. Altogether, whether or not these differences justify the extra cost of ultrasound guidance should probably also take into account the anaesthesiologist's expertise and local resources. The five ongoing studies may alter the conclusions of the review once published and assessed.

Implications for research

The number of trials available is now sufficient to allow us to conclude that ultrasound guidance probably offers some advantages regarding most of our beneficial outcomes: success rate (Analysis 1.1), reduced pain at one hour after surgery (Analysis 1.2), and prolonged block duration (Analysis 1.3). It seems unlikely that additional research will substantially affect these conclusions. However, there is still not enough information to determine if ultrasound guidance could help reduce complications from regional anaesthesia in children. Due to a fortunately extremely low incidence of major complications, it seems unlikely that efforts in trying to demonstrate a difference (or not) in the risk of major complications with ultrasound guidance using randomized controlled trials would be worthwhile. Large prospective trials could be the best option for this (Walker 2018). Future research should probably focus on two minor complications: transient paraesthesia for peripheral nerve blocks and bloody punctures in children undergoing caudal block. A reduced risk of bloody puncture with caudal blocks would seem more likely to be clinically relevant.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Abasbassi 2017

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: written parental informed consents obtained Site: Leuven, Belgium Dates of data collection: between September 2012 and November 2016 Funding: not reported Registration: EU Clinical Register AT032012, EUDRACT 2012-001217-16
Participants	310 ASA 1 or 2 children; median age: 2.4 years **Inclusion criteria** 1. Aged between 52 weeks postconception and 11 years old undergoing circumcision **Exclusion criteria** 1. Intolerance or allergic reaction against any product used in the study, psychomotorretardation, and the inability to give written informed consent

Abasbassi 2017 *(Continued)*

Interventions	**Intervention:** ultrasound-guided penile block (N = 155) **Comparator:** landmark penile block (N = 155)
Outcomes	**Relevant to this review** 1. Failed blocks (rescue postoperative analgesia) 2. Pain scores 3. Complications (haematoma, gangrene of the glans due to arterial compression, and signs of local anaesthetic systemic toxicity) **Others** 1. Anaesthesia induction time (13 versus 11 minutes) 2. Rescue analgesia 3. Nausea and vomiting 4. Length of hospital stay (no difference) 5. Need for analgesics at home (no difference)
Notes	Conference abstract Correspondence: addition information received from study authors Conflict of interest: no conflicts of interest declared DOI: 10.1111/pan.13429

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random table"
Allocation concealment (selection bias)	Low risk	Quote: "allocation concealment was ensured by enclosing assignments in sealed opaque, sequentially numbered envelopes, which were brought to the operation room by a study nurse and opened only after the arrival of the patient in the operating theatre by the investigator"
Blinding of participants and personnel	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Observer-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants underwent the allocated technique. 62 participants were lost to follow-up after 24 hours (landmark group: 29; ultrasound group: 33, P = 0.67) Outcomes for the present review were taken in hospital.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Groups had similar demographic data.

Ahiskalioglu 2018

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Turkey Dates: not reported Funding: departmental/institutional Registration: NCT03337191
Participants	134 children; mean age 6.72 years **Inclusion criteria** 1. ASA physical status 1 or 2, between the ages of 5 and 12 years old who underwent elective circumcision 2. Surgery for phimosis **Exclusion criteria** 1. Children with severe systemic disease 2. Previous neurological or spinal disorder 3. Coagulation anomaly 4. Allergy against local anaesthetics 5. Local infection at block site 6. History of premature birth
Interventions	**Intervention:** ultrasound-guided caudal block (N = 68) **Comparator:** landmark caudal block (N = 66)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Time to perform the block 3. Number of needle passes 4. Complications (systemic local anaesthetic toxicity) **Others** 1. Success at first puncture: first puncture success rate was higher for ultrasound (80% vs 63%, respectively; P = 0.026) 2. Nausea and vomiting (none)
Notes	Correspondence: email sent to authors 9 March 2018 Conflict of interest: none DOI: 10.1016/j.jclinane.2017.11.011

Risk of bias

Bias	Authors' judgement	Support for judgement

Ahiskalioglu 2018 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "randomization list by a computerized program"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "all data are collected by an anaesthetist blinded to the group classification"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up All participants enrolled were analysed.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Groups had similar demographic data.

Dingeman 2013

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: tertiary-referral urban children's hospital, USA Dates: November 2009 through May 2011 Funding: charity: a pilot grant from Harvard Catalyst/The Harvard Clinical and Translational Science Center, Boston Children's Hospital Surgical Foundation and the Department of Anesthesiology, Perioperative and Pain Medicine Registration: NCT01015053
Participants	52 children; mean age: 6.1 years **Inclusion criteria** 1. From 3 to 12 years of age undergoing elective umbilical hernia repair **Exclusion criteria** 1. ASA physical status ≥ 3 2. History of a complex regional pain syndrome 3. History of long-term analgesic use 4. Use of any analgesic (e.g. an opioid medication, paracetamol, a non-steroidal anti-inflammatory agent) within 24 hours before surgery 5. History of renal insufficiency or a bleeding disorder 6. Concurrent additional surgery at another anatomical site 7. Being a ward of the state

Dingeman 2013 *(Continued)*

	8. A non-English- or non-Spanish-speaking patient or primary caregiver 9. Inability to document postoperative pain level using FACES scores 10. Inability of the primary caregiver to comply with home instructions
Interventions	**Intervention:** bilateral rectus sheath block with real-time ultrasonographic guidance (N = 27) **Comparator:** infiltration by the surgeon (subcutaneous or intradermal) (N = 25)
Outcomes	**Relevant to this review** 1. Pain in PACU at ≥ 40 minutes measured with FACES pain rating scale (accepted as at 1 hour) **Others** 1. Rescue opioid and non-opioid analgesia 2. Length of stay in PACU
Notes	Correspondence: study authors were contacted on 8 and 27 February 2015 and in 2018: no reply Conflict of interest: none reported DOI: 10.1001/jamasurg.2013.1442

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization scheme was created using a uniform (0 or 1) random number generator in commercially available statistical software incorporating an age-stratified permuted block method of size 4 to achieve optimal balance (patient age strata, 3 - 7 and 8 - 12 years)"
Allocation concealment (selection bias)	Low risk	Quote: "randomization proceeded after written informed consent was obtained in the preoperative area and was assigned by a research team member blinded to the group allocation. Sealed envelopes for each age stratum containing the random allocations were opaque and tamperproof"
Blinding of participants and personnel	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the patient and family, recovery room nurses, and study coordinator who collected the data from families were blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up. Data were obtainable for 19/27 and 10/25 participants at 10 minutes.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Groups well balanced.

Elnour 2009

Methods	Parallel RCT

Elnour 2009 *(Continued)*

	Ethics committee: approved Informed consent: written parental informed consents obtained Setting: university hospital, Egypt Funding: unspecified Date of data collection: November 2007 through August 2008 Registration: not reported
Participants	50 children; mean age: 7.2 years **Inclusion criteria** 1. ASA 1 or 2 children from 5 to 10 years scheduled for forearm and hand surgery **Exclusion criteria** 1. Parent or participant refusal 2. Known or suspected sensitivity to amide local anaesthetics (bupivacaine) 3. Evidence of soft tissue infection near the proposed injection site 4. History of coagulopathy 5. Unco-operative or mentally unstable child 6. Axillary lymphadenopathy 7. Significant neurological disorder of the upper extremity
Interventions	**Intervention:** axillary brachial plexus with ultrasound (N = 25) **Control group:** axillary brachial plexus with nerve stimulator (N = 25)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores (no data at 1 hour) 3. Block duration (results given as categorical data, not included in the analysis; favoured ultrasound-guided technique but not significant) 4. Time to perform the block 5. Complications (lasting neurological deficit, systemic local anaesthetic toxicity) **Others** 1. Haemodynamic parameters 2. Parent satisfaction
Notes	Correspondence: email sent to authors 9 March 2018, no reply Conflict of interest: not reported DOI: NA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly allocated by a computer-generated table"

Elnour 2009 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "the randomization sequence was concealed in sealed envelopes"
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 participants were excluded because of cancelled surgery (n = 2), change in anaesthetic plan (n = 2), or incomplete participant information (n = 1). Among the remaining 45 participants, 5 had a performance time longer than 20 minutes, leaving 40 complete participant data sets available for analysis. 2 of these participants belonged to the ultrasound group, and 3 belonged to the nerve stimulator group. We included them as failed blocks for this meta-analysis.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat No significant differences in demographic data between study groups

Faraoni 2010

Methods	Parallel RCT Ethics committee: approved by the ethics committee Consents: parental informed consents obtained Setting: Belgium Funding: departmental resources Date of data collection: July 2009 until November 2009 Registration: not registered
Participants	40 boys, mean age 3.0 years **Inclusion criteria** 1. 1 to 14 years old who were scheduled for circumcision **Exclusion criteria** 1. Allergy to amino-amide local anaesthetics and a general contraindication for peripheral nerve block
Interventions	**Intervention:** ultrasound-guided penile block (N = 20) **Comparator:** penile block based on landmarks (N = 20)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Postoperative pain scale at 1 hour (SD for ultrasound group 0 entered as 0.001)

Faraoni 2010 *(Continued)*

	3. Block duration (time of first required dose of paracetamol) **Others** 1. Surgical time 2. Length of stay in PACU 3. Time to first micturition
Notes	Correspondence: additional information received from study authors 30 January 2015 (data) and 13 March 2018 Conflict of interest: no conflict of interest DOI: 10.1111/j.1460-9592.2010.03405.x

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed using a computerized randomization table"
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of participants and personnel	Low risk	Blocks performed under general anaesthesia. Staff anaesthesiologists and PACU nurses in charge were not aware of the technique used.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the nurse in charge of the patient was blinded to the regional anaesthesia technique used. On arrival and every 30 min, the modified Objective Pain Scale (OPS) without the arterial pressure measures was recorded by the nurse trained to use this scale"
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	Unclear risk	Not intention-to-treat Groups had similar demographic data.

Flack 2014

Methods	Parallel RCT Ethics committee: approved Consents: written informed parental consents obtained Setting: university hospital, USA Funding: government: supported in part by National Institutes of Health Grant ULI RR025014-01 of the University of Washington Institute of Translational Health Sciences

Flack 2014 *(Continued)*

	Date of data collection: not reported Registration: NCT00836134
Participants	40 children; mean age: 5.4 years **Inclusion criteria** 1. Undergoing umbilical hernia repair **Exclusion criteria** 1. Younger than 1 or older than 17 years 2. Bupivacaine or morphine allergy 3. Local infection 4. Coagulopathy 5. Emergency surgery 6. Additional surgical procedures 7. Participant or parent refusal
Interventions	**Intervention:** ultrasound-guided rectus sheath block (N = 20) **Comparator:** wound infiltration (N = 20)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration 3. Complications (local anaesthetic toxicity) **Others** 1. Length of surgery 2. Rescue analgesia 3. Rescue antiemetics 4. Plasma bupivacaine concentrations
Notes	Correspondence: study authors contacted on 28 January 2015. Replied on 29 January 2015 that they would send the data but never did so, despite multiple reminders including in March 2018 Conflict of interest: no conflict of interest declared DOI: 10.1111/pan.12438

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated randomization was stratified based on age (1–3 and 4–17 years), and sequences of sealed envelopes were provided by biostatistical services"
Allocation concealment (selection bias)	Low risk	Quote: "computer-generated randomization was stratified based on age (1–3 and 4–17 years), and sequences of sealed envelopes were provided by biostatistical services"
Blinding of participants and personnel	High risk	Although observers measuring pain scores were blinded, recovery room nurses administering rescue analgesia were not. This potentially introduced bias and influenced rescue analgesia administration.

Flack 2014 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Pain scores were assessed by a blinded observer; morphine use may not have been blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Pain scores measured but not provided.
Other bias	Unclear risk	Intention-to-treat Rectus sheath blocks performed 10 minutes or longer before surgical incision and infiltration at the end of the procedure.

Gkliatis 2017

Methods	Parallel RCT Ethics committee: not reported Informed consent: obtained Site: Athens, Greece Dates: not reported Funding: unspecified Registration: not reported
Participants	28 children; mean age: not reported **Inclusion criteria** 1. ASA 1 or 2, aged 5 to 11 years old undergoing open appendicectomy **Exclusion criteria** 1. Not reported
Interventions	**Intervention:** ultrasound-guided posterior transversus abdominis plane block (N = 14) **Comparator:** wound infiltration (N = 14)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Complications (study authors mentioned that no complications were recorded) **Others** 1. Rescue analgesia 2. Nausea and vomiting
Notes	Conference abstract Correspondence: email sent to authors 9 March 2018, no reply

Gkliatis 2017 *(Continued)*

	Conflict of interest: not reported
	DOI: NA

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	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the evaluator was blinded to the intervention"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up mentioned.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	No details on demographic data

Gurnaney 2011

Methods	Parallel RCT Ethics committee: approved by the ethics committee Consents: parental informed consents obtained Setting: university hospital, USA Funding: unspecified Date of data collection: not reported Registration: NCT00578136
Participants	54 children; mean age: 7.8 years **Inclusion criteria** 1. ASA physical status 1 or 2 participants between 5 and 18 years of age who were scheduled to undergo an umbilical hernia repair. 52 completed the study. **Exclusion criteria** 1. Individuals with developmental delay that parents believed would interfere with postoperative pain score assessment and those with allergy to bupivacaine
Interventions	**Intervention:** real-time (in-plane) rectus sheath block (N = 26)

Gurnaney 2011 *(Continued)*

	Comparator: wound infiltration (N = 26)
Outcomes	**Relevant to this review** 1. Pain at rest and on movement in PACU. We retained at-rest data for consistency with other studies. 2. Block duration **Others** 1. Rescue analgesia 2. Nausea 3. Vomiting 4. Pruritus
Notes	Correspondence: additional information provided by study authors 30 January 2015 Conflict of interest: none declared DOI: 10.1093/bja/aer263

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "assigned using computer-generated random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "after obtaining written informed consent, the study patients were assigned using computer-generated random numbers"
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the PACU team was blinded to the method of administering local anaesthetic. A blinded member of the research team made the initial assessment of postoperative pain using the revised Bieri FACES pain scale"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 lost in each group. 1 child excluded after randomization for developmental delay.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat Groups well balanced

Hozella 2017

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Beaumont Health, Royal Oak, Michigan, USA

Hozella 2017 *(Continued)*

	Dates: not reported Funding: departmental/institutional Registration: NCT01698268
Participants	50 children; mean age: not reported **Inclusion criteria** 1. Aged 24 to 100 months scheduled for elective hydrocelectomy or inguinal hernia, or both **Exclusion criteria** 1. Not reported
Interventions	**Intervention:** ultrasound-guided transverse abdominis plane block (N = 23) **Comparator:** wound infiltration (N = 24)
Outcomes	**Relevant to this review** 1. Pain **Others** 1. Rescue analgesia 2. Parental satisfaction 3. Adverse events included nausea, urinary urgency, and agitation
Notes	Conference abstracts Correspondence: email sent to authors 9 March 2018, no reply Conflict of interest: none DOI: NA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "prospective, randomized", no details
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	High risk	Single-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Single-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 participants excluded from data analysis due to protocol violations.
Selective reporting (reporting bias)	Low risk	All results reported.

Hozella 2017 *(Continued)*

Other bias	Unclear risk	Not intention-to-treat No details on group characteristics

Kendigelen 2014

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Setting: university hospital, Turkey Funding: departmental Date of data collection: between January 2014 and December 2014 Registration: not reported
Participants	86 children: mean age: 7.5 years **Inclusion criteria** 1. Between 6 and 8 years of age (ASA 1 to 2) undergoing unilateral inguinal surgery **Exclusion criteria** 1. History of allergy 2. Preoperative chronic pain treatment 3. Hepatic and renal failure 4. Previous inguinal surgery 5. Not able to evaluate the pain score
Interventions	**Intervention:** ultrasound transversus abdominis plane block (N = 40) **Comparator:** wound infiltration by the surgeon (N = 40)
Outcomes	**Relevant to this review** 1. Pain scores 2. Complications (study authors reported no complications related to the blocks) **Others** 1. Rescue analgesia 2. Nausea and vomiting 3. Parent satisfaction
Notes	Correspondence: information received from study authors 12 March 2018 Conflict of interest: the authors declare that they have no conflict of interest DOI: 10.1016/j.jclinane.2015.12.027

Risk of bias

Bias	Authors' judgement	Support for judgement

Kendigelen 2014 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "randomly divided", "closed envelope technique"
Allocation concealment (selection bias)	Low risk	Closed-envelope technique kept by the nurse who informed anaesthesiologists and surgeons doing the block or infiltration.
Blinding of participants and personnel	Unclear risk	Quote: "observer blinded" Parents were not informed of the group to which they had been assigned. Blocks performed at the end of surgery. Unclear for personnel caring for participant
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "observer-blinded" Anaesthesiologist who performed the block and the surgeon who did the infiltration were not present during pain evaluation and data collection.
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants were excluded from the study: 2 did not meet the inclusion criteria (allergy and previous inguinal surgery); 2 declined to participate; 1 lost to follow-up; 1 protocol violation.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Groups had similar demographic characteristics.

