Omskæring - PICO 2 Anæstesi

Review information

Authors

Styrelsen for Patientsikkerhed[1]

[1][Empty affiliation]

Citation example: SfP. Omskæring - PICO 2 Anæstesi. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Ahiskalioglu 2018

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 79 ± 2.90 years ● *Duration of surgey*: 28.69 ± 6.17 min kontrol 1 ● *Age*: 5 ± 3.31 years ● *Duration of surgey*: 28.82 ± 5.56 min **Included criteria:** The study included a total of 140 ASA I-II children aged between 5and 12 years old who underwent elective phimosis and circumcisionsurgery **Excluded criteria:** Children with severe systemic disease, previous neuro-logical or spinal disorder, coagulation anomaly, allergy against local an-esthetics, local infection at blocksite or witha history of premature birthwere excluded from the study **Pretreatment:** There were no significant differences between the two groups interms of age, height, weight, ASA class, and duration of operation
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Caudal block was performed by ultrasound guided in Group U. Aftersterilization of the region and USG with sterile plastic cover and gel, thesacral hiatus was visualized at the level of the sacral cornus at the out of plane via the lineer transducer of Esaote MyLab30 (Florence, Italy) ul-trasound machineat18 MHz depth and gain was adjusted tooptimal vi-sual quality (Fig. 2). When the inserted needle reached the center of theultrasound image, a 20–22 gauge caudal needle (Epican® Paed caudalB·Braun Melsungen AG) was inserted at the transverse view using theout-of-plane technique (Fig. 3). After confirming the absence of anyblood or cerebrospinalfluid in the aspiration, the caudal solution calcu-lated as0.5 ml/kg wasinjected with hemodynamic and ECG monitoring. ● *Dose*: Caudal solution was prepared as 0.125% levobupivacaine(Chirocaine 50 mg/10 ml ampule, Nycomed Pharma AS, Norway) plus10 mcg/kg morphine (total volume: 0.5 ml/kg), and was administeredto both groups. kontrol 1 ● *Description*: Caudal block was performed in Group C by conventional method.The sacral cornus and the sacral hiatus were palpated. After sterilizationof the region, a 20–22 gauge caudal needle (Epican® Paed caudalB·Braun Melsungen AG) was inserted into the skin with a 60–80 degreeangle and until the sacrococcygeal ligament was passed with a“pop”feeling (puncture of the sacrococcygeal ligament). Then, the angle oftheneedle wasreduced to20–30 degrees and inserted further for an ad-ditional 2–3 mm, entering into the sacral canal. After confirming the ab-sence of any blood or cerebrospinalfluid in the aspiration, the caudalsolution calculated as 0.5 ml/kg was injected with hemodynamic andECG monitorin ● *Dose*: Caudal solution was prepared as 0.125% levobupivacaine(Chirocaine 50 mg/10 ml ampule, Nycomed Pharma AS, Norway) plus10 mcg/kg morphine (total volume: 0.5 ml/kg), and was administeredto both groups.
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Adverse events* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Notes	One hundred-thirty four children, American Society of Anesthesiologists I-II, between the ages of 5 and 12, scheduled for elective phimosis and circumcision surgery

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "agent was administered for pre-medication. The patients were assigned to two groups as the con- ventional caudal block (Group C) and the ultrasound-guided caudal block (Group U) according to the randomization list by a computerized program. Anesthesia induction was performed via" Judgement Comment: Randomisation list from a computerised program
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information on allocation concealment.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding of personnel not possible (two different ultrasound guided caudal block or conventional block groups). No information on blinding of patients.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "All datas are collected by an anesthetist blinded to the group classification." Judgement Comment: Outcome assessor blinded
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No patients discontinued. All patients randomised were included in the analysis (no loss to follow up after randomisation)
Selective reporting (reporting bias)	Low risk	Quote: "(ClinicalTrials.gov. identifier NCT03337191)." Judgement Comment: Outcomes are reported as stated on clinicalTrials.gov.
Other bias	Low risk	Judgement Comment: The study seems to be free from other sources of bias

Al Qahtani 2014

Methods	RCT
Participants	
Interventions	
Outcomes	
Notes	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Allocation concealment (selection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of participants and personnel (performance bias)	High risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of outcome assessment (detection bias)	High risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Incomplete outcome data (attrition bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Selective reporting (reporting bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Other bias	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Anouar 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 30 ±3.12 months ● *Duration of surgey*: 16 ± 2.4 min ● *Anesthesia duration*: 22 ±2.2 min intervention 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration*:

	kontrol 1 ● *Age*: 25.2 ± 5 months ● *Duration of surgey*: 17 ± 1.8 min ● *Anesthesia duration*: 23 ±1.5 min kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration*: Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration*: **Included criteria:** ASA I (American society of anesthesiologists) unpremedicated children, aged from 1 to 5 years (µg20 kg) and undergoing day-case male circumcision. **Excluded criteria:** Exclusion criteria were allergy to local anesthetic, genital malformation, past history of penile surgery, preoperative incident and additional surgical procedure other than circumcision. **Pretreatment:** Demographic parameters were similar in both groups.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: received 0.1 ml/Kg of bupivacaine 0.5% with 1µg/kg of clonidine in each side. Dorsal penile nerve block was performed in the operation room, with standard monitoring, under general anesthesia. General anesthesia was induced with Sevoflurane 6% and maintained with sevoflurane 3% in oxygen /air gas flow. ● *Dose*: 0.1 ml/Kg of bupivacaine 0.5% with 1µg/kg of clonidine in each side. ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: received 0.1 ml/kg of bupivacaine 0.5 % with placebo in each side. dorsal penile nerve block was performed in the operation room, with standard monitoring, under general anesthesia. General anesthesia was induced with Sevoflurane 6% and maintained with sevoflurane 3% in oxygen /air gas flow. ● *Dose*: 0.1 ml/kg of bupivacaine 0.5 % with placebo in each side ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each patient was randomly assigned to one of the two groups by drawing from a sealed envelope." Judgement Comment: Sequence generation is not described
Allocation concealment (selection bias)	Low risk	Quote: "Each patient was randomly assigned to one of the two groups by drawing from a sealed envelope." Judgement Comment: Sealed envelope
Blinding of participants and personnel (performance bias)	Low risk	Quote: "after the block was completed. If, at the time of incision or during surgery, there was a rise in the heart rate or respiratory rate of >25% from baseline, an intravenous bolus of Alfentanyl (20 µg/kg) was given by an anesthetist, blinded to the injected solution in the block. As multimodal analgesia is the" Judgement Comment: It is not clear if the patients were blinded however they state that it is a double-blinded study and the syringes were labeled "DPNB study"
Blinding of outcome assessment (detection bias)	Unclear risk	