Li 2016

Methods	Parallel RCT Ethics committee: not reported Informed consent: not reported Site: Second Affiliated Hospital of Wenzhou Medical University, China Dates of data collection: not reported Funding: departmental/institutional Registration: not reported
Participants	80 children; mean age: not reported **Inclusion criteria** 1. ASA 1, aged from 5 to 12 years, weight between 15 kg and 52 kg and undergoing circumcision **Exclusion criteria** 1. Not reported
Interventions	**Intervention**: ultrasound-guided dorsal penile block (N = 40) **Comparator:** landmark dorsal penile block (N = 40)

Li 2016 *(Continued)*

Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Time to perform the block **Others** 1. Nausea and vomiting 2. Bradycardia, nausea, vomiting, restlessness, urinary retention, and pruritus 3. Respiratory depression between the 2 groups
Notes	Conference abstract Correspondence: email sent to authors 9 March 2018, no reply received Conflict of interest: none declared DOI: 10.1213/01.ane.0000492645.57194.ae

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly divided", no details
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	No failed block No details on group demographic data

Litz 2017

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Johns Hopkins All Children's Hospital, St Petersburg, FL, USA

Litz 2017 *(Continued)*

	Dates of data collection: from July 2014 through February 2016 Funding: departmental/institutional Registration: NCT02341144
Participants	61 children: mean age: 6.2 years **Inclusion criteria** 1. From 3 to 18 years old with a diagnosis of umbilical hernia **Exclusion criteria** 1. Pregnancy, strangulated or incarcerated umbilical hernia 2. Allergy to bupivacaine/ropivacaine 3. Undergoing concurrent surgical procedures 4. Developmental delay or neurologic diagnosis that would interfere with postoperative pain score assessment 5. Chronic pain medication use 6. Chronic pain disorder or complex regional pain syndrome 7. ASA physical status classification of 3 or greater
Interventions	**Intervention:** ultrasound-guided rectus sheath block (N = 28) **Comparator:** surgeon-administered rectus sheath block (N = 30)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration **Others** 1. Operating room time 2. Rescue analgesia 3. Length of hospital stay
Notes	Correspondence: email sent to authors 9 March 2018 Conflict of interest: none DOI: 10.1016/j.jpedsurg.2017.03.007

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	1:1 non-stratified randomization was computer generated.
Allocation concealment (selection bias)	Low risk	The random assignments to treatment groups were placed in identical, opaque, sealed envelopes. Envelopes were consecutively numbered with a study identification number and opened in order when a participant arrived in the operating room.
Blinding of participants and personnel	Unclear risk	The surgeon, anaesthesiologist, and operating room staff were not blinded to the intervention; however, the participant, participant's family, PACU nurses, and the research team members collecting the data were blinded.

Litz 2017 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	The surgeon, anaesthesiologist, and operating room staff were not blinded to the intervention; however, the participant, participant's family, PACU nurses, and the research team members collecting the data were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no missing data for primary or secondary outcome variables. 1 participant in the intervention group did not receive the intervention and was excluded as a study anaesthesiologist was not available. 1 participant in the same group was excluded from analysis after receiving the intervention due to fascial dehiscence upon awakening from anaesthesia that required re-operation. In the comparator group, 1 participant was excluded due to the administration of a non-protocol local anaesthetic.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat Groups had similar demographic characteristics.

Liu 2012

Methods	Parallel RCT Ethics committee: approved Informed consent: written parental informed consent obtained Setting: Tianjin Children's Hospital, Tianjin 300074, China Funding: unspecified Date of data collection: not reported Registration: unspecified
Participants	102 children; mean age: 3.8 years **Inclusion criteria** 1. ASA 1 or 2 paediatric participants from 1 month to 8 years of age and scheduled for urological or perineal surgery **Exclusion criteria** 1. Children with pulmonary, neurological, or coagulation dysfunction 2. History of multiple surgeries 3. Spinal or sacral malformation or skin abnormalities
Interventions	**Intervention:** caudal anaesthesia with ultrasound for pre-scanning (N = 52) **Comparator:** caudal anaesthesia with landmarks (N = 50)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Time to perform the procedure 3. Number of attempts

Liu 2012 *(Continued)*

	Others 1. Success rate at first attempt 2. Swoosh test
Notes	Correspondence: email sent 9 March 2018, no reply Conflict of interest: not reported DOI: NA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly divided random number table"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All results provided.
Other bias	Low risk	Groups well balanced

Liu 2018

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Children's Hospital of Chongqing Medical University, Chongqing, China Dates of data collection: from November 2016 to January 2017 Funding: institutional resources Registration: ChiCTR-INR-16010134
Participants	100 children; mean age: 2.1 years **Inclusion criteria** 1. ASA 1 children aged 1 to 3 years undergoing trigger thumb repair

Liu 2018 *(Continued)*

	Exclusion criteria 1. History of seizures or neurological disease 2. Neuromuscular disorders 3. Psychiatric disorders 4. Blood-clotting disorders 5. Malformation or history of trauma of the palm, wrist, and forearm 6. Parents refused to participate in trial
Interventions	**Intervention:** ultrasound-guided median nerve block (N = 50) **Comparator:** landmark median nerve block (N = 50)
Outcomes	**Relevant to this review** 1. Failed blocks **Others** 1. Volume of local anaesthetic used 2. Surgical time 3. Length of stay in PACU 4. Intra- or postoperative adverse events of urine retention, pruritus, nausea and vomiting, respiratory depression 5. Satisfaction
Notes	Correspondence: email sent to authors 9 March 2018 Conflict of interest: authors declare they have no conflicts of interest to disclose DOI: 10.1111/pan.13296

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using computational random number generator"
Allocation concealment (selection bias)	Low risk	Quote: "the random information was sealed in an oblique envelope until the child entered the operating room"
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Subjective satisfaction surveys of the anaesthetic experience were conducted by a nurse who was blinded to the study design.
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	Intention-to-treat Groups had similar demographic characteristics.

Lorenzo 2014

Methods	Parallel RCT Ethics committee: approved Consents: parental consents obtained Setting: university hospital, Canada Funding: departmental/institutional Date of data collection: 2.5-year period; approximately 2011 to 2013 Registration: NCT01243593
Participants	32 children; mean age: 0.9 years **Inclusion criteria** 1. Birth to 6 years old and ASA 1 to 3 undergoing open unilateral pyeloplasty **Exclusion criteria** 1. Children who underwent additional unrelated surgical procedures and children with a solitary kidney 2. History of pyeloplasty 3. History of or concern for malignant hyperthermia 4. Previous adverse reaction to bupivacaine 5. History of chronic pain requiring opioid analgesics
Interventions	**Intervention:** ultrasound-guided transversus abdominis plane block (N = 16) **Comparator:** wound infiltration (N = 16)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration 3. Complications (systemic local anaesthetic toxicity) **Others** 1. Surgical time 2. Rescue analgesia 3. Nausea and vomiting 4. Pruritus 5. Length of hospital stay
Notes	Correspondence: additional information obtained from study authors (30 January 2015 and March 2018) Conflict of interest: no conflict of interest DOI: 10.1016/j.juro.2014.01.026

Risk of bias

Bias	Authors' judgement	Support for judgement

Lorenzo 2014 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "randomization was carried out using a schedule derived from a table of random numbers with a simple 1:1"
Allocation concealment (selection bias)	Low risk	Quote: "recruited patients were assigned in a concealed fashion (sequentially numbered, sealed envelopes) to 1 of 2 groups"
Blinding of participants and personnel	Unclear risk	Quote: "blinded (to assessor, post-anaesthesia care unit health care provider(s), statistician, patient and family)"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a blinded assessor regularly captured pain scores in the recovery room using the FLACC (Face, Legs, Activity, Cry, Consolability) scale." Quote: "All patients had an identical bandage to maintain blinding of the assessors"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Quote: "at the first interim analysis (a third of recruitment attained), there was a highly clinically and statistically significant difference in the primary outcome measurements as well as secondary outcome measurements. Therefore, the study was stopped early due to lack of benefit"
Other bias	Low risk	Quote: "the groups were balanced for patient demographics, operating time and hospital stay. In both groups, the local anaesthetic was administered before the surgical incision"

Marhofer 2004

Methods	Parallel RCT Ethics committee: approved Consents: written parental informed consents obtained Setting: university hospital, Austria Funding: unspecified Date of data collection: not reported Registration: not reported
Participants	40 children; median age: 6 years **Inclusion criteria** 1. ASA physical status 1 or 2, 1 to 10 years of age; children scheduled for arm and forearm surgery for traumatic conditions **Exclusion criteria** 1. Coagulopathy 2. Cardiac, hepatic, renal, or neurological disease 3. Malformations of the upper limb and surgical contraindications to regional anaesthesia
Interventions	**Intervention:** ultrasound-guided infraclavicular lateral brachial plexus blocks (N = 20)

Marhofer 2004 *(Continued)*

	Comparator: infraclavicular brachial plexus blocks with a nerve stimulation (N = 20)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Block duration 3. Complications (bloody puncture, infection) **Others** 1. Onset times
Notes	Correspondence: study authors were contacted 11 February 2015. Original data have been destroyed (> 10 years). Conflict of interest: not reported DOI: 10.1111/j.1365-2044.2004.03669.x

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomised to one of two study groups by sealed envelope"
Allocation concealment (selection bias)	Low risk	Quote: "randomised to one of two study groups by sealed envelope"
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Sensory and motor blockades were assessed by an anaesthetist who was not involved in the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	High risk	Pain scores measured but not provided. Study authors contacted, and original data destroyed.
Other bias	Low risk	Intention-to-treat Groups well balanced

Nan 2012

Methods	Parallel RCT Ethics committee: approved by the ethics committee Consents: written parental informed consents obtained Setting: university hospital, Whenzou Medical College, China Funding: government: Research Foundation of Zhejiang Provincial Health Department (2009A145)

Nan 2012 *(Continued)*

	Date of data collection: July through September 2010 Registration: not reported
Participants	100 children; mean age: 5.6 years **Inclusion criteria** 1. ASA status 1, between 4 and 8 years old, scheduled for surgery for unilateral inguinal repair or high hydrocele ligation or descent and fixation of testis for cryptorchidism **Exclusion criteria** 1. Children with cardiovascular, respiratory, or kidney disease 2. History of allergy to local anaesthetic 3. Coagulation abnormalities 4. Neuromuscular disease
Interventions	**Intervention:** ilioinguinal or iliohypogastric block under ultrasonic guidance (N = 50) **Comparator:** ilioinguinal or iliohypogastric block performed according to the traditional method of anatomical localization (N = 50)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Minor complications **Others** 1. Surgical time 2. Rescue analgesia 3. Apnoea 4. Urinary retention 5. Pruritus 6. Length of stay in PACU 7. Parental satisfaction
Notes	Correspondence: study authors contacted, no reply Conflict of interest: not reported DOI: NA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a random number remainder grouping method"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias)	Unclear risk	Not mentioned

Nan 2012 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All results provided.
Other bias	Unclear risk	Lower dose of local anaesthetic in the ultrasound group

O'Sullivan 2011

Methods	Parallel RCT Ethics committee: approved Consents: written informed parental/guardian consent obtained Setting: Ireland Funding: departmental resources Date of data collection: not reported Registration: not reported
Participants	66 boys; median age: 2.6 years **Inclusion criteria** 1. ASA physical status 1 or 2 scheduled for day case circumcision **Exclusion criteria** 1. Allergy to local anaesthetic or an additional surgical procedure other than circumcision under the same general anaesthetic
Interventions	**Intervention:** penile block under ultrasound guidance (N = 34) **Comparator:** penile block with landmarks (N = 32)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Time to perform the procedure **Others** 1. Rescue analgesia
Notes	Correspondence: study authors were contacted for results at 1 hour in the postoperative care unit; data not available Conflict of interest: not reported DOI: 10.1111/j.1460-9592.2011.03722.x
Risk of bias	

O'Sullivan 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomized by drawing from a sealed envelope"
Allocation concealment (selection bias)	Low risk	Quote: "patients were randomized by drawing from a sealed envelope"
Blinding of participants and personnel	Low risk	Attending anaesthetist and nurse in PACU blinded to the treatment group.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Attending anaesthetist and nurse in PACU blinded to the treatment group.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants were excluded from the study.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Demographic data were similar in both groups.

Oberndorfer 2007

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: written informed consent obtained from parents Setting: South Africa Funding: unspecified Date of data collection: not reported Registration: not reported
Participants	46 children; median age: 5 years **Inclusion criteria** 1. Up to 8 years of age scheduled for surgery on 1 lower extremity **Exclusion criteria** 1. History of seizures or neurological, neuromuscular, psychiatric, or blood-clotting disorders
Interventions	**Intervention:** sciatic and femoral nerve blocks under ultrasound guidance (N = 23) **Comparator:** sciatic and femoral nerve blocks under nerve stimulator guidance (N = 23)
Outcomes	**Relevant to this review** 1. Failed blocks

Oberndorfer 2007 *(Continued)*

	2. Pain scores 3. Block duration 4. Complications (study authors reported no complications related to the techniques) **Others** 1. Volume of local anaesthetic used
Notes	Correspondence: additional information provided by study authors Conflict of interest: not reported DOI: 10.1093/bja/aem092

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Before randomization, participants were stratified into 2 groups based on the planned surgical procedure and the need for sciatic nerve block or sciatic nerve block plus femoral nerve block. Children were then randomized to receive nerve blocks under nerve stimulator guidance (nerve stimulator group) or ultrasound guidance (ultrasound group). Randomization was based on computer-generated codes that were kept in sequentially numbered, opaque envelopes until just before use.
Allocation concealment (selection bias)	Low risk	Randomization was based on computer-generated codes that were kept in sequentially numbered, opaque envelopes until just before use.
Blinding of participants and personnel	Unclear risk	OPS scores were evaluated by an anaesthetist who was blinded to the randomization.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	OPS scores were evaluated by an anaesthetist who was blinded to the randomization.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up mentioned.
Selective reporting (reporting bias)	Low risk	Pain scores provided by study authors.
Other bias	Unclear risk	Fixed dose of local anaesthetic with nerve stimulation and total dose of local anaesthetic administered were higher in this group. The volume of local anaesthetic in sciatic and femoral nerve blocks was reduced with ultrasound compared with nerve stimulator guidance (0.2 (SD 0.06) vs 0.3 mL/kg ($P < 0.001$) and 0.15 (SD 0.04) vs 0.3 mL/kg ($P < 0.001$), respectively). This could have favoured nerve stimulator guidance for time to first request of an analgesic.

Ponde 2009

Methods	Parallel RCT Ethics committee: approved Consents: written informed parental consents obtained

Ponde 2009 *(Continued)*

	Setting: India Funding: unspecified Date of data collection: not reported Registration: not reported
Participants	50 children; mean age: 1.0 year **Inclusion criteria** 1. ASA physical status 1 and 2 children, between 1 and 2 years of age, scheduled for radial club hand repair (centralization of ulna) **Exclusion criteria** 1. Cardiac disease 2. Renal diseases 3. Neurological diseases 4. Coagulopathies
Interventions	**Intervention:** real-time (in-plane) ultrasound-guided infraclavicular brachial plexus block (N = 25) **Comparator:** lateral infraclavicular brachial plexus block guided by nerve stimulator (N = 25)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Block duration **Others** 1. Rescue analgesia
Notes	Correspondence: study authors contacted; data no longer available Conflict of interest: not reported DOI: 10.1213/ane.0b013e3181a2a252

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized by sealed envelope to one of two study groups based on regional anaesthetic technique"
Allocation concealment (selection bias)	Low risk	Quote: "randomized by sealed envelope to one of two study groups based on regional anaesthetic technique"
Blinding of participants and personnel	Low risk	Quote: "an anaesthesiologist who was blinded to the block administration technique finished the case"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an anaesthesiologist who was blinded to the block administration technique finished the case" Quote: "the Children's Hospital Eastern Ontario Pain Scale pain score was recorded at 1, 4, 6, 8, and 10 postoperative hours by an anaesthesiologist not involved in the study"

Ponde 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	High risk	Pain scores and time to first request of an analgesic measured but not provided.
Other bias	Low risk	Groups were comparable for age, weight, and duration of surgery.

Ponde 2013

Methods	Parallel RCT Ethics committee: approved Consents: written informed parental/guardian consents obtained Setting: All India Institute of Physical Medicine and Rehabilitation Centre, Mumbai, Maharashtra, India Funding: departmental resources Date of data collection: 2009 Registration: not reported
Participants	60 children; mean age: 1.0 year **Inclusion criteria** 1. 6 months to 5 years of age diagnosed with distal arthrogryposis multiplex congenita posted for foot surgery (vertical talus correction) **Exclusion criteria** 1. Children were excluded from the study if they had coagulopathies or cardiac and renal disorders
Interventions	**Intervention:** femoral and sciatic block under real-time (in-plane) ultrasound guidance (N = 30) **Comparator:** femoral and sciatic block with nerve stimulator (N = 30)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Block duration **Others** 1. Rescue analgesia
Notes	Correspondence: email sent 9 March 2018, no reply Conflict of interest: no conflicts of interest declared DOI: 10.1111/pan.12022

Risk of bias

Bias	Authors' judgement	Support for judgement

Ponde 2013 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "randomization was performed by sealed envelopes prepared by the statistical staff"
Allocation concealment (selection bias)	Low risk	Quote: "randomization was performed by sealed envelopes prepared by the statistical staff." "The anaesthesiologist performing the block was given randomly generated group allocations within sealed opaque envelopes"
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Postoperatively, CHIPPS pain score was recorded at 1, 4, 6, 8, and 10 hours by the second anaesthesiologist on duty, who was blinded to the block technique.
Incomplete outcome data (attrition bias) All outcomes	Low risk	60 participants were recruited, all of whom completed the study.
Selective reporting (reporting bias)	Low risk	All results provided.
Other bias	Low risk	Groups well balanced

Qiu 2016

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: not reported Site: China Funding: not reported Dates of data collection: not reported Registration: not reported
Participants	150 children; mean age: not reported **Inclusion criteria** 1. ASA 1 or 2 infants scheduled for surgery on unilateral inguinal region **Exclusion criteria** 1. Not reported
Interventions	**Intervention:** ultrasound-guided transversus abdominis plane block (N = 50) **Comparator:** landmark (N = 50)
Outcomes	**Relevant to this review** 1. Pain scores **Others**

Qiu 2016 *(Continued)*

1. Haemodynamic parameters
2. Rescue analgesia
3. Satisfaction

Notes	The trial also contains a third group with ultrasound guidance and a lower injection volume not retained for this review. Conference abstract No data suitable for analysis Correspondence: letter sent to authors 9 March 2018, no reply Conflict of interest: none declared DOI: 10.1213/01.ane.0000492655.51356.36

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "chosen and divided into three groups"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Groups had similar characteristics.

Relland 2017

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Ohio State University College of Medicine, USA Dates of data collection: from September 2011 to September 2016 Funding: departmental/institutional

Relland 2017 *(Continued)*

	Registration: NCT01394523
Participants	39 children; mean age: 4.5 years **Inclusion criteria** 1. ASA 1 or 2 children undergoing umbilical hernia repair **Exclusion criteria** 1. Individuals with comorbid cardiac, pulmonary, or neurological diseases 2. Having concomitant procedures (circumcision, orchidopexy, etc.) 3. Weight over 25 kg
Interventions	**Intervention:** ultrasound-guided bilateral rectus sheath blocks (N = 13) **Comparator:** surgical site infiltration (N = 13)
Outcomes	**Relevant to this review** 1. Pain scores (Hannallah 1987) **Others** 1. Aldrete recovery scores 2. Rescue analgesia 3. Time to tracheal extubation 4. Length of hospital stay
Notes	This trial also contains a third group with caudal analgesia not retained for this review. Correspondence: additional information received from study authors Conflict of interest: the authors report no conflicts of interest in this work DOI: 10.2147/JPR.S144259

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random assignment"
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of participants and personnel	Low risk	Treatment groups were otherwise blinded from the intraoperative anaesthesiology team and recovery nurses. Quote: "all participants were draped for surgery in similar fashion to conceal what type of treatment was provided after induction of general anaesthesia" Quote: "specialized regional anesthesiology team took over care during the time of the experimental treatment (rectus sheath block vs. caudal vs. surgical site injection). The general anesthesiology team was outside the operating room and did not return until after the patient was draped for surgery." Quote: "nurses in the recovery room followed a standardized protocol without any knowledge of treatment allocation."

Relland 2017 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "an independent observer, who was blinded to the type of regional anaesthesia that was provided"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	High risk	The trial was planned to include 25 participants per group, no explanation was provided for premature termination.
Other bias	Low risk	Intention-to-treat Groups had similar demographic characteristics.

Sahin 2013

Methods	Parallel RCT Ethics committee: approved by the ethics committee Consents: informed parental written consents obtained Setting: university hospital, Turkey Funding: none declared Date of data collection: December 2010 through May 2011 Registration: ACTRN12611000585921 (7 June 2011) from Australian New Zealand Clinical Trials Registry
Participants	57 children; median age: 4 years **Inclusion criteria** 1. ASA 1 or 2 children between the ages of 2 and 8 years undergoing unilateral inguinal hernia repair **Exclusion criteria** 1. Psychiatric illness 2. Kidney failure 3. Known hypersensitivity to relevant drugs
Interventions	**Intervention:** transversus abdominis plane block with ultrasound guidance (N = 29) **Comparator:** wound infiltration (N = 28)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration **Others** 1. Haemodynamic parameters 2. Surgical time 3. Anaesthetic time 4. Rescue analgesia

Sahin 2013 *(Continued)*

	5. Nausea and vomiting
Notes	Correspondence: study authors contacted in 2015 (26 January 2015 and 14 February 2015) and 2018 but we received no reply Conflict of interest: none declared DOI: 10.1097/EJA.0b013e32835d2fcb

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised by sealed envelopes"
Allocation concealment (selection bias)	Low risk	Quote: "patients were randomised by sealed envelopes"
Blinding of participants and personnel	Unclear risk	Blinding or masking began in the recovery room.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding or masking began in the recovery room. The recovery room nurse assigned to each participant was blinded to study groups.
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 participants lost to follow-up: 1 in ultrasound group and 2 in infiltration group
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat Higher volume of local anaesthetic in the ultrasound group. Blocks performed after anaesthesia induction for the ultrasound group and during wound closure for the infiltration group.

Shaaban 2014

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Faculty of Medicine, Ain Shams University, Cairo, Egypt Dates of data collection: not reported Funding: not reported Registration: ACTRN12613000595718
Participants	44 children; mean age: not reported **Inclusion criteria**

Shaaban 2014 *(Continued)*

1. ASA 1 to 2 children aged 4 to 16 years undergoing laparoscopic appendectomy

Exclusion criteria

1. Psychiatric illness
2. Weight greater than 60 kg
3. Comorbid diseases (cardiac, pulmonary (not including asthma))
4. Neurological disease
5. Bleeding tendencies (coagulopathy)
6. Children in whom a transversus abdominis plane block is contraindicated, i.e. surgical scar or distorted anatomy at the site of injection or known hypersensitivity to relevant drugs

Interventions	**Intervention:** ultrasound-guided transversus abdominis plane block (N = 22) **Comparator:** local anaesthetic infiltration (N = 22)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration 3. Time to perform the block **Others** 1. Surgery time 2. Rescue analgesia 3. Nausea and vomiting 4. Length of stay in PACU
Notes	Conference abstract Correspondence: email sent to authors 9 March 2018, no reply received Conflict of interest: none declared DOI: 10.1016/j.egja.2014.06.005

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The allocation sequence was generated using a randomized central computer-generated sequence held by an investigator not involved with the clinical management or data collection.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	Low risk	Blinding was ensured for the participants receiving the treatment, the outcome assessors, and those analysing the results/data. Furthermore, before emergence from anaesthesia, all participants in both the TAP and local infiltration groups had opaque sticking plasters placed at the site of a TAP to enable participants, parents, and the data collectors to remain blinded to allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding was ensured for the participants receiving the treatment, the outcome assessors, and those analysing the results/data.

Shaaban 2014 *(Continued)*

		Furthermore, before emergence from anaesthesia, all participants in both the TAP and local infiltration groups had opaque sticking plasters placed at the site of a TAP to enable participants, parents, and the data collectors to remain blinded to allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 participants, 1 from each group, were excluded after enrolment due to post-operative analgesic protocol violations.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not in intention-to-treat Groups had similar demographic characteristics.

Shank 2016

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Shriners Hospital for Children – Boston, Harvard Medical School, Boston, USA Dates of data collection: not reported Funding: charity (supported by the Shriners Hospital for Children) Registration: NCT01500655
Participants	19 children; mean age: 12 years **Inclusion criteria** 1. Paediatric burn participants undergoing reconstructive skin grafting, age > 2 and ≤ 21, and lateral/anterior thigh donor site available **Exclusion criteria** 1. Requiring narcotics preoperatively 2. History of local anaesthetic allergy 3. Individuals who were morbidly obese (body mass index ≥ 30)
Interventions	**Intervention:** ultrasound-guided femoral lateral nerve block (N = 5) **Comparator:** infiltration (N = 6)
Outcomes	**Relevant to this review** 1. Pain scores 2. Block duration **Others** 1. Rescue analgesia
Notes	The trial also contains a third group with continuous infusion through a catheter (fascia iliaca).

Shank 2016 *(Continued)*

Correspondence: email sent to authors 9 March 2018, no reply

Conflict of interest: none of the authors have any conflict of interest to report

DOI: 10.1097/BCR.0000000000000174

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was via a random number generator with equal distribution to all three groups"
Allocation concealment (selection bias)	High risk	If during the surgery a decision was made to harvest skin graft from areas other than the typical sensory distribution of the lateral femoral cutaneous nerve - and that participant had been designated group 2 (single shot lateral femoral cutaneous nerve block) - then that participant would be re-randomized to either group 1 (local infiltration) or group 3 (fascia iliaca block/catheter).
Blinding of participants and personnel	Unclear risk	All blocks/catheter placements were performed at the end of the surgery, while the child was still asleep.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	High risk	Block duration measured, not reported.
Other bias	Low risk	Groups had similar demographic characteristics.

Tachibana 2012

Methods	Parallel RCT Ethics committee: approved Consents: written informed consent obtained from children and their parents Setting: Sapporo Medical University School of Medicine, Japan Funding: unspecified Date of data collection: not reported
Participants	20 children; mean age: 9 years **Inclusion criteria** 1. ASA physical status classification 1 children from 5 to 7 years of age and scheduled to undergo the minimally invasive Nuss procedure for pectus excavatum **Exclusion criteria** 1. Neurological disease

Tachibana 2012 *(Continued)*

2. Local infection
3. Coagulation abnormality
4. Seizures
5. Allergy to a local anaesthetic
6. Anatomical malformation of centroaxial structures

Interventions	**Intervention:** thoracic epidural analgesia; pre-scanning with ultrasound (N = 10) **Comparator:** thoracic epidural analgesia; landmarks (N = 10)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Time to perform the procedure 3. Number of epidural puncture attempts 4. Complications (study authors reported that no participants experienced severe side effects) **Others** 1. Needle depth to epidural space 2. Difficulty score
Notes	Correspondence: study authors contacted 3 times (14 and 27 February 2015 and letter sent 9 March 2018), no response Conflict of interest: not reported DOI: 10.1007/s00540-011-1279-0

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	No details
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
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	Intention-to-treat Groups were similar with respect to all demographic variables.

Uchinami 2017

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: Graduate School of Medicine, Hokkaido University, Sapporo, Japan Dates of data collection: from May 2014 to January 2015 Funding: departmental (the study received no external funding) Registration: UMIN000020912
Participants	34 children; mean age: 4.1 years **Inclusion criteria** 1. ASA 1 or 2 children aged from 10 months to 9 years who were scheduled to undergo elective laparoscopic extraperitoneal closure surgery **Exclusion criteria** 1. ASA classification 3 or worse 2. Psychiatric illness 3. Use of analgesics before surgery or allergy to ropivacaine
Interventions	**Intervention:** ultrasound-guided rectus sheath block (N = 17) **Comparator:** local anaesthetic infiltration (N = 17)
Outcomes	**Relevant to this review** 1. Pain scores 2. Time to perform the procedure **Others** 1. Surgery time 2. Nausea and vomiting (2 participants in each group)
Notes	Correspondence: email sent to authors 9 March 2018, no reply Conflict of interest: no conflicts of interest declared DOI: 10.1111/pan.13085

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "The group into which patients were allocated was revealed to each anesthesiologist via a sealed envelope on the day of the surgery"
Blinding of participants and personnel	Unclear risk	Quote: "the patients, parents, or guardians of the patients, and postanaesthesia care unit (PACU) staff were blinded because the places of incision and local anaesthetic placement were covered by clean gauze"

Uchinami 2017 *(Continued)*

		Quote: "Surgeons, anaesthesiologists, statistical analysts, and medical staff in the operating room were not blinded to the treatment group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "observer-blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	37 enrolled: 3 participants excluded: 1 for ASA physical status > 3 and 1 for history of febrile seizure; 35 randomized: 1 excluded for incomplete data
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat Groups had similar demographic characteristics.

Wang 2013

Methods	Parallel RCT Ethics committee: approved Consents: informed parental consents obtained Setting: Jiaxing Maternity and Child Care Hospital, Jiaxing, China Funding: departmental resources Date of data collection: over a 5-month period Registration: not reported
Participants	140 children; median age: 2.2 years **Inclusion criteria** 1. ASA 1 to 2 children, up to 72 months of age, weighing up to 25 kg, undergoing elective inguinal hernia repair **Exclusion criteria** 1. Individuals were excluded from this study if they had contraindications to caudal block 2. Lack of parental consent
Interventions	**Intervention:** ultrasound-guided caudal blocks (N = 70) **Comparator:** caudal blocks based on landmarks (N = 70)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Block duration 3. Complications (bloody puncture, systemic local anaesthetic toxicity) **Others** 1. Desaturation

Wang 2013 *(Continued)*

Notes	Correspondence: study authors contacted on 15 and 27 February 2015 and in March 2018, no reply Conflict of interest: no conflicts of interest declared DOI: 10.1111/pan.12104

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomization was based on computer-generated codes with SPSS 13.0 (SPSS Inc., Chicago, IL, USA)"
Allocation concealment (selection bias)	Low risk	Quote: "maintained in sequentially numbered opaque envelopes"
Blinding of participants and personnel	Low risk	Quote: "a separate anaesthetist who then entered the operating room after the block was assigned to subsequent anaesthetic assessment and management"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "thus, the observer of anaesthetic effect was blinded with regards to the block technique"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study successfully.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Low risk	Intention-to-treat Quote: "there were no differences between two groups in terms of patients' characteristics"

Weintraud 2009

Methods	Parallel RCT Ethics committee: approved Consents: written parental informed consents obtained Setting: University Cape Town, Red Cross War Memorial Children's Hospital, Cape Town, South Africa Funding: unspecified Date of data collection: not reported Registration: not reported
Participants	70 children: mean age: 4.3 years **Inclusion criteria** 1. 8 to 84 months of age, ASA 1 to 2, scheduled for inguinal hernia repair **Exclusion criteria**

Weintraud 2009 *(Continued)*

1. Prior surgical procedures in the groin area
2. General contraindications for the blocks
3. Known allergy to amino-amide local anaesthetics
4. Inability of the parents to understand the study protocol
5. Lack of parental informed consent

Interventions	**Intervention:** ilioinguinal-iliohypogastric nerve blockade with real-time (out of-plane) ultrasound guidance (N = 37 included; 35 analysed) **Comparator:** ilioinguinal-iliohypogastric nerve blockade with landmarks (N = 33 included; 31 analysed)
Outcomes	**Relevant to this review** 1. Failed blocks **Others** 1. Rescue analgesia 2. Plasma ropivacaine concentrations
Notes	Correspondence: email sent 9 March 2018, no reply Conflict of interest: not reported DOI: 10.1213/ane.0b013e31819cb1f3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the computer-generated randomization protocol was prepared outside the study centre and delivered in opaque envelopes that were sealed and sequentially numbered"
Allocation concealment (selection bias)	Low risk	Quote: "the computer-generated randomization protocol was prepared outside the study centre and delivered in opaque envelopes that were sealed and sequentially numbered"
Blinding of participants and personnel	Low risk	Quote: "the anaesthesiologist who performed general anaesthesia was blinded to the method of performance of the treatment group"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the anaesthesiologist who performed general anaesthesia was blinded to the method of performance of the treatment group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 participants excluded, 2 in each study group.
Selective reporting (reporting bias)	Low risk	All results reported.
Other bias	Unclear risk	Not intention-to-treat Groups well balanced

Willschke 2005

Methods	Parallel RCT Ethics committee: approved Consents: written parental informed consents obtained Setting: University Cape Town, Red Cross War Memorial Children's Hospital, South Africa Funding: equipment loan from the industry Date of data collection: not reported Registration: not reported
Participants	100 children; mean age: 3.5 years **Inclusion criteria** 1. Up to 8 years of age who were scheduled for inguinal hernia repair, orchidopexy, or hydrocele repair were included in this study **Exclusion criteria** 1. History of seizures or neurological disease 2. Neuromuscular, psychiatric, or blood-clotting disorders
Interventions	**Intervention:** ultrasound-guided ilioinguinal block (N = 50) **Comparator:** ilioinguinal block using the traditional fascial click method (N = 50)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Complications (bloody puncture) **Others** 1. Nerves locations 2. Surgical time 3. Rescue analgesia 4. Length of hospital stay
Notes	Correspondence: additional information received from study authors Conflict of interest: none other than equipment loan from the industry DOI: 10.1093/bja/aei157

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was performed outside the study centre and was delivered in sequentially numbered, sealed, opaque envelopes.
Allocation concealment (selection bias)	Low risk	Randomization was performed outside the study centre and was delivered in sequentially numbered, sealed, opaque envelopes.
Blinding of participants and personnel	Unclear risk	Not mentioned

Willschke 2005 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
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	Intention-to-treat The volume of local anaesthetic administered was less in the ultrasound group, but this should not have influenced the rate of success. The amount of local anaesthetic given in the ultrasound group was significantly less than that given in the fascial click group (0.19 (0.05) vs 0.3 mL/kg; P < 0.0001).

Willschke 2006

Methods	Parallel RCT Ethics committee: approved Consents: parental consents obtained Setting: University of Cape Town, Red Cross War Memorial Children's Hospital, Cape Town, South Africa Funding: equipment loan from the industry Date of data collection: not reported Registration: not reported
Participants	64 children; mean age: 1.0 year **Inclusion criteria** 1. Undergoing major abdominal or thoracic surgery, ranging from neonates to children 6 years of age **Exclusion criteria** 1. Neurological disorders, seizures, local infection, or coagulopathies
Interventions	**Intervention:** ultrasound-guided epidural catheters insertions (N = 30) **Comparator:** epidural catheters insertions with standard loss-of-resistance technique with air or saline (N = 34)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores 3. Time to perform the procedure 4. Complications (bloody puncture) **Others** 1. Skin-epidural distance

Willschke 2006 *(Continued)*

Notes	Correspondence: additional information received from study authors Conflict of interest: none other than equipment loan from the industry DOI: 10.1093/bja/ael121

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomization protocol was prepared outside the study centre and delivered in opaque envelopes that were sealed and sequentially numbered"
Allocation concealment (selection bias)	Low risk	Quote: "the randomization protocol was prepared outside the study centre and delivered in opaque envelopes that were sealed and sequentially numbered"
Blinding of participants and personnel	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
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	Intention-to-treat Quote: "the patient characteristic data and epidural puncture level were similar in both groups"

Yang 2015

Methods	Parallel RCT Ethics committee: approved by the ethics committee Informed consent: obtained Site: The First Affiliated Hospital of Zhengzhou University, China Date of data collection: not reported Funding: departmental/institutional Registration: not reported
Participants	90 children; mean age: 5.3 years **Inclusion criteria**

Yang 2015 *(Continued)*

1. Scheduled for selective unilateral inguinal surgeries (including high ligation of the hernia sac and high ligation of hydrocele of the tunica vaginalis), aged 4 to 6 years, weighed 15 kg to 22 kg, and belonged to ASA physical status 1 or 2

Exclusion criteria

1. Coagulation abnormalities
2. Respiratory infection
3. Allergies to local anaesthetic

Interventions	**Intervention:** ultrasound-guided ilioinguinal/iliohypogastric nerve block (N = 30) **Comparator:** traditional Schulte-Steinberg ilioinguinal/iliohypogastric (N = 30)
Outcomes	**Relevant to this review** 1. Failed blocks 2. Pain scores **Others** 1. Haemodynamic parameters 2. Pulse oximetry 3. Surgery time 4. Nausea and vomiting
Notes	The trial also contains a third group without block not retained for this review. Correspondence: email sent to authors 9 March 2018 Conflict of interest: the authors declare that they have no competing interests DOI: 10.1007/s12262-015-1301-0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly divided"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Operative time and recovery time were also recorded, and the FLACC behavioural tool was used for postoperative pain scoring by an anaesthesiologist not participating in 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	Unclear risk	Higher dose of local anaesthetic in the landmark group

ASA: American Society of Anesthesiologists; **CHIPPS**: Children's and Infants' Postoperative Pain Scale; **DOI**: digital object identifier; **EU**: European Union; **FACES**: score on the FACES pain rating scale: **FLACC**: Face, Legs, Activity, Cry, and Consolability Pain Scale; **IV**: intravenous; **LA**: local anaesthetic; **MAC**: minimal alveolar concentration; **NA**: not available; **OPS**: objective pain scale; **PACU**: post-anaesthesia care unit; **RCT:** randomized controlled trial; **SD**: standard deviation; **TAP**: transversus abdominis plane block.