Incomplete outcome data (attrition bias)	Unclear risk	Quote: "CHEOPS score was inferior to 7 for all included patients during the first six post operative hours. CHEOPS (Children's Hospital of Eastern Ontario Pain Scale) was significantly lower in group 1 from H2 to H24 in comparison with group 2 (Table 2)." Judgement Comment: Total number of patients included in the analysis is not described.
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No protocol
Other bias	Low risk	Quote: "The authors declare no competing interests." Judgement Comment: No other sources of bias

Arnett 1990

Methods	RCT
Participants	52 male NB; FT; BW > 2000 g; 5 min Apgar scores >/= 6
Interventions	0.4 ml lidocaine DPNB (n=23) 0.4 ml saline DPNB (n=22) no treatment control (n=7) WT not reported; mean length for entire procedure was 4.4 minutes
Outcomes	HR, infant irritability, O2sat
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Inadequate procedure: "The infants were divided by random selection through the use of cards into three groups."
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Likely the procedure (injection) was blinded for the operator and staff.
Blinding of outcome assessment (detection bias)	Low risk	Likely nurses and surgeon grading the procecure were blinded. "Physicians could correctly identify the anesthetized infant 81% of the time (17/21) and 100% of the infants that did not receive anesthesia were correctly identified."
Incomplete outcome data (attrition bias)	Unclear risk	However unclear, 2-3 patients were excluded from analysis due to missing data points. No analysis of the failure to analyze the patients in the group they were allocated. Not clear if any droped out and not reffering to a flowchart
Selective reporting (reporting bias)	Low risk	Nor reffering to a protocol but report on relevant outcomes No protocol however, data from all time points are presented.
Other bias	Low risk	No reason to suspects other sources of bias.

Awori 2019

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 16.9(7.3) years ● *Duration of surgey*: ● *Anesthesia duration* : intervention 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 1 ● *Age*: 16.7(7.5) years ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** We recruited men and boys 10 years of age and above. To be eligible, participants needed to be uncircumcised, in good general health and free of any active sexually transmitted infections. **Excluded criteria:** Participants with known sensitivity to injectable lidocaine or topical cream, or a congenital abnormality or other condition which in the opinion of the medical staff prevented safe participation in the study were excluded **Pretreatment:**

Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Up to 5 grams of a cream containing 2.5% prilo-caine and 2.5% lidocaine were applied to participants in the TA group ,who were then asked to rest as the anaesthesia took effect. ● *Dose*: 5 grams of a cream containing 2.5% prilo-caine and 2.5% lidocaine ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: Participants assigned to the IA group underwent dorsal penile nerveblock with a penile shaft ring block, using 1% lidocaine without epinephrine ● *Dose*: 1% lidocaine without epinephrine ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	*Styrelsen for Patientsikkerhed Britta Bjerrum Mortensen* on 08/10/2019 20:42 **Select** Kirsten: Suppl. - klik på link i View Fulltext *Britta Tendal* on 15/10/2019 16:45 **Select** Raw data available

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "IA during their ShangRing circumcision. We used age stratified block randomisation with varying block sizes in a 2:1 ratio (TA:IA). The random allocation sequence was computer generated by a researcher unaffiliated with the study. In each treatment group, we" Judgement Comment: Computer generated.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Computer generated by a researcher unaffiliated with the study. Not described
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: One group received topical and the other injectable anaesthesia. Not possible to blind personnel
Blinding of outcome assessment (detection bias)	High risk	Quote: "are shown in Table 1. The primary outcome measure was pain, as reported by participants, at various points around the time of circumcision. We used the 11-point visual analogue scale that ranged from 0 = no pain to 10 = worst pain possible. Secondary outcomes included procedure time," Judgement Comment: self-reported pain
Incomplete outcome data (attrition bias)	High risk	Quote: "total of 16 participants were lost to follow-up; 12 (5.3%) in the TA and 4 (3.4%) in the IA group." Judgement Comment: Reasons for loss to follow up not stated.
Selective reporting (reporting bias)	Low risk	Judgement Comment: Outcome as reported in protocol. Protocol at clinicaltrials.gov
Other bias	Low risk	Judgement Comment: The study seem to be free from other sources of bias

Benini 1993

Methods	RCT
Participants	28 male NB; FT; BW > 2500g; 5 min Apgar > 7; < 7 d age
Interventions	0.5 ml (0.5g) LP cream (n=14) 0.5 ml (0.5 g) petroleum jelly (n=14) applied and covered with occlusive dressing 45 - 60 min prior
Outcomes	HR, O2sat, % time crying, facial action

Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only stated the newborns were randomized. No information about sequence generation
Allocation concealment (selection bias)	Unclear risk	No information about allocation concealment.
Blinding of participants and personnel (performance bias)	Unclear risk	No information about blinding of specific personnel or parents. The application of EMLA or sterile petroleum jelly described (but not who applied) and likely the pediatrician were blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Blinded outcome assessor evaluating facial expressions and crying. Cyring was recorded usind a microphone.
Incomplete outcome data (attrition bias)	Low risk	One newborn excluded post follow up.
Selective reporting (reporting bias)	Low risk	No protocol however relevant and thorough outcomes reported
Other bias	Low risk	No reasons to suspect other sources of bias.

Beyaz 2011

Methods	RCT
Participants	50 male children DPNB, n=23, age: 8.5yr (SD:3.5) Caudal, 0.5 ml/kg.), n=24, 7.4yr (SD:3.1)
Interventions	DPNB (0.25% levobupivacaine, 0.5 ml/kg.) Caudal block (0.25% levobupivacaine, 0.5 ml/kg.)
Outcomes	Flacc Pain Scale, analgesic amounts, times, and probable local or systemic complications were recorded.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Patients were randomized by the closed-envelope technique into 2 groups."
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Patients were randomized by the closed-envelope technique into 2 groups."
Blinding of participants and personnel (performance bias)	Unclear risk	SUPPORTING ANNOTATIONS: "Drug solutions were prepared by another anesthetist." COMMENTS: "No information about blinding." COMMENTS: "No information about blinding."
Blinding of outcome assessment (detection bias)	High risk	SUPPORTING ANNOTATIONS: "In the recovery room, all children were observed and recorded for pain, sedation, and side effects (nausea, vomit, agitation, penile hematoma, bleeding, motor block, urinary retention) at 5, 15, and 30 minutes. Then, the children were transferred to wards. They were observed and recorded for the same parameters at 1, 3, and 6 hours." COMMENTS: "No information who monitored the outcomes nor how in terms of blinding."
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "Two patients in group 1 and 1 patient in group 2 were excluded from the study." COMMENTS: "Excluded due to need of extra analgesic Rx."
Selective reporting (reporting bias)	Unclear risk	COMMENTS: "No protocol however. Outcomes marginally reported (Fig. 1 and 2 identical?) Not reffering to a protocol but report on relevant outcomes"
Other bias	Low risk	COMMENTS: "No reasons to suspect other sources of bias."Other bias