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

Study	Reason for exclusion
Abdellatif 2012	Different intervention: comparison of ilioinguinal nerve blocks versus caudal analgesia
Ahmed 2014	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia
Alsadek 2015	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia versus no block
Atta 2008	Different intervention: ilioinguinal/iliohypogastric nerve block versus caudal block
Aveline 2011	Different intervention: comparison of transversus abdominis plane block versus ilioinguinal nerve block
Bryskin 2015	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia
Erbuyun 2016	Different study design: retrospective trial
Fiocca 2013	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia
Fusco 2016	Different study population: adults
Hamill 2015	Different intervention: rectus sheath block with local anaesthetics versus saline
Harju 2016	Different intervention: randomized to blockade before surgical incision or at the end of surgery
Jagannathan 2009	Different intervention: addition of ilioinguinal nerve block with local anaesthetic or saline to caudal and general anaesthesia
Laserre-Sartre 2009	Different study design: children were allocated to treatment groups according to the anaesthesiologist's usual clinical practice
Lloyd 2016	Different study design: retrospective chart review
Matinyan 2015	Different intervention: comparison of paravertebral blockade versus epidural analgesia
Micic 2011	Different intervention: comparison of femoral nerve block versus caudal block
Mirjalili 2015	Different intervention: description of the anatomical relationship of the posterior superior iliac spines to the sacral cornua in infants using ultrasound
Narasimhan 2017	Different intervention: comparison of paravertebral blockade versus caudal analgesia
NCT03427437	Study authors informed us that the trial will never be published due to failure to register the trial before starting participant recruitment.
Oksuz 2017	Different intervention: comparison of transversus abdominis plane block versus quadratus lumborum block
Ponde 2017	Different study design: descriptive observational study

Study	Reason for exclusion
Pérez-Pradilla 2015	Different study design: descriptive observational study
Sahin 2015	Different intervention: comparison of transversus abdominis plane block versus ilioinguinal nerve block versus caudal analgesia
Sethi 2016	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia
Sherif 2011	Different intervention: comparison of transversus abdominis plane block versus caudal analgesia versus no block
Shin 2009	Different intervention: randomized to the puncture site
Sohn 2010	This study was withdrawn by the trialists due to problems related to data collection.
Triffterer 2012	Different intervention. The aim of this study was to measure the cranial spread of caudally administered local anaesthetics in infants and children by means of real-time ultrasonography, with a special focus on comparing the effects of using 2 different speeds of injection.
Tutuncu 2017	Different intervention: comparison of ilioinguinal/iliohypogastric nerve block versus caudal block

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

ACTRN12608000488303

Trial name or title	Comparison of ultrasound guided placement of local anaesthetic in the abdominal muscle and local anaesthetic under the skin for pain relief during and following surgical repair of belly button hernias in children
Methods	RCT
Participants	Children
Interventions	**Intervention:** bilateral ultrasound-guided rectus sheath blocks with a predetermined volume of 1% lignocaine and 1% ropivacaine will be injected following a negative aspiration test. A total of 0.3 mL/kg (to a maximum of 5 mL) of combined 1% lignocaine and 1% ropivacaine will be infiltrated bilaterally 5 minutes before skin incision. **Comparator:** once general anaesthesia has been established, the surgeon will perform all subcutaneous periumbilical local anaesthetic infiltrations. Following aseptic preparation of the site, a total of 0.3 mL/kg (to a maximum of 5 mL) of combined 1% lignocaine and 1% ropivacaine will be infiltrated 5 minutes before skin incision.
Outcomes	**Primary outcomes** 1. Number of intraoperative fentanyl doses 2. Number of morphine doses in PACU 3. Time to first dose of paracetamol and ibuprofen
Starting date	18 February 2008
Contact information	Michael Fredrickson, Newmarket, Auckland
Notes	Retrospectively registered

ACTRN12608000488303 *(Continued)*	Accessed 3 March 2018: last update 5 April 2011: recruitment status noted as complete; email sent to contact author 3 March 2018; invalid email address; email resent to michaelfredrickson@yahoo.com. Author replied that the trial was never finished and never published.

CTRI/2014/09/005023

Trial name or title	A comparative evaluation of the analgesic efficacy of ultrasound guided transversus abdominis plane block (TAP), caudal epidural and wound infiltration in children undergoing unilateral infra umbilical abdominal surgery
Methods	Parallel RCT
Participants	**Inclusion criteria** 1. Age 3 to 10 years and weight less than 20 kg 2. ASA physical status 1 or 2 3. Unilateral lower abdominal surgery such as hernia repair, orchidopexy **Exclusion criteria** 1. Contraindications to caudal or TAP block, e.g. coagulation defect, systemic or local infection, and anatomical abnormalities preventing giving any of the above block 2. Allergy to bupivacaine and amide local anaesthetic 3. Undergoing bilateral lower abdominal surgery 4. Additional surgical procedure at anatomical location not covered by either TAP block or caudal block 5. Refusal to give consent for study
Interventions	**Intervention:** ultrasound-guided transversus abdominis plane block **Comparator:** caudal block **Comparator:** wound infiltration
Outcomes	1. Haemodynamic parameters 2. Anaesthetic drugs consumption 3. Pain scores 4. Rescue analgesia 5. Nausea and vomiting
Starting date	25 January 2014
Contact information	Mukesh Singh Rautela, VMMMC AND Safdarjung Hospital New Delhi, email: ameetaas@yahoo.com
Notes	Last refreshed 26 February 2018, recruiting. Email sent to study authors 8 March 2018.

CTRI/2018/01/011534

Trial name or title	Comparison of ultrasound guided abdominal plane block to the one done under direct vision by surgeon himself in children undergoing abdominal surgeries for post surgery pain relief.
Methods	Parallel RCT
Participants	28 children

CTRI/2018/01/011534 *(Continued)*

	Inclusion criteria 1. Children aged from 0 to 10 years, listed for upper abdominal surgery, willing to be included in the study 2. ASA physical status grade 1 to 3 **Exclusion criteria** 1. Age more than 10 years 2. Refusal to participate in study 3. Psychiatric illness 4. Already using opioids for chronic pain 5. Allergic to study medication (fentanyl and bupivacaine) 6. Not extubated after surgery for any reason
Interventions	**Intervention:** ultrasound-guided subcostal transversus abdominis plane catheter **Comparator:** surgeon-placed subcostal transversus abdominis plane catheter
Outcomes	1. Rescue analgesia 2. Pain scores up to 48 hours after surgery 3. Time spent in the operating room 4. Time to readiness for tracheal extubation
Starting date	2 January 2018
Contact information	Maj Tanveerpal Singh, Department of Anaesthesiology and Critical Care AFMC Pune, email: drraiamit@gmail.com
Notes	Last refreshed 26 February 2018, not recruiting

NCT02321787

Trial name or title	Ultrasonography for confirmation of caudal injection
Methods	RCT
Participants	Children younger than 8 years and weighing ≤ 20 kg who are undergoing lower abdominal, lower extremity orthopaedic, or urological procedures
Interventions	**Intervention:** ultrasound caudal block **Comparator:** landmark caudal block
Outcomes	**Primary outcome measures** 1. Rate of block success (within 4 hours as estimated by ultrasound spread, heart rate, need for additional medications, and pain scores) **Secondary outcome measures** 1. Opioid administration (within 4 hours)
Starting date	December 2014
Contact information	Justin B Long, MD, and John Hajduk; Ann & Robert H Lurie Children's Hospital of Chicago

NCT02321787 *(Continued)*

Notes	Accessed 3 March 2018; recruitment completed; last updated 15 January 2016

NCT02352519

Trial name or title	A comparison of ultrasound guided rectus sheath block and local infiltration
Methods	Parallel RCT
Participants	50 children aged from 6 to 17 years undergoing appendicectomy **Inclusion criteria** 1. Acute appendicitis 2. Age 6 to 17 years 3. ASA physical status 1 to 3 4. Judged by parents, physicians, and other caretakers as being capable of using the patient-controlled analgesia device **Exclusion criteria** 1. Allergies to local anaesthetics 2. Do not understand or cannot use the pain rating scale because of developmental delay, language, or other issues 3. Concomitant major cardio-respiratory disorders
Interventions	**Intervention:** ultrasound-guided rectus sheath block **Comparator:** local infiltration
Outcomes	1. Amount of morphine used during the first 48 hours after surgery 2. Pain scores during the first 48 hours after surgery 3. Time to first rescue analgesia 4. Rescue analgesia used in the PACU 5. Incidence of side effects of opioids such as respiratory depression, itching, nausea, and vomiting, dysphoria 6. Time to achieving discharge readiness in PACU 7. Time to achieving discharge readiness from the hospital 8. Participant and parental satisfaction with pain management
Starting date	April 2011
Contact information	Yang Liu, Baylor College of Medicine, Texas Children's Hospital, Texas, USA 77030, email: yxliu@texaschildrenshospital.org
Notes	Last update posted 21 July 2015, recruitment completed. Email sent to study authors 8 March 2018.

ASA: American Society of Anesthesiologists; **FACES**: Score on the FACES pain rating scale; **PACU**: post-anaesthetic care unit; **RCT**: randomized controlled trial; **TAP:** transversus abdominis plane.

DATA AND ANALYSES

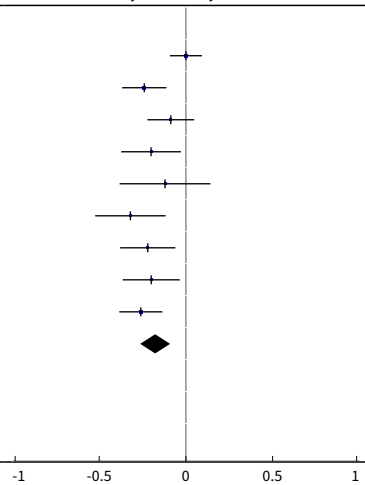
Comparison 1. Ultrasound versus no ultrasound

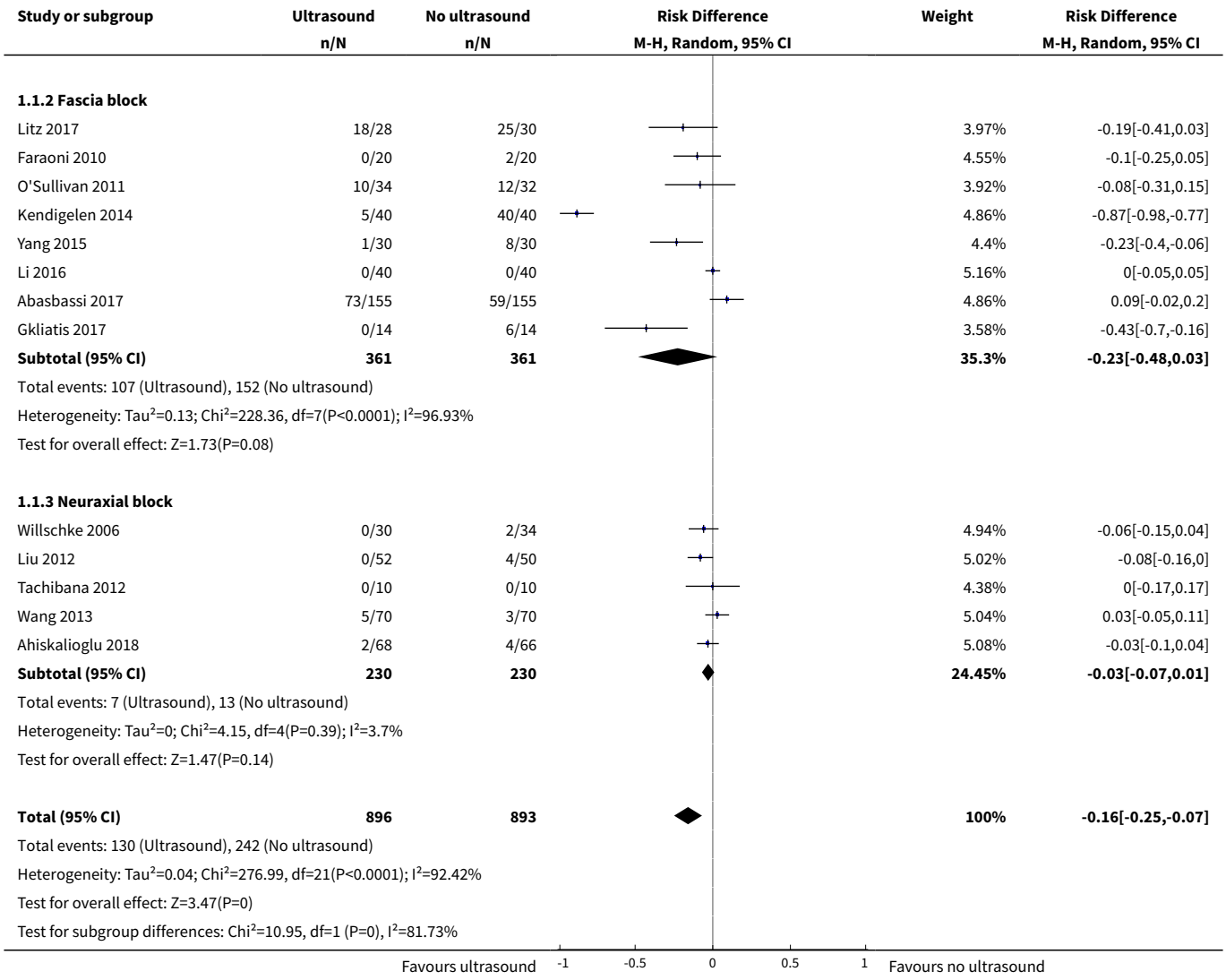
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Success (event = failed block)	22	1789	Risk Difference (M-H, Random, 95% CI)	-0.16 [-0.25, -0.07]
1.1 Peripheral nerve block	9	607	Risk Difference (M-H, Random, 95% CI)	-0.18 [-0.26, -0.09]
1.2 Fascia block	8	722	Risk Difference (M-H, Random, 95% CI)	-0.23 [-0.48, 0.03]
1.3 Neuraxial block	5	460	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.07, 0.01]
2 Pain at 1 hour after surgery	15	982	Std. Mean Difference (Random, 95% CI)	-0.41 [-0.74, -0.07]
2.1 Ultrasound vs landmark	4	514	Std. Mean Difference (Random, 95% CI)	-0.13 [-0.43, 0.17]
2.2 Ultrasound vs nerve stimulator	2	104	Std. Mean Difference (Random, 95% CI)	-0.29 [-0.68, 0.09]
2.3 Ultrasound vs infiltration	8	306	Std. Mean Difference (Random, 95% CI)	-0.70 [-1.41, 0.02]
2.4 Ultrasound vs surgeon administered	1	58	Std. Mean Difference (Random, 95% CI)	0.01 [-0.51, 0.52]
3 Block duration	10	460	Std. Mean Difference (Random, 95% CI)	1.24 [0.72, 1.75]
3.1 Ultrasound vs landmark	1	40	Std. Mean Difference (Random, 95% CI)	1.38 [0.69, 2.08]
3.2 Ultrasound vs nerve stimulator	3	138	Std. Mean Difference (Random, 95% CI)	1.22 [0.85, 1.59]
3.3 Ultrasound vs infiltration	5	224	Std. Mean Difference (Random, 95% CI)	1.42 [0.36, 2.48]
3.4 Ultrasound vs surgeon administered	1	58	Std. Mean Difference (Random, 95% CI)	0.45 [-0.07, 0.97]
4 Time to perform the block	9	680	Std. Mean Difference (Random, 95% CI)	-0.46 [-1.06, 0.13]
4.1 In-plane	4	220	Std. Mean Difference (Random, 95% CI)	0.15 [-0.76, 1.06]
4.2 Out-of-plane	3	338	Std. Mean Difference (Random, 95% CI)	-0.39 [-0.96, 0.19]
4.3 Pre-scanning	2	122	Std. Mean Difference (Random, 95% CI)	-1.97 [-2.41, -1.54]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Number of needle passes	3	256	Std. Mean Difference (Random, 95% CI)	-0.63 [-1.08, -0.18]
6 Minor complications: bloody puncture	13	896	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.05, 0.00]
6.1 Peripheral nerve bock	5	326	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.02]
6.2 Fascia block	5	232	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.04, 0.03]
6.3 Neuraxial block	3	338	Risk Difference (M-H, Random, 95% CI)	-0.08 [-0.15, -0.02]
7 Minor complications: transient neurological injury	18	1230	Risk Difference (M-H, Random, 95% CI)	-0.00 [-0.01, 0.01]
8 Minor complications: seizure from local anaesthetic toxicity	22	1576	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
9 Minor complications: block infection without neurological injury	18	1238	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
10 Major complications: cardiac arrest from local anaesthetic toxicity	22	1576	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]
11 Major complications: lasting neurological injury	19	1250	Risk Difference (M-H, Random, 95% CI)	0.0 [-0.01, 0.01]

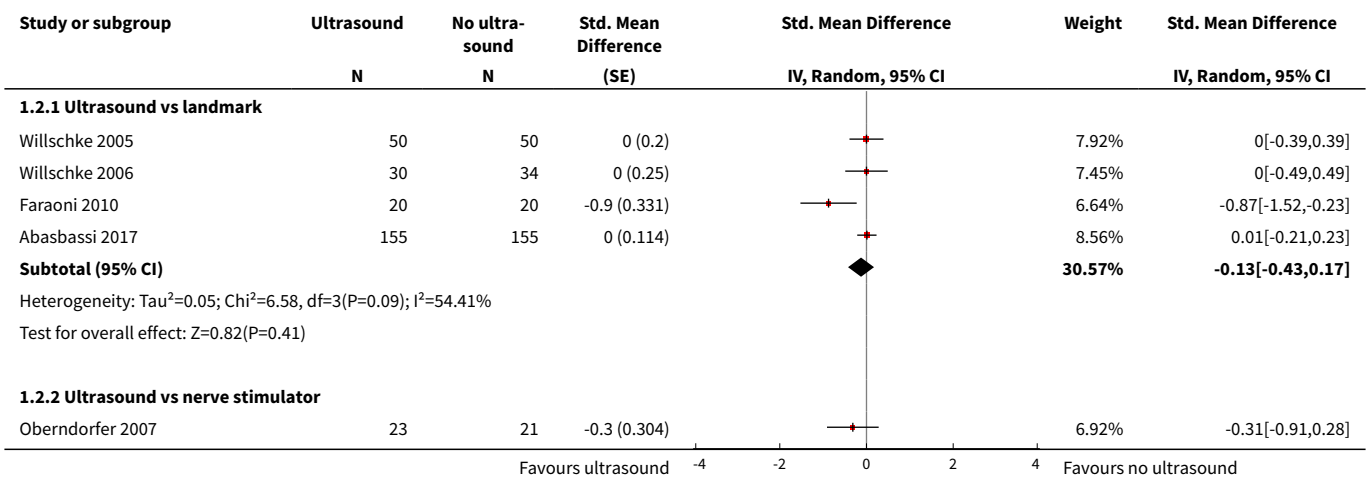
Analysis 1.1. Comparison 1 Ultrasound versus no ultrasound, Outcome 1 Success (event = failed block).