Blass 1991 A

Methods	RCT
Participants	30 male NB, FT; 28 - 54 h age; Apgars > 8
Interventions	1.5 ml 24% sucrose by nipple 1.5 ml water by nipple no treatment control *comparison is sucrose versus water (placebo) number subjects per group not specified 3 min WT after intervention
Outcomes	% time crying
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in details. Each infant was randomly assigned to a treatment condition (water vs sucrose) and brought in his or her own bassinet to a quiet corner of the nursery for testing
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (performance bias)	Low risk	everal bottles of sterile water or 24% sucrose solution were prepared daily and marked to ensure that neither experimenter nor physician knew of their contents.An experi- enced nurse who was unaware of infant treatment then collected blood in her usual manner using standard methods of heel lancing. Likely relevant personnel were blinded.
Blinding of outcome assessment (detection bias)	Low risk	Trained research assistants who were unaware of syringe contents scored the videotapes and meas- ured crying duration during blood collection and the immediate 3-minute recovery period. Crying was defined as audible crying vocalizations. An experi- enced nurse who was unaware of infant treatment then collected blood in her usual manner using standard methods of heel lancing. Trained research assistants who were unaware of syringe contents scored the videotapes and meas- ured crying duration during blood collection and the immediate 3-minute recovery period. Crying was defined as audible crying vocalizations. There was virtually no disagreement among coders in recognizing crying Outcome assessors were likely blinded.
Incomplete outcome data (attrition bias)	Unclear risk	No information
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcomes.
Other bias	Low risk	The study seems free of other sources of bias

Blass 1991 B

Methods	RCT
Participants	30 male NB, FT; 28 - 54 h age; Apgars > 8
Interventions	1.5 ml 24% sucrose by nipple 1.5 ml water by nipple no treatment control *Comparison is sucrose versus no treatment number subjects per group not specified 3 min WT after intervention
Outcomes	% time crying
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	See Blass 1991 A
Allocation concealment (selection bias)	Unclear risk	See Blass 1991 A
Blinding of participants and personnel (performance bias)	Low risk	See Blass 1991 A
Blinding of outcome assessment (detection bias)	Low risk	See Blass 1991 A
Incomplete outcome data (attrition bias)	Unclear risk	See Blass 1991 A
Selective reporting (reporting bias)	Low risk	See Blass 1991 A
Other bias	Low risk	See Blass 1991 A

Bramwell 1982

Methods	RCT
Participants	90 inpatients aged 1-12 years having elective circumcision. Exclusions: caudal contra-indicated e.g. spina bifida, local sepsis. Setting: UK
Interventions	CAUDAL versus PARENTERAL Caudal (n = 46) 0.25% bupivacaine 0.5 ml/kg up to 40 ml (0.1875% used for volumes over 40 ml). Parenteral analgesia (n = 45): Dihydrocodeine 1 mg/kg IM after induction of anaesthesia and prior to surgery.
Outcomes	Pain: Two 8-cm linear analogue scales were marked by a nurse every 5 minutes for 30 minutes and then every 15 minutes for the next 90 minutes, indicating the patient's level of pain from none to severe and level of consciousness (unrousable to alert), respectively. Rescue analgesia (dihydrocodeine 1mg/kg) was administered in the first 2 hours after surgery as needed at the nurses' discretion. Other outcomes: Vomiting, drinking, administration of analgesics and weakness.

Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Each patient was allocated by random numbers to the analgesic or to the caudal group. The two groups were similar in age and weight
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	No information on blinding of participants and personnel
Blinding of outcome assessment (detection bias)	High risk	Ithough the chart did not show which analgesic the patient had received, this information was available on the ward so that any complication could have been dealt with quickly.The nursing staff had participated in the design of this chart and had been instructed in its use.
Incomplete outcome data (attrition bias)	Unclear risk	statistical calculations were based on the true number of readings.COMMENTSIt is not stated how many were excluded from analysis due to the nurse allocated elsewhere. Per protocol analysis.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol, but report on relevant outcomes
Other bias	Low risk	No reasons to suspect other sources of bias.

Butler O'Hara 1998

Methods	RCT
Participants	50male infants inNICU; >/= 34.5 weeks (post-menstrual) at time of circumcision and stable for discharge participants were 3 -105 days age at time of circumcision
Interventions	0.5 ml (0.5g) LP cream (n=25) 0.7 - 1.0 ml lidocaine DPNB + placebo cream (n=25) creams applied 60 min prior and covered with occlusive dressing 3 min WT after DPNB
Outcomes	HR; RR; NIPS score (primary outcome)
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computerized randomization was performed by a randomized number generator in blocks of 10.
Allocation concealment (selection bias)	Unclear risk	Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	to assure that the bedside nurse remained blinded to group assignment, every infant had a cream and dressing applied to the penis 1 hour before the circumcision.
Blinding of outcome assessment (detection bias)	Low risk	the videotapes were then reviewed by a second individual (C.L.) unaware of the in- fant's experimental group assignment. NIPS scores were assigned for each of the six events on all 44 randomized.
Incomplete outcome data (attrition bias)	Low risk	4 infants were excluded from the EMLA group and 2 infants from the DPNB due to technical difficulties with the recording equipment.
Selective reporting (reporting bias)	Low risk	No reference to study protocol, but appears to report on all outcomes of interest
Other bias	Low risk	The study appears to be free from other sources of bias

Canakci 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 6.05±13.1 years ● *Duration of surgey*: 20.7±3.5 min ● *Anesthesia duration* : intervention 2 ● *Age*: 9.62±11.6 years ● *Duration of surgey*: 19.5±2.5 min ● *Anesthesia duration* : kontrol 1 ● *Age*: 8.82±7.6 years ● *Duration of surgey*: 19.8±3.1 min

	● *Anesthesia duration* : kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** ASA I physical status without any additional disorders **Excluded criteria:** Children or parents who did not accept our analgesia techniques when explained to them were excluded. Likewise,those who also had some additional urological problems such as paraphimosis reduction, hypospadias repair, epispadias repair, undescended testicles surgery; and who were planned to be operated for those reasons and to be circumcised at the same time were al so excluded. And so were patients who had allergy against localanaestheticsoropioidsorthosewithatendencytohaveallergies.AlsoexcludedwerechildreninASAII/IIIphysicalstatussufferingfromadditionaldisorderssuchaschildhoodasthma,diabetes,epilepsy, liverdisease, congenital hear tdiseaseetc.;children who had bleeding, coagulation disorders or haematological problems such as anaemia; morbidly obese children with body weight above the 90th percentile according to the percentile curves; children diagnosed with growth development retardation under the 3rd percentile according to the percentile curves; children diagnosed with some additional endocrinological problems;children who were followed by a paediatric psychiatrist and taking medication for any mental health problem like attention deficit hyperactivity syndrome,depression etc.;children with neurological,neuromuscula rdisorders;and children out side the 6-12age bracket. **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: group M: Following standard general anaesthesia, 100mcg/kg of subcutaneous morphine was injected into the deltoid muscle by means of a 26-gauge insulin needle. ● *Dose*: 100 mcg/kg ● *Duration*: ● *Follow-up time*: 24 hours postoperative intervention 2 ● *Description*: dorsal penile nerve block with 1mg/kg of bupivacaine 0.25% ● *Dose*: Injecting bupivacaine 0.25% in 1mg/kg dose (maximum upper limitis 50mg) ● *Duration*: ● *Follow-up time*: 24 hours postoperative kontrol 1 ● *Description*: Group C: caudal block with bupivacaine 0.25% in a total volume of 0.50ml/kg in lateral position ● *Dose*: Bupivacaine 0.25% of 0.5 ml/kg volume in 1mg/kg dose (maximum 50mg, 20cc volume) was administered by the anaesthesiologist into the sacral hiatus by means of a 22-gauge caudal needle. ● *Duration*: ● *Follow-up time*: 24 hours postoperative kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The selected sample was randomised into 3 equal groups: DP, C and M. All the" Judgement Comment: Sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Allocation concealment not described
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Not possible to blind personnel
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: All cases included in analysis. Loss to follow up not described
Selective reporting (reporting bias)	Low risk	Judgement Comment: Not reffering to a protocol, however it seems like the report on all relevant outcome
Other bias	Low risk	Quote: "Conflict of Interest: None." Judgement Comment: The study seems to be free from other sources of bias

Concha 1994

Methods	RCT
Participants	40 boys, mean age 4.7 years in caudal group and 5.6 years in fentanyl/rectal acetaminophen group, undergoing day surgery for circumcision. Setting: Chile
Interventions	CAUDAL versus RECTAL/IV Caudal: 0.25% bupivacaine 0.5 ml/kg (n = 20). Rectal/IV: Fentanyl 2 ug/kg IV after induction, and rectal acetaminophen 15 mg/kg (n = 20), repeated during 6 postoperative hours. All children received the same general anaesthetic.
Outcomes	Episodes of nausea and vomiting, passing of urine, quality of pain relief on a visual analogue scale, all measured by anaesthetist. Extra dose of acetaminophen given at anaesthetist's discretion.
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear (Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005)
Allocation concealment (selection bias)	Unclear risk	Unclear (Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005)
Blinding of participants and personnel (performance bias)	Unclear risk	Cited from Cyna et al. 2008: "In both White 1983 and Concha 1994 an anaesthetist assessed the need for analgesia postoperatively and was apparently blinded to the technique, however it is unclear as to whether the patients (or parents) were aware of the type of analgesia used." (Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005)
Blinding of outcome assessment (detection bias)	Unclear risk	Cited from Cyna et al. 2008: "In both White 1983 and Concha 1994 an anaesthetist assessed the need for analgesia postoperatively and was apparently blinded to the technique, however it is unclear as to whether the patients (or parents) were aware of the type of analgesia used." (Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005)
Incomplete outcome data (attrition bias)	Unclear risk	Not reported. No ITT. (Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005)
Selective reporting (reporting bias)	Unclear risk	Unclear
Other bias	Unclear risk	Unclear

Dixon 1984

Methods	
Participants	31 male NB, FT, AGA, < 7 days age, > 2500 gm, 5 min Apgar > 7
Interventions	0.8 ml lidocaine DPNB (n=15) 0.8 ml saline DPNB (n=8) no treatment control (n=8) 4 - 5 min WT
Outcomes	Brazelton Neonatal Assessment Scale
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	

Other bias	Unclear risk	

Dostbil 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 7.9±2.1 ● *Duration of surgey*: 24.6±4.2 ● *Anesthesia duration* : intervention 2 ● *Age*: 7.8±1.9 ● *Duration of surgey*: 25.5±4.9 ● *Anesthesia duration* : kontrol 1 ● *Age*: 8.0±1.9 ● *Duration of surgey*: 25.5±5.3 ● *Anesthesia duration* : kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** Two hundred and forty patients who were between the ages of 5 and 12 years, of American Society of Anesthesiologists class 1 to 2 and scheduled for circumcision were included in the study **Excluded criteria:** Patients who had severe systemic disease, a previously known neurologic or spinal disease, bleeding diathesis, amide-type local anaesthetic allergy, local skin site infection, family history of postoperative nausea and vomiting (POnV) or motion sickness, or chronic upper airway obstruction and habitual snoring, were excluded from the study **Pretreatment:** No differences at baseline
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: The sacral hiatus was located using an aseptic technique, and a 25-gauge needle advanced approximately 3 to 4 mm into the epidural space. After the negative aspiration of blood or cerebro-spinal fluid, 0.125% levobupivacaine (volume 0.5 ml/kg) was injected, with the addition of 7.5, 10 or 15 μg/kg morphine ● *Dose*: 7,5 μg/kg morphine ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: The sacral hiatus was located using an aseptic technique, and a 25-gauge needle advanced approximately 3 to 4 mm into the epidural space. After the negative aspiration of blood or cerebro-spinal fluid, 0.125% levobupivacaine (volume 0.5 ml/kg) was injected, with the addition of 7.5, 10 or 15 μg/kg morphine ● *Dose*: 10 μg/kg morphine ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: The sacral hiatus was located using an aseptic technique, and a 25-gauge needle advanced approximately 3 to 4 mm into the epidural space. After the negative aspiration of blood or cerebro-spinal fluid, 0.125% levobupivacaine (volume 0.5 ml/kg) was injected, with the addition of 7.5, 10 or 15 μg/kg morphine ● *Dose*: 15 μg/kg morphine ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	*Jeanett Rohde* on 23/10/2019 18:18 **Select** Er det ok at populationen er Two hundred and forty patients who were between the ages of 5 and 12 years, of AmericanSociety of Anesthesiologists class 1 to 2

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "This randomised, double-blind, three-arm con- trolled clinical trial" Quote: "Patients were divided into three equal groups according to the random- isation list created using a computer-based random- isation program." Judgement Comment: Computer-generated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Allocation concealment not described
Blinding of participants and personnel (performance bias)	Low risk	Quote: "After loss of consciousness, children were placed in the lateral position and caudal block was performed by one of two anaesthetists experienced in this field, who did not know which caudal study solution was used." Judgement Comment: Personnel and patients were blinded
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The pain scores of each child were assessed by an independent blinded observer using the Wong-Baker FACeS Pain rating Scale from 0 to 5 (0=no pain, 1=hurts a little bit, 2=hurts a little more, 3=hurts even more, 4=hurts a whole lot, 5=hurts worst) 7. This scale was also explained to the family or guardian of the child so that observations could be continued at home." Judgement Comment: Pain was obtained by a blinded observer.
Incomplete outcome data (attrition bias)	Low risk	Quote: "All patients completed the study and there were no significant differences between groups in terms of age, weight and duration of surgery" Judgement Comment: I flowchartet er der dog 1 patient, der falder fra i "Group 7,5", og 2 patienter falder fra i "Group 10" på grund af "protocol violations".
Selective reporting (reporting bias)	Low risk	Judgement Comment: Not possible to check registration but relevant outcomes are reported
Other bias	Low risk	Judgement Comment: The study seem to be free from other sources of bias