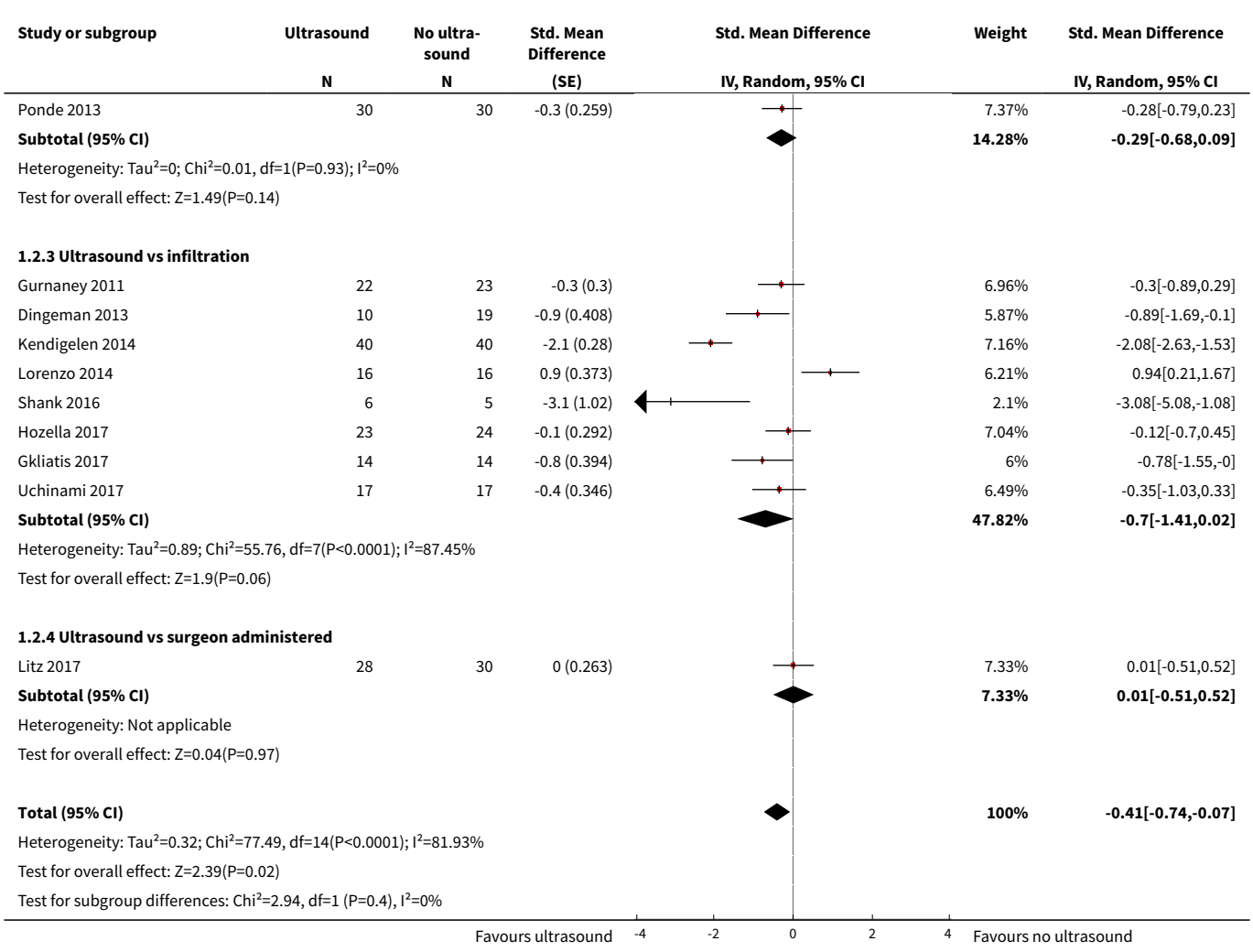
Study or subgroup	Ultrasound n/N	No ultrasound n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.1.1 Peripheral nerve block					
Marhofer 2004	0/20	0/20		4.96%	0[-0.09,0.09]
Willschke 2005	1/50	13/50		4.74%	-0.24[-0.37,-0.11]
Oberndorfer 2007	0/23	2/23		4.68%	-0.09[-0.22,0.05]
Weintraud 2009	2/35	8/31		4.39%	-0.2[-0.37,-0.03]
Elnour 2009	5/22	8/23		3.62%	-0.12[-0.38,0.14]
Ponde 2009	1/25	9/25		4.13%	-0.32[-0.52,-0.12]
Nan 2012	6/50	17/50		4.5%	-0.22[-0.38,-0.06]
Ponde 2013	1/30	7/30		4.46%	-0.2[-0.36,-0.04]
Liu 2018	0/50	13/50		4.76%	-0.26[-0.38,-0.14]
Subtotal (95% CI)	**305**	**302**		**40.24%**	**-0.18[-0.26,-0.09]**
Total events: 16 (Ultrasound), 77 (No ultrasound)					
Heterogeneity: Tau^2=0.01; Chi^2=24.14, df=8(P=0); I^2=66.87%					
Test for overall effect: Z=4.03(P<0.0001)					



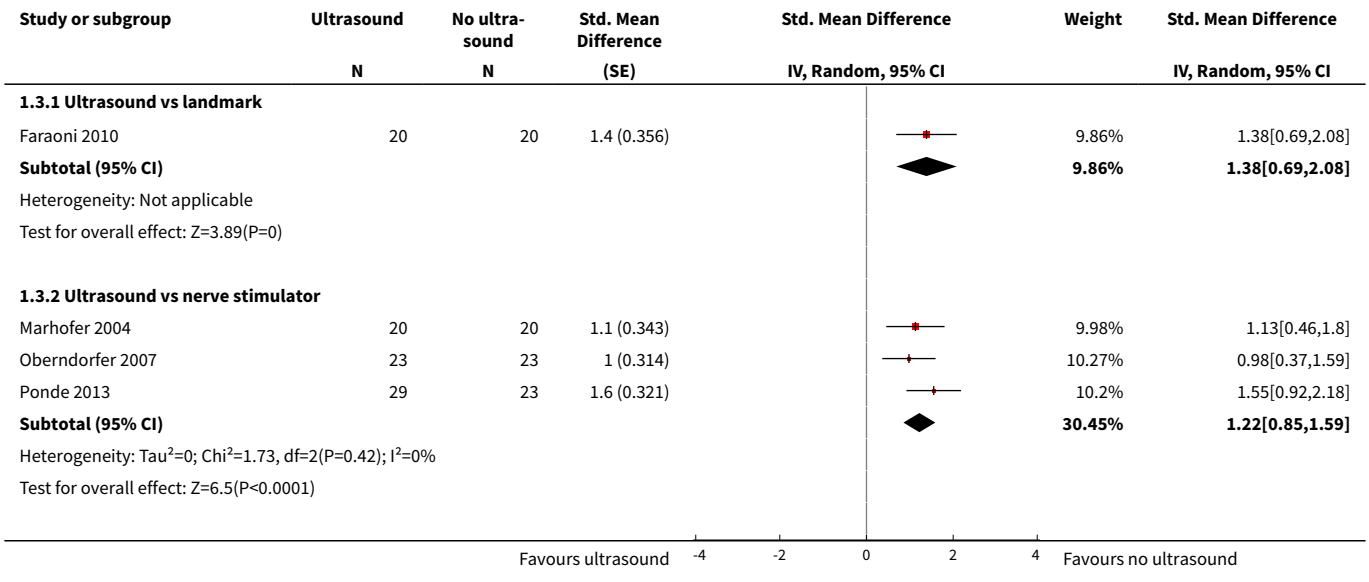


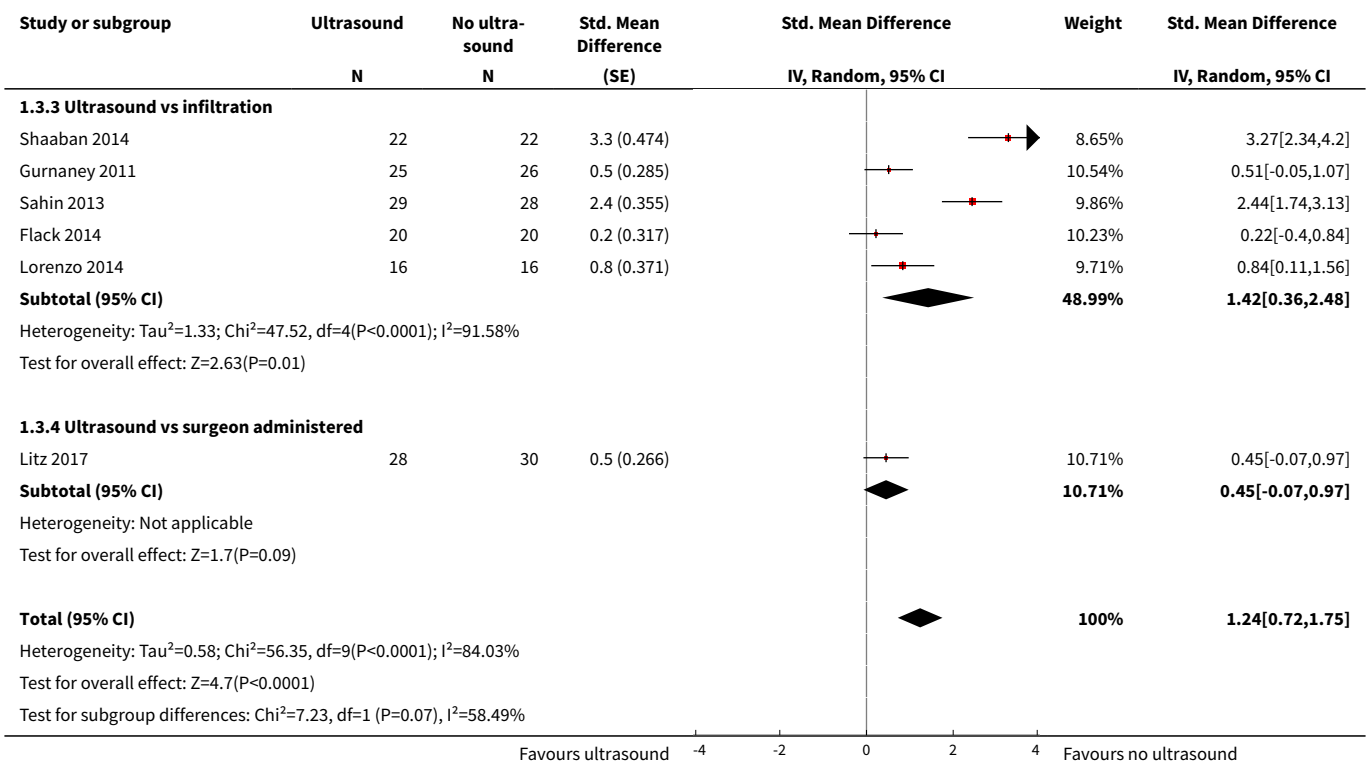
Analysis 1.2. Comparison 1 Ultrasound versus no ultrasound, Outcome 2 Pain at 1 hour after surgery.



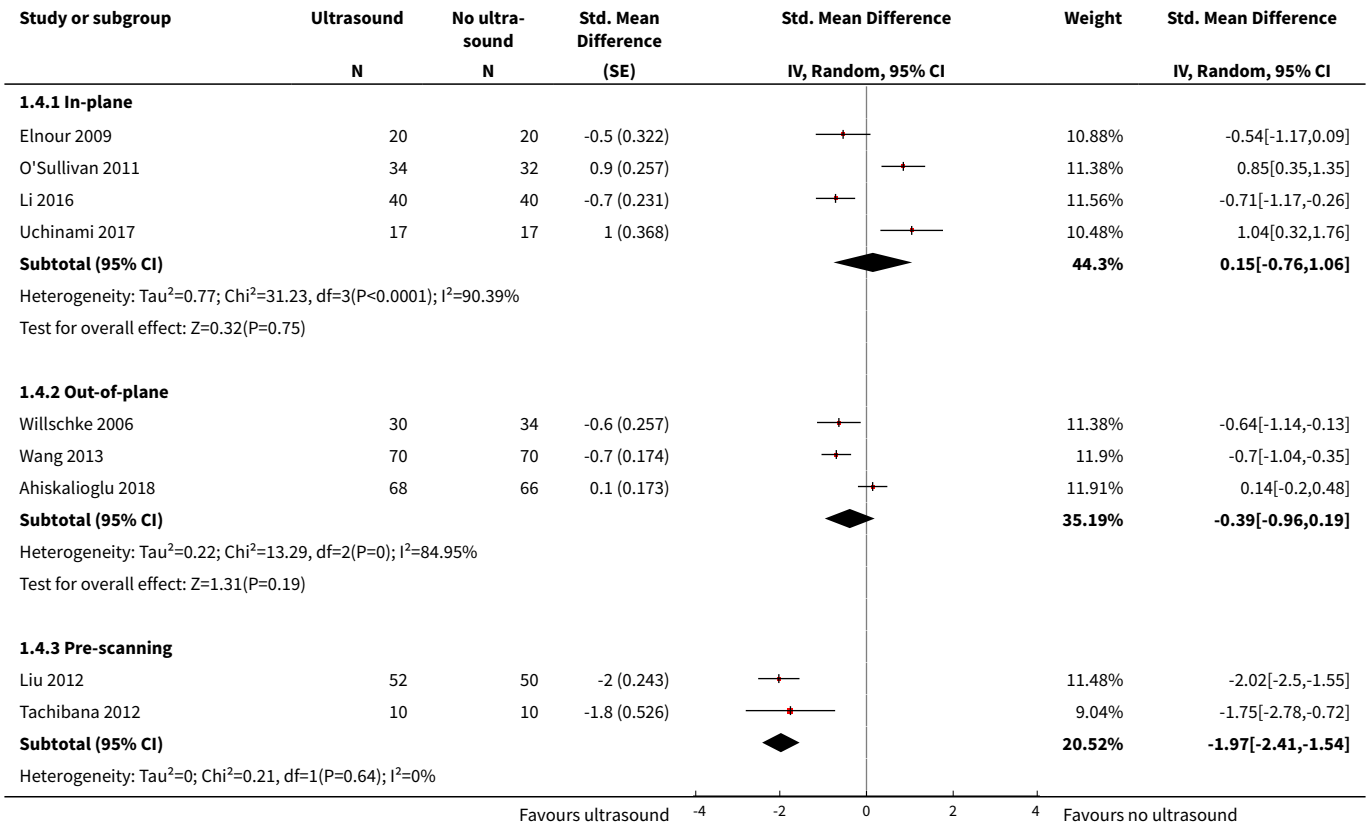


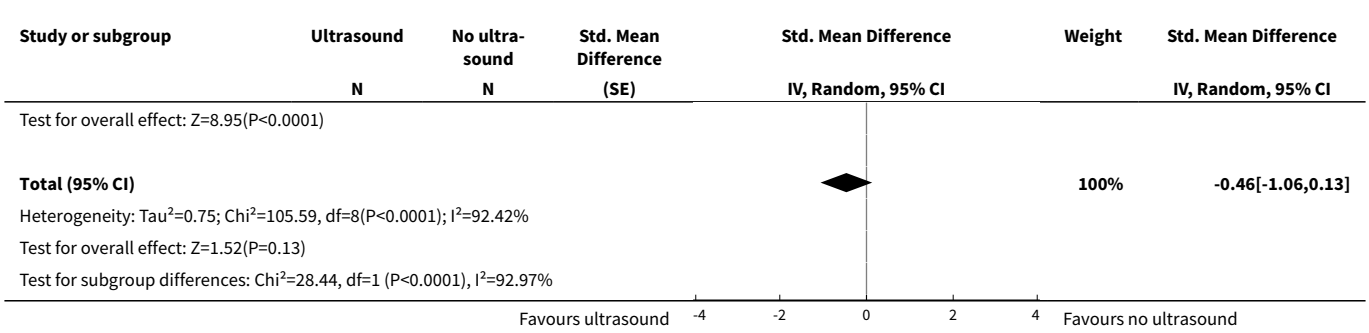
Analysis 1.3. Comparison 1 Ultrasound versus no ultrasound, Outcome 3 Block duration.



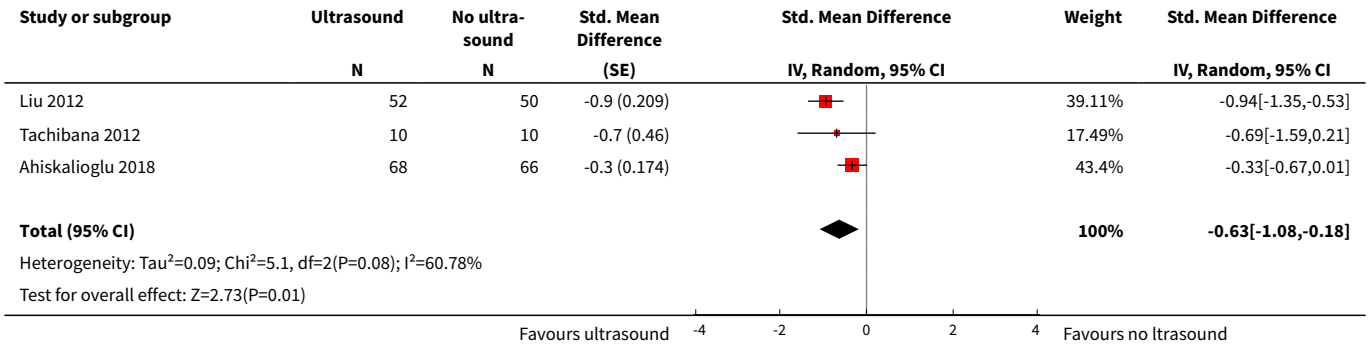


Analysis 1.4. Comparison 1 Ultrasound versus no ultrasound, Outcome 4 Time to perform the block.