Garry 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 (DPNB group) ● *Age*: 39.3 weeks (SD: 1.0) ● *Duration of surgery*: ● *Anesthesia duration*: Intervention 2 ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: Control 1 ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: Control 2 (Lidocaine-prilocaine) ● *Age*: 39.2 weeks (SD: 0.89) ● *Duration of surgery*: ● *Anesthesia duration*: Overall ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: **Included criteria:** Over a 3-week period, 18 term male newborns were recruited forstudy participation after parental consent was obtained for avideotaped circumcision **Excluded criteria:** viewing process might have been a potential confounding variable.Exclusion criteria for the newborns were a gestational age <37weeks, any contraindication to circumcision, use of sedative or painmedication, and parental refusal to participate. **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Group 1 was six newborns undergoing circumcisionafter a dorsal penile nerve block.The dorsal penile nerve block was performed with0.3 – 0.5 ml of 1% lidocaine injected at 2 and 10 o'clock positionsat the base of the penis 5 min before the procedure. ● *Dose*: 0.3 – 0.5 ml of 1% lidocaine injected ● *Follow-up time*: Intervention 2 ● *Description*: Group 2 was six newbornsundergoing circumcision after topical lidocaine – prilocaine.A topicalmixture of lidocaine (2.5%) and prilocaine (2.5%) cream (EMLAanesthetic cream, AstraZeneca Pharmaceuticals, Wilmington, DE,USA) was applied to the shaft of the penis with an occlusivedressing 1 h before the procedure.

	● *Dose*: lidocaine (2.5%) and prilocaine (2.5%) cream ● *Follow-up time*: Control 1 ● *Description*: Group3 was six newborns undergoing a sham procedure with threehaving dorsal penile nerve block and three having topicallidocaine – prilocaine.A sham procedure was administration of anesthesia with theusual draping followed by gentle manipulation with touch and nocircumcision performed. The neonates undergoing the shamprocedures had the circumcision performed immediately after thevideotaping was completed. A randomized listing was followed fordetermination of the sham procedure versus the actualcircumcision. ● *Dose*: ● *Follow-up time*: Control 2 ● *Description*: ● *Dose*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "with the circumcision procedure. Methods The study was a prospective, randomized, reviewer blinded comparison of anesthetic methods used in neonatal male circumcision. The Institutional Review Board approved" Judgement Comment: Not described in details how sequence generation was perfomed
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information of concealment of the allocation sequence
Blinding of participants and personnel (performance bias)	High risk	Quote: "1 h before the procedure. A sham procedure was administration of anesthesia with the usual draping followed by gentle manipulation with touch and no circumcision performed. The neonates undergoing the sham procedures had the circumcision performed immediately after the videotaping was completed. A randomized listing was followed for determination of the sham procedure versus the actual circumcision. This divided the neonates into" Judgement Comment: No blinding of participants and personel
Blinding of outcome assessment (detection bias)	Low risk	Evaluater was blinded
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No missing data
Selective reporting (reporting bias)	Low risk	Judgement Comment: No protocol available, no signs of selective reporting
Other bias	Low risk	Judgement Comment: The study apperas to be free of other sources of bias

Gauntlett 2003

Methods	RCT
Participants	60 boys aged 1 to 10 years undergoing elective circumcision. Exclusions: contraindications to either type of block or parental inability to assess pain scores.
Interventions	CAUDAL versus DNBP Caudal (n = 30) 0.5 ml/kg bupivacaine 0.15% with ketamine 0.5 mg/kg: DNBP (n = 30); bupivacaine 0.5%, 3-5 ml according to age. Children were not premedicated other than with EMLA cream applied to the back of their hands. GA: IV propofol or inhalation of sevoflurane in nitrous oxide and oxygen as clinically appropriate. Anaesthetic maintenance was with nitrous oxide, oxygen and sevoflurane. All local anaesthetic procedures were performed by one experienced paediatric anaesthetist. Children were not premedicated other than with EMLA cream applied to the dorsum of both hands.
Outcomes	Rescue analgesia (as time to paracetamol - could not be used in meta-analysis, number of failed blocks used to measure this) Failed blocks Motor weakness (scale of 0-4) Nausea and vomiting (including severe PONV) Eating disturbance Sleep disturbance Behavioural disturbance Urinary retention
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	After induction of anaes- thesia, patients were randomly allocated into one of two groups.Sequence generation not clearly described
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Personnel was not blinded
Blinding of outcome assessment (detection bias)	Low risk	Parents and ward nurses were blinded to which of the blocks the boys received by small spot dressings applied below the symphysis pubis and over the sacrococcygeal membrane, to conceal the injection site. Parents were asked not to disturb the dressing for 24 h. They were told that the local anaesthetic may cause some motor weakness, and the nurses on the paediatric day ward were instructed not to discuss any details of the two kinds of block with parents.
Incomplete outcome data (attrition bias)	Unclear risk	there were three failed blocks in the caudal group and none in the DNB group. These were excluded from subsequent analysis. For one child in the caudal group, the time taken to first dose of paracetamol was recorded on the data chart incorrectly (the time recorded was earlier than the time the block was given), and his data set was excluded from analysis of time to first analgesia There were three failed blocks in the caudal group and none in the DNB group. These were excluded from subsequent analysis. For one child in the caudal group, the time taken to first dose of paracetamol was recorded on the data chart incorrectly (the time recorded was earlier than the time the block was given), and his data set was excluded from analysis of time to first analgesia
Selective reporting (reporting bias)	Low risk	No protocol (no heart rate, oxygen saturation)
Other bias	Low risk	The study seems to be free from other sources of bias

Gulec 2015

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : intervention 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 1 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** 60 ASA physical status I-II children, aged between 3 and 9 years, undergoing circumcision operations under sedation were recruited according to a randomize and double-blind institutional review board-approved protocol. **Excluded criteria:** Patients with clinically significant neurological, respiratory, cardiovascular and psychiatric diseases were excluded from the study **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: mixture of midazolam 0.05 mg/kg+ketamine3mg/kg+atropine 0.02mg/kg intra muscular lyinthe presence of parents in the pre-operative holding area. Patients were induced with propofol---ketamine in Group I ● *Dose*: ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:

	kontrol 1 ● *Description*: mixture of midazolam 0.05 mg/kg+ketamine3mg/kg+atropine 0.02mg/kg intra muscular lyinthe presence of parents in the pre-operative holding area. Patients were induced ketamine alone in Group II. ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	*Jeanett Rohde* on 16/10/2019 16:32 **Select** Population: physical status I---II children