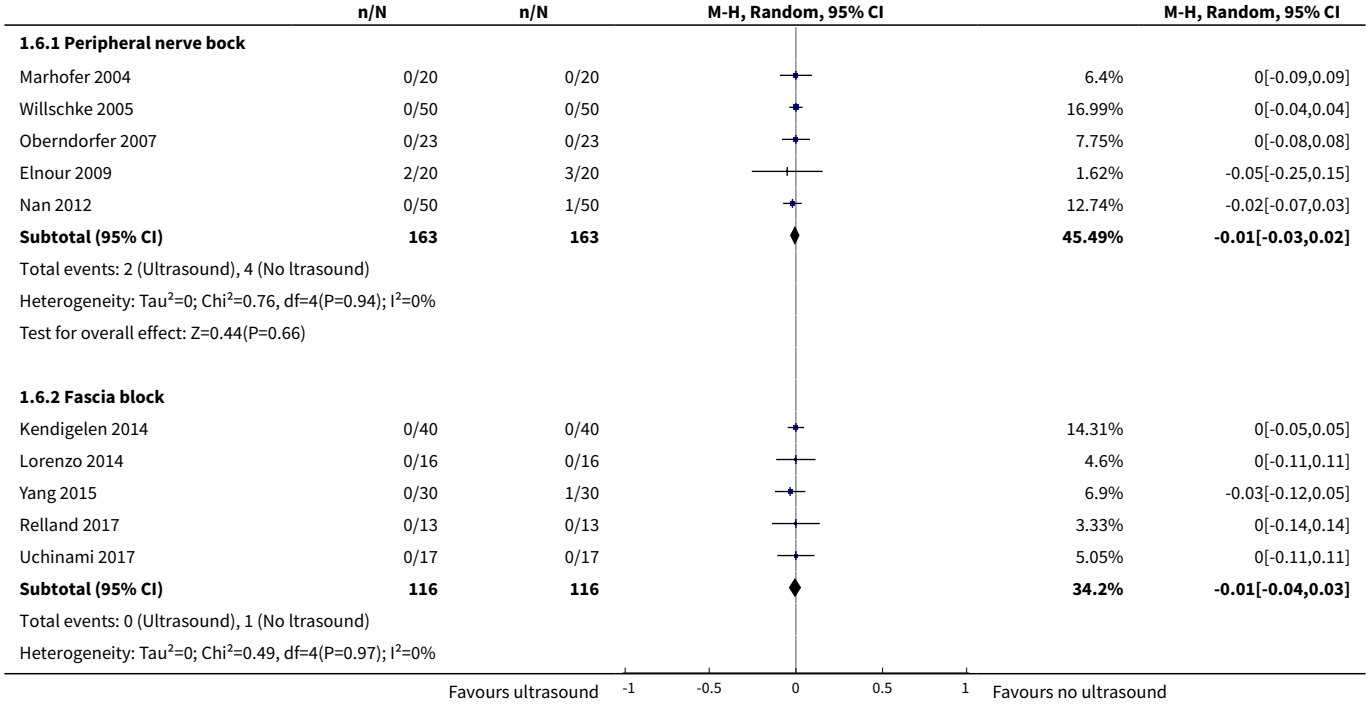


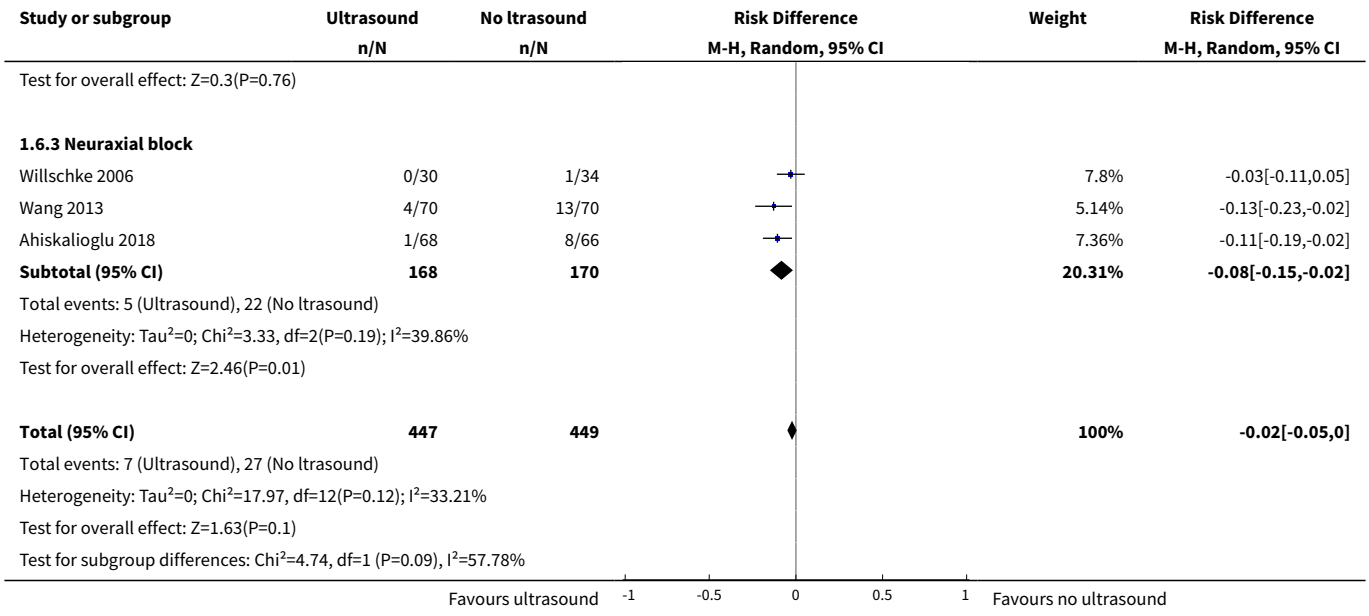


Analysis 1.5. Comparison 1 Ultrasound versus no ultrasound, Outcome 5 Number of needle passes.

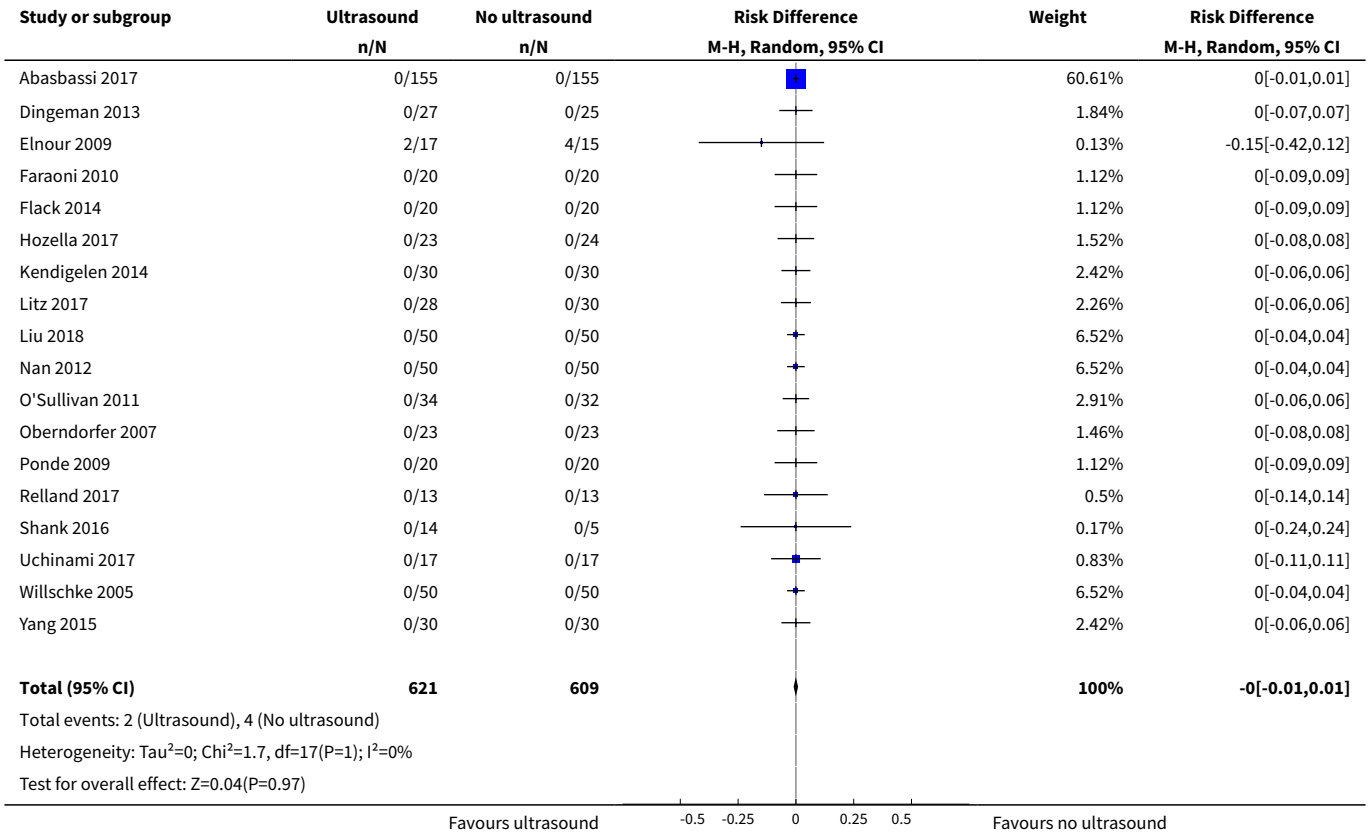


Analysis 1.6. Comparison 1 Ultrasound versus no ultrasound, Outcome 6 Minor complications: bloody puncture.



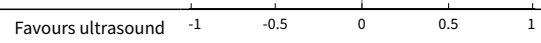


Analysis 1.7. Comparison 1 Ultrasound versus no ultrasound, Outcome 7 Minor complications: transient neurological injury.



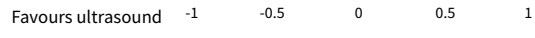
Analysis 1.8. Comparison 1 Ultrasound versus no ultrasound, Outcome 8 Minor complications: seizure from local anaesthetic toxicity.

Study or subgroup	Ultrasound n/N	No ultrasound n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Abasbassi 2017	0/155	0/155		47.63%	0[-0.01,0.01]
Ahiskalioglu 2018	0/68	0/66		9.08%	0[-0.03,0.03]
Dingeman 2013	0/27	0/25		1.44%	0[-0.07,0.07]
Elnour 2009	0/17	0/15		0.58%	0[-0.11,0.11]
Faraoni 2010	0/20	0/20		0.88%	0[-0.09,0.09]
Flack 2014	0/20	0/20		0.88%	0[-0.09,0.09]
Hozella 2017	0/23	0/24		1.19%	0[-0.08,0.08]
Kendigelen 2014	0/30	0/30		1.91%	0[-0.06,0.06]
Litz 2017	0/28	0/30		1.78%	0[-0.06,0.06]
Liu 2018	0/50	0/50		5.12%	0[-0.04,0.04]
Lorenzo 2014	0/16	0/16		0.58%	0[-0.11,0.11]
Nan 2012	0/50	0/50		5.12%	0[-0.04,0.04]
O'Sullivan 2011	0/34	0/32		2.28%	0[-0.06,0.06]
Ponde 2009	0/20	0/20		0.88%	0[-0.09,0.09]
Relland 2017	0/13	0/13		0.4%	0[-0.14,0.14]
Shank 2016	0/14	0/5		0.13%	0[-0.24,0.24]
Tachibana 2012	0/10	0/10		0.25%	0[-0.17,0.17]
Uchinami 2017	0/17	0/17		0.65%	0[-0.11,0.11]
Wang 2013	0/70	0/70		9.91%	0[-0.03,0.03]
Weintraud 2009	0/35	0/31		2.27%	0[-0.06,0.06]
Willschke 2005	0/50	0/50		5.12%	0[-0.04,0.04]
Yang 2015	0/30	0/30		1.91%	0[-0.06,0.06]
Total (95% CI)	**797**	**779**		**100%**	**0[-0.01,0.01]**
Total events: 0 (Ultrasound), 0 (No ultrasound)					
Heterogeneity: Tau^2=0; Chi^2=0, df=21(P=1); I^2=0%					
Test for overall effect: Not applicable					



Analysis 1.9. Comparison 1 Ultrasound versus no ultrasound, Outcome 9 Minor complications: block infection without neurological injury.

Study or subgroup	Ultrasound n/N	No ultrasound n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Abasbassi 2017	0/155	0/155		60.01%	0[-0.01,0.01]
Dingeman 2013	0/27	0/25		1.82%	0[-0.07,0.07]
Faraoni 2010	0/20	0/20		1.11%	0[-0.09,0.09]
Flack 2014	0/20	0/20		1.11%	0[-0.09,0.09]
Hozella 2017	0/23	0/24		1.5%	0[-0.08,0.08]
Kendigelen 2014	0/30	0/30		2.4%	0[-0.06,0.06]
Litz 2017	0/28	0/30		2.24%	0[-0.06,0.06]
Liu 2018	0/50	0/50		6.46%	0[-0.04,0.04]
Marhofer 2004	0/20	0/20		1.11%	0[-0.09,0.09]
Nan 2012	0/50	0/50		6.46%	0[-0.04,0.04]
O'Sullivan 2011	0/34	0/32		2.88%	0[-0.06,0.06]
Oberndorfer 2007	0/23	0/23		1.45%	0[-0.08,0.08]
Ponde 2009	0/20	0/20		1.11%	0[-0.09,0.09]



Study or subgroup	Ultrasound n/N	No ultrasound n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Relland 2017	0/13	0/13		0.5%	0[-0.14,0.14]
Shank 2016	0/14	0/5		0.17%	0[-0.24,0.24]
Uchinami 2017	0/17	0/17		0.82%	0[-0.11,0.11]
Willschke 2005	0/50	0/50		6.46%	0[-0.04,0.04]
Yang 2015	0/30	0/30		2.4%	0[-0.06,0.06]
Total (95% CI)	**624**	**614**		**100%**	**0[-0.01,0.01]**
Total events: 0 (Ultrasound), 0 (No ultrasound)					
Heterogeneity: Tau^2=0; Chi^2=0, df=17(P=1); I^2=0%					
Test for overall effect: Not applicable					

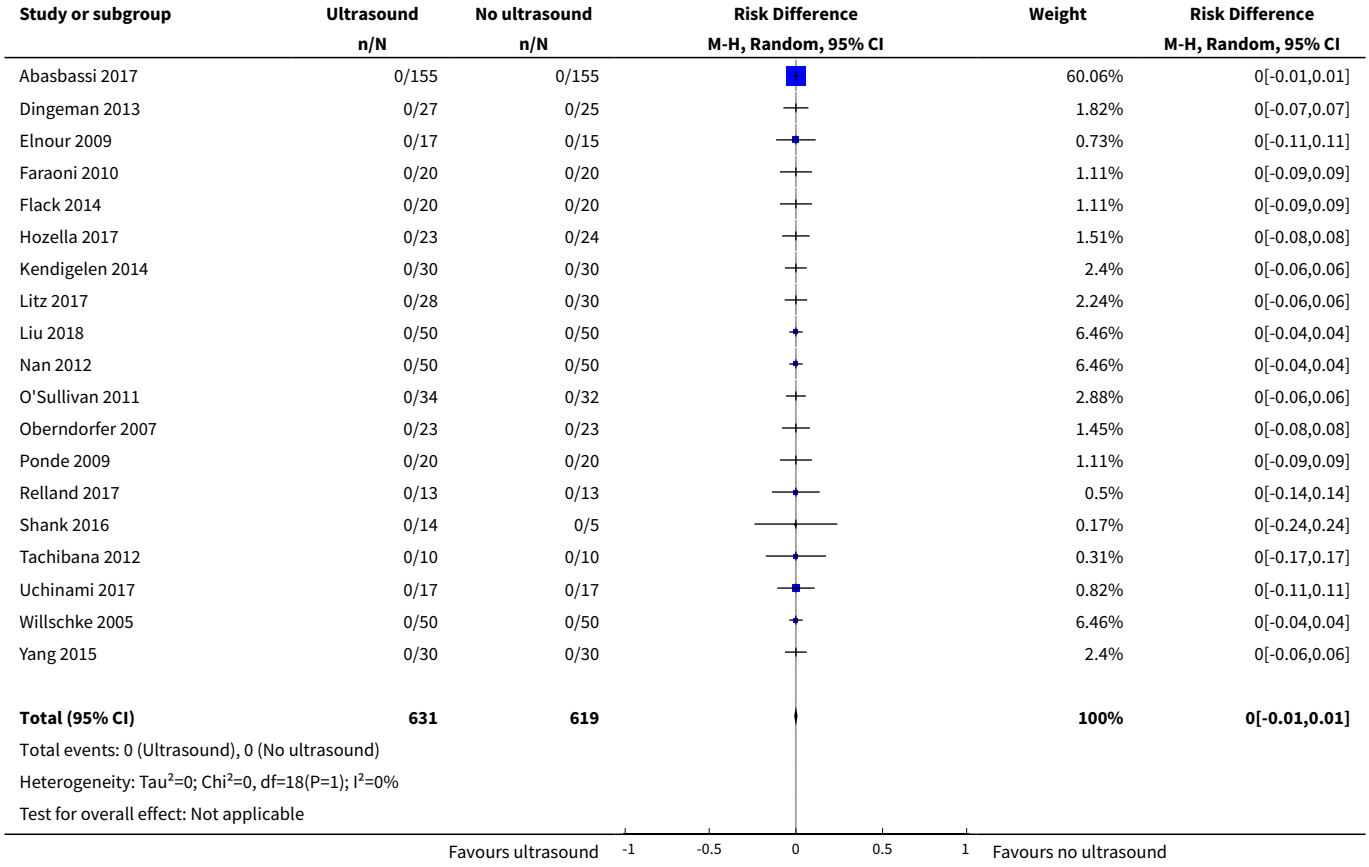
Favours ultrasound -1 -0.5 0 0.5 1 Favours no ultrasound

Analysis 1.10. Comparison 1 Ultrasound versus no ultrasound, Outcome 10 Major complications: cardiac arrest from local anaesthetic toxicity.