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomized into two groups via sealed envelope assignment."
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomized into two groups via sealed envelope assignment. Both groups"
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Double-blinded and the knowledge of the intervention is not likely to influence (measured) outcomes
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Double-blinded and the knowledge of the intervention is not likely to influence (measured) outcomes
Incomplete outcome data (attrition bias)	Unclear risk	Judgement Comment: Insufficient information on missing data
Selective reporting (reporting bias)	Low risk	Judgement Comment: No reference to study protocol, but appears to report on outcomes of interest
Other bias	Low risk	Quote: "The authors declare no conflicts of interest." Judgement Comment: The study appears to be free from other sources of bias

Haliloglu 2013

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Randomization was performed by NCSS software from a single centre."
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	COMMENTS: Unclear if personnel were blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "CHEOPS scores were measured by a single nurse at each hospital. Physicians performing the penile or caudal block were not involved in CHEOPS score measurement."
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "159 patients were evaluated. <b>Seven patients were excluded from the study. In 4 of these patients cardiac arrythmia was observed during anesthesia induction and their circumcisions were postponed. In the other 3 patients laryngeal spasm developed after the procedure and as anesthesia resolution was delayed in these patients, their pain scoring was tought to have been effected so they were excluded."
Selective reporting (reporting bias)	Low risk	COMMENTS: No protocol, however stated primary and secondary outcomes reported. Still limited reporting, as they inlude no variations (SD/SEM/CI)
Other bias	Low risk	COMMENTS: No reasons to suspect other sources of bias

Hardwick Smith 1998

Methods	RCT
Participants	40 male NB; FT; Apgar >/= 7; 6 hr - 5 days age; fasting 30 -120 min prior; normal exam
Interventions	1.0 ml 5% lidocaine RB (n=20) no treatment control (n=20) 3 min WT
Outcomes	HR; RR; O2sat; behavioral state; cry time
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Infants were comparable in terms of demographic data (Table 1), fasting time, baseline vital signs, and behav- ioral state (Table 2). There was no significant difference in the procedure duration with or without anesthesia (10.43 1.29 minutes for the anesthetized group versus 9.7 1.05 minutes for controls).newborns undergoing circumcision were assigned. randomly through drawing of cards to receive either ring block (n 20) or no anesthesia (n 20). Admission criteria included 37– 42
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	ing block then was performed by a single oper- ator using 1 mL of 0.5% lidocaine without epinephrine, delivered subcutaneously and circumferentially at the base of the penis with a 25-gauge needle (Figure 1). After a 3-minute waiting period, circumcision was performed by the same operator using a Gomco clamp.
Blinding of outcome assessment (detection bias)	Unclear risk	ndices of perceived pain including behavioral state, heart rate, respiratory rate, and oxygen saturation were recorded by one of several trained assistants at baseline (2 minutes after monitors were applied), at ten intervals during the procedure, and 2 hours postoperatively.Eight observ- ers assigned behavioral states to the recorded infants,Heart and respiratory rates were monitored continu- ously using an apnea-bradycardia monitor
Incomplete outcome data (attrition bias)	Low risk	During certain portions of the procedure, oxygen saturation was not recorded in up to 50% of the infants. A trend toward greater oxygen desaturation in the control group was present.COMMENTSLikely no deviations or drop outs from groups.
Selective reporting (reporting bias)	Low risk	No protocol. Apparently thorough outcome reporting.
Other bias	Low risk	No reasons to suspect other sources of bias.

Herschel 1998

Methods	RCT
Participants	120 male NB; FT; > 2500g; Apgar >/= 8 at 5 min; >/= 12 hr age
Interventions	0.8 ml 1% lidocaine DPNB (n=40) 10 ml 50% oral sucrose via nipple (n=40) no treatment control (n=40) 3 min WT for DPNB; 2 min WT for sucrose group
Outcomes	HR; O2sat (%)
Notes	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Allocation concealment (selection bias)	High risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of participants and personnel (performance bias)	High risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Blinding of outcome assessment (detection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Incomplete outcome data (attrition bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Selective reporting (reporting bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Other bias	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Holliday 1999

Methods	RCT
Participants	50 male preterm/low birthweight NICU patients, subjects weighed 1600 to 2500g at time of circumcision 25-27 days age, 36 week GA at circumcision
Interventions	0.8 ml 1% lidocaine DPNB + placebo cream (n= 19) LP cream (n=12) (group enrollment stopped, excluded from data analyses) placebo cream (n=19) DPNB 5 min WT cream applied 1 hr prior and covered with occlusive dressing
Outcomes	HR, RR, O2sat, systolic BP, behavioral score, serum B-endorphin
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	After informed consent was obtained, infants were randomized, using randomization tables, to the DPNB, EMLA, or control group.
Allocation concealment (selection bias)	Unclear risk	Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	To maintain the blinded nature of the study, the DPNB and control groups received placebo (acid mantle) cream and the EMLA group received EMLA cream.COMMENTSVery likely relevant personnel are blinded
Blinding of outcome assessment (detection bias)	Low risk	The investigator (M.H. or S.K.) monitoring the infant's physi- ologic variables and behavior was not present during ap- plication of the placebo or EMLA cream or during admin- istration of the DPNB injection.COMMENTSVery likely outcome assessors were blinded.
Incomplete outcome data (attrition bias)	Unclear risk	the institutional review board requested discon- tinuation of EMLA enrollment, and the study contin- ued with only the DPNB and control groups. Because of the small number of patients in the EMLA group, no meaningful statistical comparisons could be made, and these patients were excluded from further analysis.COMMENTSNo analysis of the effect of not analysing the group excluded. Likely all outcome data are available for the remaining groups.
Selective reporting (reporting bias)	High risk	No reference to study protocol, but appears to report on outcomes of interest No protocol available. Post hoc exclusion of one intervention group. Unclear reporting of outcomes in terms of assessing effect size and varians.
Other bias	Low risk	The study appears to be free from other sources of bias