Study or subgroup	Ultrasound n/N	No ultrasound n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Litz 2017	0/28	0/30		1.78%	0[-0.06,0.06]
Willschke 2005	0/50	0/50		5.12%	0[-0.04,0.04]
Elnour 2009	0/17	0/15		0.58%	0[-0.11,0.11]
Ponde 2009	0/20	0/20		0.88%	0[-0.09,0.09]
Weintraud 2009	0/35	0/31		2.27%	0[-0.06,0.06]
Faraoni 2010	0/20	0/20		0.88%	0[-0.09,0.09]
O'Sullivan 2011	0/34	0/32		2.28%	0[-0.06,0.06]
Nan 2012	0/50	0/50		5.12%	0[-0.04,0.04]
Tachibana 2012	0/10	0/10		0.25%	0[-0.17,0.17]
Wang 2013	0/70	0/70		9.91%	0[-0.03,0.03]
Dingeman 2013	0/27	0/25		1.44%	0[-0.07,0.07]
Lorenzo 2014	0/16	0/16		0.58%	0[-0.11,0.11]
Flack 2014	0/20	0/20		0.88%	0[-0.09,0.09]
Kendigelen 2014	0/30	0/30		1.91%	0[-0.06,0.06]
Yang 2015	0/30	0/30		1.91%	0[-0.06,0.06]
Shank 2016	0/14	0/5		0.13%	0[-0.24,0.24]
Abasbassi 2017	0/155	0/155		47.63%	0[-0.01,0.01]
Hozella 2017	0/23	0/24		1.19%	0[-0.08,0.08]
Uchinami 2017	0/17	0/17		0.65%	0[-0.11,0.11]
Relland 2017	0/13	0/13		0.4%	0[-0.14,0.14]
Liu 2018	0/50	0/50		5.12%	0[-0.04,0.04]
Ahiskalioglu 2018	0/68	0/66		9.08%	0[-0.03,0.03]
Total (95% CI)	**797**	**779**		**100%**	**0[-0.01,0.01]**
Total events: 0 (Ultrasound), 0 (No ultrasound)					
Heterogeneity: Tau^2=0; Chi^2=0, df=21(P=1); I^2=0%					
Test for overall effect: Not applicable					

Favours ultrasound -1 -0.5 0 0.5 1 Favours no ultrasound

Analysis 1.11. Comparison 1 Ultrasound versus no ultrasound, Outcome 11 Major complications: lasting neurological injury.



ADDITIONAL TABLES

Table 1. Block techniques

Study	Intervention	Comparator
Abasbassi 2017	Ultrasound-guided out-of-plane dorsal penile nerve block with 0.2 mL/kg of levobupivacaine 0.5%	Landmark dorsal penile nerve block with 0.2 mL/kg of levobupivacaine 0.5% (Dalens 1989)
Ahiskalioglu 2018	Ultrasound-guided out-of-plane caudal block with 0.125% levobupivacaine plus 10 mcg/kg morphine (total volume: 0.5 mL/kg)	Landmark caudal block with 0.125% levobupivacaine plus 10 mcg/kg morphine (total volume: 0.5 mL/kg)
Dingeman 2013	Bilateral rectus sheath block with real-time ultrasonographic guidance with 0.5 mL/kg per side of ropivacaine 0.25%, cephalad to the umbilicus	Infiltration by the surgeon (subcutaneous or intradermal) with 0.4 mL/kg of ropivacaine 0.5%
Elnour 2009	Axillary brachial plexus with ultrasound, 13-6 MHz linear probe, real-time in-plane technique, circumferential spread around each target nerve	Axillary brachial plexus with nerve stimulator 0.5 mA, 0.3 ms distal response for median, radial, and ulnar nerves. A triceps response could also be accepted for the radial nerve.

Table 1. Block techniques *(Continued)*

Faraoni 2010	Real-time (in-plane) ultrasound guidance was used to guide bilateral injections into the subpubic space, deep to Scarpa's fascia, with ropivacaine 0.75% 0.1 mL/kg per side plus 0.05 mL/kg at the base of the penis	Landmark dorsal penile nerve block with same volume and locations
Flack 2014	Real-time (in-plane) ultrasound-guided rectus sheath block with 0.2 mL/kg 0.25% bupivacaine (1 mg/kg) to each side at least 10 minutes before incision	Wound infiltration of 0.4 mL/kg 0.25% bupivacaine (1 mg/kg) at the end of surgery
Gkliatis 2017	Ultrasound-guided posterior transversus abdominis plane block Total dose of 0.3 mL/kg ropivacaine 0.2%	Wound infiltration Total dose of 0.3 mL/kg ropivacaine 0.2%
Gurnaney 2011	Real-time (in-plane) rectus sheath block, 1 cm cephalad to the umbilicus with 0.25% bupivacaine, volume according to a table Total volume: < 12 kg = 0.5 mL/kg; ≥ 12 to 30 = 12 mL; ≥ 30 to 40 = 16 mL; ≥ 40 = 20 mL	Infiltration of 0.25% bupivacaine at the end of surgery. Volume according to a table Total volume: < 12 kg = 0.5 mL/kg; ≥ 12 to 30 = 12 mL; ≥ 30 to 40 = 16 mL; ≥ 40 = 20 mL
Hozella 2017	Transverse abdominis plane block with 0.5 mL/kg of 0.25% ropivacaine placed with in-plane ultrasound guidance	Wound infiltration with 0.5 mL/kg of 0.25% ropivacaine
Kendigelen 2014	Transverse abdominis plane block with 2 mg/kg of 0.25% bupivacaine (maximal volume 30 mL) placed with in-plane ultrasound guidance	Wound infiltration with 2 mg/kg of 0.25% bupivacaine
Li 2016	Ultrasound-guided in-plane penile block, probe beneath the scrotum with 0.1 mL/kg of lidocaine 1% and ropivacaine 0.375%	Landmark traditional penile block with 0.2 mL/kg of lidocaine 1% and ropivacaine 0.375%
Litz 2017	Ultrasound-guided rectus sheath block with 0.5 mL/kg (maximal volume 10 mL) per side of ropivacaine 0.2%	0.5 mL/kg (maximal volume 10 mL) per side of ropivacaine 0.2% injected under direct visualization into the rectus sheaths bilaterally by the attending surgeon
Liu 2012	Caudal anaesthesia with ultrasound for pre-scanning; positive reaction in caudal space was monitored simultaneously by ultrasound	Caudal anaesthesia with landmarks; positive reaction in caudal space was monitored simultaneously by classic swoosh test
Liu 2018	Ultrasound-guided in-plane median nerve block with 0.2% ropivacaine (maximal volume 0.5 mL/kg)	Landmark median nerve block with 0.2% ropivacaine (maximal volume 0.5 mL/kg) plus skin incision infiltration
Lorenzo 2014	Real-time, in-plane, ultrasound-guided transversus abdominis plane block with 0.4 mL/kg bupivacaine 0.25% with 1:200,000 epinephrine before incision	Wound infiltration with 0.4 mL/kg bupivacaine 0.25% with 1:200,000 epinephrine before incision
Marhofer 2004	Infraclavicular lateral brachial plexus blocks with 0.5% ropivacaine 0.5 mL/kg guided by ultrasound visualization (out-of-plane), injection around the brachial plexus	Infraclavicular brachial plexus blocks with 0.5% ropivacaine 0.5 mL/kg guided by nerve stimulation (coracoid process, 0.3 mA and 0.3 ms)
Nan 2012	ilioinguinal or iliohypogastric block under ultrasonic guidance (linear 5 to 10 MHz probe; real time; out-of-plane)	Ilioinguinal or iliohypogastric block performed according to the traditional method (Schulte-Steinberg's method) of anatomical

Table 1. Block techniques *(Continued)*

	with a mixture of 0.8% lidocaine and 0.25% levobupivacaine at 0.2 mL/kg	localization with the same local anaesthetic at 0.3 mL/kg
O'Sullivan 2011	Penile block under ultrasound guidance. Hockey-stick probe (6 to 13 MHz, 25 mm), real-time (in-plane; information from study authors) guidance. 2 puncture techniques with 0.5% bupivacaine 1 to 2 mL up to 3 years and 1 additional mL per each additional 3 years up to a maximum of 5 to 6 mL	Penile block with landmarks with the same doses
Oberndorfer 2007	Sciatic and femoral nerve block under ultrasound guidance using a multiple-injection technique until the nerves were surrounded by levobupivacaine. Portable ultrasound unit with a 5 to 10 MHz linear hockey stick probe, real-time (out-of plane) technique	Sciatic and femoral nerve blocks under nerve stimulator guidance using a predefined dose of 0.3 mL/kg of levobupivacaine injected when a current of 0.3 mA over 0.3 ms at 2 Hz elicited plantar flexion (sciatic) or cephalic movement of the patella (femoral)
Ponde 2009	Real-time (in-plane) ultrasound-guided infraclavicular brachial plexus block with a 38-millimetre linear 5 to 10 MHz probe and with 0.5 mL/kg of 0.5% of bupivacaine as a 1-injection technique	Lateral infraclavicular brachial plexus block guided by nerve stimulator with 0.5 mL/kg of 0.5% bupivacaine injected at 0.5 mA over 250 ms. If after 3 redirections a wrist response could not be obtained, an elbow response was accepted.
Ponde 2013	Femoral and sciatic block under real-time (in-plane) ultrasound guidance with a 5 to 10 MHz probe and 0.5 mL/kg of 0.25% bupivacaine for the sciatic nerve and 0.7 mL/kg of lidocaine 1% for the femoral nerve. The procedure was abandoned in the absence of visualization of the sciatic nerve.	Femoral and sciatic block with nerve stimulator. Procedure abandoned if sciatic nerve stimulation was not obtained after 3 attempts (each pass was counted as an attempt). Injection of 0.5 mL/kg of bupivacaine 0.25% with plantar or dorsiflexion (ankle movement for the sciatic block) and 0.7 mL/kg of lidocaine 1% with a quadriceps contraction (femoral block) obtained at 0.5 mA. A fascia iliaca block (loss-of-resistance technique) was administered to children in whom a femoral block could not be performed.
Qiu 2016	Transverse abdominis plane block with 0.5 mL/kg of 0.25% ropivacaine placed with in-plane ultrasound guidance	Landmark (triangle of Petit) transverse abdominis plane block with 0.5 mL/kg of 0.25% ropivacaine
Relland 2017	In-plane ultrasound-guided rectus sheath block with 0.1 mL/kg of 0.2% ropivacaine with 5 mcg/mL of epinephrine per side and administered at the T9–T10 level	The surgeon injected either 0.5 mL/kg of 0.5% bupivacaine or 1 mL/kg of 0.25% bupivacaine with 5 mcg/mL of epinephrine based on the surgeon's discretion in line with his or her standard practice.
Sahin 2013	Transversus abdominis plane block with ultrasound (real time; in-plane) and 0.5 mL/kg of 0.25% levobupivacaine. The block was performed after anaesthesia induction with a 10 to 18 MHz probe placed between the iliac crest and the subcostal area at the mid-axillary line and the needle directed posteriorly. The surgical procedure began 5 to 10 minutes after local anaesthetic administration.	Wound infiltration with 0.2 mL/kg of 0.25% levobupivacaine between external aponeurosis and the skin was performed by surgeons during wound closure.
Shaaban 2014	In-plane ultrasound-guided transversus abdominis plane block with 0.4 mL/kg of bupivacaine 0.25% with 1:200,000	Wound infiltration with 0.4 mL/kg of bupivacaine 0.25% by the surgeon at the end of surgery

Table 1. Block techniques *(Continued)*

	epinephrine. Total dose of bupivacaine will not exceed 2 mg/kg, and total volume will not be more than 20 mL.	
Shank 2016	Ropivacaine 0.2% (without epinephrine) around the lateral femoral cutaneous nerve via ultrasound guidance; dose = 20 mL or 1 mL/kg for children < 20 kg	Donor site infiltration with bupivacaine 0.25% with epinephrine 1:200,000; dose = 1 mL/kg (no maximum)
Tachibana 2012	Thoracic epidural. Ultrasound was used to determine the level, the wider space, and the puncture point (shortest depth from the skin).	Landmarks
Uchinami 2017	In-plane ultrasound-guided rectus sheath block with 0.2 mL/kg of 0.375% ropivacaine per side in the posterior rectus sheath compartment	Local anaesthetic infiltration with 0.2 mL/kg of 0.75% ropivacaine
Wang 2013	Ultrasound guidance. Pre-scanning with a 5 to 10 MHz linear 38 millimetre probe, real time (out of-plane), confirmed with upward displacement of the sacrococcygeal ligament upon injection	Landmarks
Weintraud 2009	Ilioinguinal-iliohypogastric nerve blockade with real-time (out of-plane) ultrasound guidance using a 5 to 10 MHz linear hockey stick probe	Ilioinguinal-iliohypogastric nerve blockade with landmarks (single-pop)
Willschke 2005	Real-time (out of-plane) ultrasound-guided ilioinguinal block with levobupivacaine 0.25% in amount sufficient to surround the nerves	Ilioinguinal block using the traditional fascial click method. The needle was inserted vertically through the tented skin, 1 to 2 cm medial and 1 to 2 cm inferior to the anterior superior iliac spine. After the first fascial click was detected, and following a negative aspiration, levobupivacaine 0.25% (0.3 mL/kg) was injected. The spread of local anaesthetic was examined with ultrasound after injection but with no further intervention consequential to this information.
Willschke 2006	Epidural catheter placement was guided by direct ultrasound visualization (real time, out-of-plane for needle placement). Images obtained by an assistant with 5 to 10 MHz hockey stick probe to obtain a paramedian longitudinal view. Midline needle insertion. Confirmation of the position of the tip of the catheter and spread of local anaesthetics through the catheter. Levobupivacaine 0.25% for confirmation of needle placement and through the catheter (0.2 mg/kg for the latter)	Epidural catheter with standard loss-of-resistance technique with air or saline. Levobupivacaine 0.2% 0.2 mg/kg through the needle and 0.2 mg/kg through the catheter
Yang 2015	In-plane ultrasound-guided ilioinguinal nerve block with 0.2 mL/kg mixture of 0.8% lidocaine with 0.25% levobupivacaine	Landmark-based ilioinguinal nerve block (van Schoor 2005), with 0.3 mL/kg mixture of 0.8% lidocaine with 0.25% levobupivacaine

T9–T10: vertebral thoracic level 9-10

Table 2. Definitions used by study authors for failed blocks

Study	Type of block	Timing of blockade	Definition

Table 2. Definitions used by study authors for failed blocks *(Continued)*

Abasbassi 2017	Dorsal nerve penile block	Not reported	Proportion of participants that needed piritramide (Objective Pain Scale score > 3) were considered as failed blocks.
Ahiskalioglu 2018	Caudal block	Under general anaesthesia before surgical incision in both groups	Failed block was defined as significant motor movements following surgical induction or heart and respiratory rates increasing > 20% of the basal levels.
Elnour 2009	Axillary brachial plexus block	Under general anaesthesia before surgical incision in both groups	The procedure was considered a failure when: 1. performance time exceeded 20 minutes; or 2. increase in heart rate and arterial blood pressure > 20% of baseline values, non-specific body movements, and/or withdrawal of the blocked limb in response to surgical stimulus.
Faraoni 2010	Penile nerve block	Under general anaesthesia before surgical incision in both groups	Ineffective block was defined as an increase in heart rate and mean arterial pressure > 20% above baseline values.
Gkliatis 2017	Transversus abdominis plane block	Not reported	Proportion of participants that needed tramadol were considered as failed blocks.
Kendigelen 2014	Transversus abdominis plane block	End of surgery	Proportion of participants that needed tramadol during the first 5 minutes after surgery were considered as failed blocks.
Li 2016	Penile block	Not reported	Not reported
Litz 2017	Rectus sheath block	Before surgical incision for ultrasound-guided technique and before skin closure for the surgeon-administered technique	Pain scores ≥ 4 in post-anaesthesia care unit
Liu 2012	Caudal block	Under general anaesthesia 10 to 15 minutes before surgical incision in both groups	Unsuccessful caudal puncture after 4 attempts (n = 2 in the control group) or signs of pain, such as body movement, tachycardia, and tachypnoea during surgery
Liu 2018	Median nerve block	Before surgical incision	A block was considered unsuccessful if the children met any of the following criteria: 1. withdrawal reflex related to operation stimulation; 2. 2 or more additional doses of propofol or sufentanil were required during the operation; 3. the heart rate or mean arterial blood pressure increased more than 20% as soon as the surgery began; or 4. instant feeling of intense pain or modified-CHEOPS score > 5 after anaesthesia recovery.
Marhofer 2004	Infraclavicular brachial plexus block	Propofol sedation, 30 minutes before surgical incision in both groups	Procedure was considered a failure if ≥ 2 of the 4 nerves (ulnar, radial, median, and musculocutaneous) could not be blocked effectively.
Nan 2012	Ilioinguinal and iliohypogastric nerve blocks	Under general anaesthesia before surgical incision in both groups	Inadequate analgesia was defined as an increase of heart rate > 10% of baseline level, which required elevation of the sevoflurane concentration to 3% to 4% during surgery.