Holve 1983

Methods	RCT
Participants	31 male NB; FT, < 7 days age, > 2500 gm, 5 min Apgar > 7
Interventions	0.8 ml 1% lidocaine DPNB (n=15) 0.8 ml saline DPNB (n=8) no treatment control (n=8) 4-5 min WT
Outcomes	HR; % time crying per interval; clinical observation of anesthesia effectiveness (good, fair, poor)
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	controlled, double-blind investigation wasSubjects were assigned to one of three groups by use of a random numbers table.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Operations were performed in a relatively isolated area of the newborn nursery. A single physician did all circumcisions using a Gomco bell and clamp. Two researchers were present at each procedure and were blind as to which subjects had DPNB with lidocaine versus saline, but they were aware of which infants did not receive any injection. All other researchers remained completely blind to infant group assignment until the end of the study.
Blinding of outcome assessment (detection bias)	Low risk	The two researchers who were present at each cir- cumcision observed infant response to operative pro- cedures and together categorized each newborn as having &dquo;good&dquo; (minimal to no crying or signs of dis- tress), &dquo;fair&dquo; (slightly more agitation), or &dquo;poor&dquo; an- esthetic effect (significant agitation and distress). Heart rate and crying data were analyzed by a member of the research team who was not present at the circum- cisions and who was blind to infant group assignment.
Incomplete outcome data (attrition bias)	Unclear risk	Follow-up data at 1 to 2 months of age were obtained on 23 of the 31 subjects. Eight subjects were not brought back for follow-up appointments and could not be reached by telephone.All infants randomized in this study are included in this report.COMMENTSNo analysis done to evaluate the impact of the failure to analyse the participants in the group they were allocated.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcoms
Other bias	Low risk	seems free of other sources of bias

Howard 1994

Methods	RCT
Participants	44 male NB, healthy, AGA, FT, Apgars > 7, >/= 24 h age
Interventions	acetaminophen 15 mg/kg/dose (n= 23) placebo (n= 21) given 2 hr prior and q 6H X 24 hr following Infants were brought to a quiet room near the nursery. They were placed on the Circumstraint (Olympic Medical Co, Seattle, Wash) board, and their legs were restrained. A nurse held the infants' arms in flexion on the chest, and all infants were offered pacifiers. Infants were allowed to settle for up to 5 minutes before data collection was begun.
Outcomes	HR; RR; cry time; post-operative comfort score; feeding behavior pre/post
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Using a computer-generated random number list, neonates were randomized to either an acetaminophen or placebo group.
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Low risk	All nurses and physicians involved in the study were blinded to the group assignments.
Blinding of outcome assessment (detection bias)	Low risk	All nurses and physicians involved in the study were blinded to the group assignments. Two of the authors (C.R.H. and F.M.H.), both blinded to in- fants' circumcision status, performed a pilot test of the Postopera- tive Comfort Score in a group of 55 well, full-term newborns, 15 of whom were postcircumcision. Intraobserver reliability for this in- strument was r = .90, and interobserver reliability was r = .85. A comfort score of <16 from <1 hour to 70 hours postcircumcision identified neonates who had undergone circumcision with a posi- tive predictive value of 85%, a sensitivity of 73%, and specificity of 96%. In the subgroup of circumcised neonates, a score of <16 predicted with 85% sensitivity and 100% specificity those neonates who were <24 hours postcircumcision. Interobserver reliability was reverified (r > .90) in the later half of the current study in a subgroup of 13 neonates. Feeding behavior was evaluated before
Incomplete outcome data (attrition bias)	Unclear risk	Drop outs not reported
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol, but report on relevant outcomes
Other bias	Low risk	The study seems to be free from other sources of bias

Howard 1999

Methods	RCT
Participants	62 male NB; healthy; AGA; FT

Interventions	1g LP cream + 0.8 ml saline DPNB (n=31) 0.8 ml 1% lidocaine DPNB + 1g placebo cream (n=31) 4 min WT for DPNB creams applied 1 hr prior and covered with occlusive dressing
Outcomes	HR; RR; behavioral distress score
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Parental informed consent was obtained. <b>Infants were randomized in a double-blind fashion to 1 of 2 study groups according to a random number list maintained in the hospital pharmacy. A total of 62 in- fants were randomized
Allocation concealment (selection bias)	Low risk	Pharmacy personnel responsible for randomization and the application and dispensing of medications had no other responsibilities in this study. The list was maintained in the hospital pharmacy
Blinding of participants and personnel (performance bias)	Low risk	One hour before the procedure and in accord with study group assignment, a pharmacy research nurse ap- plied 1 g of either a placebo or EMLA cream to the distal half of the infant's penis. 19 The cream was then covered with an occlusive dressing. The placebo cream was se- lected to resemble EMLA cream as nearly as possible. Prefilled tuberculin syringes containing either sodium chloride solution or 1% lidocaine without epinephrine. Personnel performing the surgery were blinded. Both groups had DPNB and the surringes were masked.
Blinding of outcome assessment (detection bias)	Low risk	A single observer (C.tH.), blinded to study group assignment and trained in Brazelton behavioral state assessment, reviewed each tape and assigned dis- tress scores. Behavioural distress was assessed by a blinded observer. It is not clear who assessed the heart rate or respiratory rate.
Incomplete outcome data (attrition bias)	Low risk	A total of 62 in- fants were randomized; however, only 60 infants com- pleted the protocol. Before the procedure, tachypnea de- veloped in 1 infant and another infant's parents withdrew permission for study participation. 60 infants completed the protocol.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol
Other bias	Low risk	The study seems to be free from other sources of bias.

Joyce 2001

Methods	RCT
Participants	23 male NB, FT; 5 min Apgar > 7; BW > 2500 g; age < 7 d
Interventions	LP cream (1 - 2 g) + music (n=6) LP cream + no music (n=5) placebo cream + music (n=7) placebo cream + no music (n=5) cream applied 1 hr prior and covered with occlusive dressing music started just prior to procedure and continued to 10 min post procedure
Outcomes	HR, O2sat, cry duration; RR, Riley Infant pain scale, salivary cortisol, infant state
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomized, researcher-blinded study was conducted in the newborn nursery of a large Midwest city hospi- tal.Twenty-three male neonates were ran- domly assigned to the study groups us- ing a random numbers table.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Acid Mantle cream, (Doak Dermatologies, Bradley Pharma- ceuticals, Inc, Fairfield, NJ), which is similar in appearance to EMLA but is inert with no active properties, was used as the placebo cream. To control for variability in the dose of EMLA, both the EMLA and placebo creams were drawn into syringes prior to ap- plication. Nurses were instructed to apply the entire contents of the syringe using a standard protocol. The syringes were labeled A and B, and data collec- tors did not know which was EMLA and which was placebo cream. Likely participants and personnel were blinded.
Blinding of outcome assessment (detection bias)	Low risk	To allow for blinded ratings of pain intensity, the procedure was recorded on videotape with the following pre- cautions taken to ensure blinded con- ditions: (a) a placebo cream similar to EMLA in appearance was applied to the penis for the control conditions; (b) observational data were obtained from the videotapes by research assistants who were not present during the pro- cedure and who were blinded to the type of cream applied; and (c) blank compact discs were played for neo- nates in control conditions, allowing for the same sequencing of activities

		to provide the appearance of audio stim- ulation for all neonates. the syringes were labeled A and B, and data collec- tors did not know which was EMLA and which was placebo cream." Likely the outcome assessors were blinded. Pain subjective assessed and HR and OS objectively assessed
Incomplete outcome data (attrition bias)	Unclear risk	No information
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol.
Other bias	Unclear risk	No reasons to suspect other sources of bias