Table 2. Definitions used by study authors for failed blocks *(Continued)*

O'Sullivan 2011	Penile nerve block	Under general anaesthesia ≥ 10 minutes before surgical incision in both groups	Procedure was considered a failure if a rise in heart rate or respiratory rate > 25% from baseline occurred in response to surgical stimulus.
Oberndorfer 2007	Sciatic and femoral nerve blocks	Under general anaesthesia ≥ 20 minutes before surgical incision in both groups	Procedure was considered a failure if a rise in heart rate > 15% of baseline value occurred at skin incision or during surgery.
Ponde 2009	Infraclavicular brachial plexus block	Under general anaesthesia before surgical incision in both groups	Procedure was considered a failure if a pain response to surgical stimulus occurred, defined as an increase in heart rate and arterial blood pressure > 20% of basal rate or non-specific body movement in response to surgical stimulus and withdrawal of blocked limb in response to incision.
Ponde 2013	Sciatic and femoral nerve blocks	Under general anaesthesia ≥ 20 minutes before surgical incision in both groups	Procedure was considered a failure when: 1. sciatic nerve stimulation response could not be elicited after 3 attempts (each pass was counted as an attempt) with the neurostimulator, or nerve could not be convincingly visualized under ultrasound guidance; or 2. response to surgical stimulus: increase in pulse rate and blood pressure > 20% of basal rate.
Tachibana 2012	Thoracic epidural anaesthesia	Under general anaesthesia before surgical incision in both groups	Procedure was considered a failure if a participant complained of severe postoperative pain despite sufficient epidural administration of local anaesthetics.
Wang 2013	Caudal block	Under general anaesthesia ≥ 15 minutes before surgical incision in both groups	Procedure was considered a failure if a child had motor or haemodynamic response, as indicated by an increase in mean arterial pressure or heart rate > 15% compared with baseline values obtained just before skin incision and subsequent to surgical procedure.
Weintraud 2009	Ilioinguinal and iliohypogastric nerve blocks	Under general anaesthesia ≥ 15 minutes before surgical incision in both groups	Procedure was considered a failure if child had an increase in heart rate or mean arterial blood pressure > 10% compared with baseline during operation.
Willschke 2005	Ilioinguinal and iliohypogastric nerve blocks	Under general anaesthesia ≥ 15 minutes before surgical incision in both groups	Procedure was considered a failure if child had an increase in heart rate or mean arterial pressure > 10% after skin incision or during surgery.
Willschke 2006	Thoracic or lumbar epidural anaesthesia	Under general anaesthesia ≥ 15 minutes before surgical incision in both groups	An increase in heart rate or blood pressure > 20% from baseline was considered to reflect inadequate analgesia and was managed by bolus administration of levobupivacaine 0.25% 0.3 mL/kg of body weight through the epidural catheter. If this was unsuccessful, the epidural block was considered to have failed.
Yang 2015	Ilioinguinal nerve block	Under general anaesthesia after induction	Pain score of > 3 was considered a sign of inadequate analgesia.

CHEOPS: Children's Hospital of Eastern Ontario Pain Scale

Table 3. Complications

Peripheral nerve block

Study	Type of block	Minor complications	Major complications
Elnour 2009	Axillary brachial plexus block	No intravascular injection. Local bruising 2/17 in the ultrasound group vs 3/15 in the nerve stimulator group. Local axillary pain 3/17 in the ultrasound group and 8/15 in the nerve stimulator group. Transient postblock paraesthesia 2/17 in the ultrasound group and 4/15 in the nerve stimulator group (which resolved within 5 days as reported by parents and participants in the follow-up surgical clinic 1 week later).	Major complications (e.g. unintentional intravascular injection, persistent neurological deficit) did not occur in either group.
Liu 2018	Median nerve block	No adverse events were observed in the 2 groups.	No adverse events were observed in the 2 groups.
Marhofer 2004	Infraclavicular brachial plexus block	No clinical signs of inadvertent puncture of major vessels	No clinical signs of pneumothorax, infection, or haematoma
Nan 2012	Ilioinguinal or iliohypogastric nerve block	1 case in no-ultrasound group had needle puncturing into blood vessels.	No other adverse event was observed in the 2 groups.
Oberndorfer 2007	Sciatic and femoral nerve blocks	No clinical signs of inadvertent puncture of major vessels	No clinical signs of nerve damage, infection, or haematoma
Ponde 2009	Infraclavicular brachial plexus block	No complications were related to the regional anaesthetic technique.	No complications were related to the regional anaesthetic technique.
Ponde 2013	Sciatic and femoral nerve blocks	Not reported	Not reported
Shank 2016	Lateral femoral cutaneous block or fascia-iliaca block	No adverse events occurred performing these blocks.	No adverse events occurred performing these blocks.
Weintraud 2009	Ilioinguinal-iliohypogastric nerve block	Not reported	The ultrasound-guided technique resulted in higher C_{max} (SD) and AUC values (C_{max}: 1.78 (0.62) vs 1.23 (0.70) mcg/mL, $P < 0.01$; AUC: 42.4 (15.9) vs 27.2 (18.1) mcg 30 min/mL, $P < 0.001$). No signs of clinical toxicity
Willschke 2005	Ilioinguinal block	All anaesthetic procedures were uneventful; no clinical evidence of complications such as small bowel or major vessel puncture.	All anaesthetic procedures were uneventful.

Table 3. Complications *(Continued)*

Yang 2015	Ilioinguinal nerve block	No adverse events other than 1 bloody puncture (landmark) were reported during or after the operation.	No adverse events other than 1 bloody puncture (landmark) were reported during or after the operation.
Fascia block			
Study	**Type of block**	**Minor complications**	**Major complications**
Abasbassi 2017	Penile nerve block	No adverse events were reported.	No adverse events were reported.
Dingeman 2013	Rectus sheath block	No adverse events requiring immediate medical attention associated with the surgical procedure or the postoperative course were reported in either group.	No adverse events requiring immediate medical attention associated with the surgical procedure or the postoperative course were reported in either group.
Faraoni 2010	Penile nerve block	No complications	No complications
Flack 2014	Rectus sheath block	Not reported	Peak plasma bupivacaine concentration was higher following ultrasound rectus sheath block (median 631.9 ng/mL, IQR: 553.9 to 784.1 vs 389.7 ng/mL, IQR: 250.5 to 502.7; P = 0.002). Time to peak concentration was longer in the USGRSB group (median 45 minutes, IQR: 30 to 60 vs 20 minutes, IQR: 20 to 45; P = 0.006). No measured plasma bupivacaine concentration exceeded 1 mcg/mL. No adverse events and no clinical evidence of toxicity were noted.
Gkliatis 2017	Posterior transversus abdominis plane block	No complication was recorded in transversus abdominis plane block group.	No complication was recorded in transversus abdominis plane block group.
Gurnaney 2011	Rectus sheath block	Not reported	Not reported
Hozella 2017	Transversus abdominis plane block	No adverse events due to research interventions	No adverse events due to research interventions
Kendigelen 2014	Transversus abdominis plane block	No adverse effects related to the transversus abdominis plane block were identified. No complications were observed during or after the block intervention.	No major complications
Li 2016	Penile block	No significant difference in the incidence of respiratory depression between the 2 groups	No significant difference in the incidence of respiratory depression between the 2 groups
Litz 2017	Rectus sheath block	1 child in the surgeon-administered rectus sheath block group developed a superficial surgical site infection; there were no complications in the ultrasound-guided group.	No anaesthetic complications reported.

Table 3. Complications *(Continued)*

Lorenzo 2014	Transversus abdominis plane block	None reported.	No local anaesthetic-specific adverse events were noted.
O'Sullivan 2011	Penile nerve block	No complications were reported of either technique.	No complications were reported of either technique.
Qiu 2016	Transversus abdominis plane block	Not reported	Not reported
Relland 2017	Rectus sheath block	No complications	No complications
Sahin 2013	Transversus abdominis plane block	Not reported	Not reported
Shaaban 2014	Transversus abdominis plane block	There were no complications attributable to the ultrasound-guided block.	There were no complications attributable to the ultrasound-guided block.
Uchinami 2017	Rectus sheath block	No procedure-related complications were observed in either group.	No procedure-related complications were observed in either group. No adverse events associated with the nerve block procedure such as neuropathy or local anaesthetic intoxication were reported for any child.
Neuraxial block			
Study	**Type of block**	**Minor complications**	**Major complications**
Ahiskalioglu 2018	Caudal block	Dural puncture and systemic local anaesthetic toxicity were not observed in any of the groups. No intraoperative desaturation was observed.	Dural puncture and systemic local anaesthetic toxicity were not observed in any of the groups. No intraoperative desaturation was observed.
Liu 2012	Caudal	Not reported	Not reported
Tachibana 2012	Thoracic epidural	Not reported	No children experienced severe side effects.
Wang 2013	Caudal	There was an incidence of bloody puncture of 18.6% in group landmarks and 5.7% in group ultrasound ($P < 0.05$).	No dural puncture or systemic reaction to local anaesthetic was reported in either group.
Willschke 2006	Thoracic (n = 59) or lumbar (n = 5) epidural	Blood was aspirated in 1 child in the control group.	No dural puncture occurred in either group.

AUC: area under the curve for blood concentrations of local anaesthetics; **C_{max}**: maximal blood concentration of local anaesthetic; **IQR**: interquartile range; **SD**: standard deviation; **USGRSB**: ultrasound-guided rectus sheath block.

APPENDICES

Appendix 1. CENTRAL (the Cochrane Library) search strategy

#1. MeSH descriptor: [Ultrasonography] explode all trees
#2. (ultrasound* or ultrasonog*) near (guid* or assess* or assist*)
#3. #1 or #2
#4. MeSH descriptor: [Nerve Block] explode all trees
#5. MeSH descriptor: [Anesthesia, Local] explode all trees
#6. MeSH descriptor: [Anesthesia, Spinal] explode all trees
#7. (nerv* near block*) or (regional near (an?est* or techniq* or block*))
#8. #4 or #5 or #6 or #7
#9. (child* or neonat* or preschool* or adolescen* or infant* or p*ediatric*)
#10. #3 and #8 and #9
#11. #10 in Trials

Appendix 2. MEDLINE (OvidSP) search strategy

1. exp ULTRASONOGRAPHY/ or ((ultrasound* or ultrasonog*) adj10 (guid* or assess* or assist*)).mp.
2. exp Nerve Block/ or exp Anesthesia, Local/ or exp Anesthesia, Spinal/ or (nerv* adj5 block*).mp. or (regional adj5 (an?est* or techniq*or block*)).mp.
3. exp child/ or exp infant/ or (child* or neonat* or preschool* or adolescen* or infant* or p?ediatric*).af.
4. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab. or (meta?analysis or review or systematic review).mp.) not (animals not (humans and animals)).sh.
5. 1 and 2 and 3 and 4

Appendix 3. Embase (OvidSP) search strategy

1. ultrasound/ or ((ultrasonog* or ultrasound*) adj10 (guid* or assess* or assist*)).mp.
2. exp nerve block/ or exp local anesthesia/ or exp spinal anesthesia/ or (nerv* adj5 block*).mp. or (regional adj5 (an?est* or techniq* or block*)).mp.
3. exp child/ or (child* or neonat* or preschool* or adolescen* or infant* or p?ediatric*).af.
4. (randomized-controlled-trial/ or randomization/ or controlled-study/ or multicenter-study/ or phase-3-clinical-trial/ or phase-4-clinical-trial/ or double-blind-procedure/ or single-blind-procedure/ or (random* or cross?over* or multicenter* or factorial* or placebo* or volunteer*).mp. or ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)).ti,ab. or (latin adj square).mp.) not (animals not (humans and animals)).sh.
5. 1 and 2 and 3 and 4

Appendix 4. Pain scales used by study authors

1. Objective pain scale from 0 to 15

Objective behavioural variables (crying, facial expression, position of torso and legs, motor restlessness) are assessed.

Each pain variable is scored on a three-point scale (1 = none, 2 = moderate, 3 = severe) to give a maximum cumulative score of 15.

This scale was used for Oberndorfer 2007, Willschke 2005, and Willschke 2006.

2. Objective pain scale from 0 to 10

Objective behavioural variables (crying, facial expression, position of torso and legs, motor restlessness) are assessed.

Each pain variable is scored on a two-point scale (1 = absent, 2 = present) to give a maximum cumulative score of 10.

This scale was used for Abasbassi 2017 and Faraoni 2010.

3. Children's and Infants' Postoperative Pain Scale (CHIPPS)

Item	Behavioural	Score	Definition
Cry	No cry	1	Child is not crying.

(Continued)

	Moaning	2	Child is moaning or quietly vocalizing silent cry.
	Crying	2	Child is crying, but the cry is gentle or whimpering.
	Scream	3	Child is in a full-lunged cry; sobbing; may be scored with complaint or without complaint.
Facial	Composed	1	Neutral facial expression
	Grimace	2	Score only if definite negative facial expression
	Smiling	0	Score only if definite positive facial expression
Child verbal	None	1	Child not talking
	Other complaints	1	Child complains, but not about pain, e.g. “I want to see mommy” of “I am thirsty”.
	Pain complaints	2	Child complains about pain.
	Both complaints	2	Child complains about pain and about other things, e.g. “It hurts; I want my mommy”.
	Positive	0	Child makes any positive statement or talks about others things without complaint.
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive.
	Shifting	2	Body is in motion in a shifting or serpentine fashion.
	Tense	2	Body is arched or rigid.
	Shivering	2	Body is shuddering or shaking involuntarily.
	Upright	2	Child is in a vertical or upright position.
	Restrained	2	Body is restrained.
Touch	Not touching	1	Child is not touching or grabbing at wound.
	Reach	2	Child is reaching for but not touching wound.
	Touch	2	Child is gently touching wound or wound area.
	Grab	2	Child is grabbing vigorously at wound.
	Restrained	2	Child’s arms are restrained.
Legs	Neutral	1	Legs may be in any position but are relaxed; includes gentle swimming or separate-like

(Continued)

		movements.
Squirm/kicking	2	Definitive uneasy or restless movements in the legs and/or striking out with foot or feet
Drawn up/tensed	2	Legs tensed and/or pulled up tightly to body and kept there
Standing	2	Standing, crouching, or kneeling
Restrained	2	Child's legs are being held down.

A score greater than four indicates pain.

This scale was use for Ponde 2013.

4. Wong and Baker

Original scale: 0 = No pain, 1 = Mild, 2 = Moderate, 3 = Quite a lot, 4 = Very bad, and 5 = Worst pain

The scale used by Dingeman 2013 could be this one or Wong and Baker from 0 to 10.

Litz 2017 used this scale but from 0 to 10: 2 = Mild, 4 = Moderate, 6 = Quite a lot, 8 = Very bad, and 10 = Worst pain.

The scale can be presented visually to the child or used by the person caring for the child. The tool may include five drawings of faces expressing variable degrees of pain/discomfort.

5. Revised Bieri FACES pain scale

The Bieri pain scale contains seven schematic faces depicting changes in severity of expressed pain from no pain to the most pain possible. The revised FACES pain scale excludes smiles and tears.

This scale was used for Gurnaney 2011.

6. Face, Legs, Activity, Cry, Consolability (FLACC) scale

The FLACC Pain Assessment Tool incorporates five categories of pain behaviours: facial expression, leg movement, activity, cry, and consolability.

This scale was used for Hozella 2017, Lorenzo 2014, and Uchinami 2017.

7. Visual analogue pain scale (VAS) from 0 to 10

This scale was used for Kendigelen 2014.

8. FLACC or VAS

These scales were used for Shank 2016.

9. FLACC, FACES, or numerical rating scale (NRS) (range unspecified)

Used for Gkliatis 2017

Appendix 5. Block duration (trials extracted as means and standard deviations)

		Ultrasound guidance (hours)			Comparator (hours)		
		Mean	SD	Number	Mean	SD	Number
1	Oberndorfer 2007	8.47	2.97	20	5.58	2.82	20
2	Ponde 2013	8.60	0.66	29	7.62	0.57	23
3	Shaaban 2014	10.40	1.50	22	5.40	1.50	22
4	Gurnaney 2011	0.83	0.62	25	0.54	0.49	26
5	Sahin 2013	17.00	6.80	25	4.70	1.60	26
6	Lorenzo 2014	0.43	0.38	16	0.18	0.15	16

SD: standard deviation

	Ultrasound guidance (hours)	Comparator (hours)
Mean	7.622	4.003
Standard deviation	6.248	2.987

Appendix 6. Time to perform the block (trials extracted as means and standard deviations)

	Ultrasound guidance (minutes)			Comparator (minutes)		
	Mean	SD	Number	Mean	SD	Number
Elnour 2009	14.55	3.39	20	16.10	2.24	20
Li 2016	3.90	1.60	40	5.50	2.70	40
Uchinami 2017	5.30	2.20	17	3.20	1.70	17
Willschke 2006	2.70	1.25	30	3.90	2.30	34
Wang 2013	2.42	0.38	70	2.73	0.52	70
Ahiskalioglu 2018	1.83	0.83	68	1.72	0.75	66
Liu 2012	1.40	0.40	52	3.20	1.20	50

SD: standard deviation

	Ultrasound guidance (minutes)	Comparator (minutes)
Mean	4.586	5.193
Standard deviation	4.587	4.946

Appendix 7. Number of needle passes (trials extracted as means and standard deviations)

	Ultrasound guidance			Comparator		
	Mean	SD	Number	Mean	SD	Number
Liu 2012	1.10	0.3	52	1.6	0.6	50

(Continued)

Ahiskalioglu 2018	1.32	0.7	68	1.4	0.7	66

SD: standard deviation

	Ultrasound guidance	Comparator
Mean	1.210	1.500
Standard deviation	0.1556	0.1414

WHAT'S NEW

Date	Event	Description
7 March 2018	New citation required but conclusions have not changed	Conclusions unchanged.
7 March 2018	New search has been performed	We included 13 new trials in this version. In total we included 33 trials with 2293 participants.

HISTORY

Protocol first published: Issue 12, 2014
Review first published: Issue 2, 2016

Date	Event	Description
3 January 2017	Amended	Co-published in *Anesthesia and Analgesia* (Guay 2016b)
1 March 2016	Amended	Peer's name corrected.

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Screening retrieved papers against inclusion criteria: JG and SK.

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Abstracting data from papers: JG and SK.

Writing to authors of papers to ask for additional information: JG.

Obtaining and screening data from unpublished studies: JG.

Managing data for the review: JG.

Entering data into Review Manager 5 (Review Manager 2014): JG.

Analysing Review Manager 5 statistical data: JG.

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Writing the review: JG, SS, and SK.

Securing funding for the review: departmental resources only.

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

Serving as guarantor for the review (one review author): JG.

Taking responsibility for reading and checking the review before submission: JG, SS, and SK.

DECLARATIONS OF INTEREST

Joanne Guay: none known.

Santhanam Suresh: I am co-author of one excluded trial, Sohn 2010, and one ongoing trial (NCT02321787).

Sandra Kopp: none known.

SOURCES OF SUPPORT

Internal sources

- University of Sherbrooke, Canada.

  University of Sherbrooke granted access to electronic databases and to major medical journals.
- University of Quebec in Abitibi-Temiscamingue, Canada.

  University of Quebec in Abitibi-Temiscamingue provided access to electronic databases and medical journals.
- Cochrane Anaesthesia Review Group, Denmark.

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- Laval University, Canada.

  Laval University granted access to electronic databases and to major medical journals.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made no changes to our published protocol (Guay 2014).

INDEX TERMS

Medical Subject Headings (MeSH)

*Ultrasonography, Interventional; Nerve Block [adverse effects] [*methods]; Perioperative Care [methods]; Peripheral Nervous System; Randomized Controlled Trials as Topic; Surgical Procedures, Operative; Time Factors

MeSH check words

Child; Child, Preschool; Humans; Infant