Karasu 2018

Methods	RCT
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Kass 2001

Methods	RCT
Participants	71 healthy male NB
Interventions	lidocaine DPNB (n=24) 2ml D50W orally (n=23) 2 ml H2O orally (n=24) WT 2 to 6 min
Outcomes	time cry (primary outcome); HR; O2sat ; modified behavioral pain scale
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The infants were randomized (by computer modeling) to 1 of the 3 arms of the study. Despite baseline imbalances in time since last fed and heart rate the randomization was likely successfully performed.
Allocation concealment (selection bias)	Unclear risk	No information about allocation concealment before the procedures.
Blinding of participants and personnel (performance bias)	High risk	The base of the penis in all patients was covered with a sterile 2 × 2 gauze pad secured with tape to obscure evidence of a DPNB.
Blinding of outcome assessment (detection bias)	Low risk	The base of the penis in all patients was covered with a sterile 2 × 2 gauze pad secured with tape to obscure evidence of a DPNB. Likely blinded outcome assessors.
Incomplete outcome data (attrition bias)	Low risk	No information about attrition. Likely no missing outcome data.
Selective reporting (reporting bias)	Low risk	No protocol however, primary and secondary outcomes clearly stated and similar reported.
Other bias	Low risk	No reasons to suspect other sources of bias.

Kaufman 2002

Methods	RCT
Participants	57 NB; healthy; male; FT; Apgar > 7 at 5 min
Interventions	Mogen + water pacifier (15) Mogen + 24% sucrose pacifier (n=14) Gomco+ water pacifier (n=14) Gomco + 24% sucrose pacifier (n=14)
Outcomes	time crying; grimacing, procedure length Notes

Notes	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Allocation concealment (selection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of participants and personnel (performance bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of outcome assessment (detection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Incomplete outcome data (attrition bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Selective reporting (reporting bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Other bias	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

KazakBengisun 2012

Methods	RCT
Participants	Cadual block (n=30), age 6yr (SD:3), weight 23kg (SD:9), duration of surgery 26min (SD:9), duration of anesthesia 52min (SD:10) DPNB (n=30), age 7yr (SD:2), weight 26kg (SD:6), duration of surgery 33min (SD:2), duration of anesthesia 58min (SD:13)
Interventions	Caudal block: All caudal blocks were performed by one experienced anesthetist in left lateral decubitus position with a 22 G i.v. cannula and 1 mg.kg-1 of 0.25% levobupivacaine was administered from the sacral hiatus. DPNB: DPNB was applied in the supine position. All penile blocks were performed by one experienced urologist. For the penile block, 1 mg.kg-1 0.25% levobupivacaine was administered through a 21-G needle.
Outcomes	Demographic data (age, weight, duration of surgery and duration of anesthesia), the number of patients who were pain free for the first 6 hours, duration of analgesia, the time to first analgesic administration, the rescue analgesic (paracetamol) demands in 24 hours, motor blocks, the time to first walking and micturition, length of stay were followed, postoperatively. According to modified Bromage scale,motor weakness was assessed as 0=able to stand or strong leg movement, 1=able to move legs but unable to stand, 2=no leg movement. Postoperative pain and sedation scores were assessed on the 10th, 30th minutes, and 1-6 hours, by nurses and parents. Pain was evaluated by Faces Pain Rating Scale (FPRS), Observer Pain Score (OPS) and Modified Pediatric Objective Pain Scale (MPOPS). OPS and MPOPS include 5 criteria such as crying, movements, agitation, systolic blood pressure and complains of pain. Nevertheless; sedation (time to waking) was defined as the time between the end of surgery (E0) and waking. It was assessed by the Modified Aldrete-Kroulik Recovery Scores that consists of motor activity, respiration, circulation, consciousness and O2 saturation
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "in this single centre, prospective, randomized, controlled, blind study. Age, weight, surgery and anesthesiathere was no difference in respect to demographic data (age, weight, duration of surgery and duration of anesthesia)" "Randomization was done by computer generated random number sequence." COMMENTS: Unclear how sequence generation was performed
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "The allocation was concealed in a sealed envelope until the child was anesthetized"
Blinding of participants and personnel (performance bias)	Low risk	SUPPORTING ANNOTATIONS: "small spot dressings were applied to the sites of both caudal and penile injection to avoid observer bias postoperatively. During surgery, a block was." "This was a blind study: patients, nurses and parents were blinded to the type of given block." COMMENTS: Likely personnel and participants were blinded.

Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "Postoperative pain and sedation scores were assessed on the 10th, 30th minutes, and 1-6 hours, by nurses and parents.Twenty-four hours later, the parents of the children were called by a member of anesthetic team who was unaware of the kinds of blocks. The par- ents were asked for their records.This was a blind study: patients, nurses and parents were blinded to the type of given block. " COMMENTS: Likely the outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "None of the patients was withdrawn from the study with any reason"
Selective reporting (reporting bias)	Low risk	COMMENTS: Not reffering to a protocol but report on relevant outcomes
Other bias	Low risk	COMMENTS: The study seems free of other sources of bias

Kurtis 1999 A

Methods	RCT
Participants	48 male NB; FT; 5 min Apgar >/= 7
Interventions	Mogen clamp and 0.8 ml 1% lidocaine DPNB (n=16) Mogen clamp and no DPNB (n=16) Gomco clamp and 0.8 mL 1% lidocaine DPNB (n=8) Gomco clamp and no DPNB (n=8) 5 minute WT
Outcomes	time crying, HR, O2sat, salivary cortisol, RR
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insuffient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Insuffient information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Unblinded, but this is unlikely to influence reporting of outcome. the physicians performing the circumcisions were not blinded to the anesthesia status.
Blinding of outcome assessment (detection bias)	Low risk	Unblinded, but this is unlikely to influence reporting of outcome
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient information on incomplete outcome data
Selective reporting (reporting bias)	Low risk	No reference to study protocol, but appears to report on all outcomes of interest
Other bias	Low risk	The study appears to be free from other sources of bias

Kurtis 1999 B

Methods	RCT
Participants	48 male NB; FT; 5 min Apgar >/= 7
Interventions	Mogen clamp and 0.8 ml 1% lidocaine DPNB (n=16) Mogen clamp and no DPNB (n=16) Gomco clamp and 0.8 mL 1% lidocaine DPNB (n=8) Gomco clamp and no DPNB (n=8) 5 minute WT
Outcomes	Time crying, HR, O2sat, salivary cortisol, RR
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "Infants enrolled were randomized into one of the four anesthesia/clamp groups." COMMENTS: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	COMMENTS: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	SUPPORTING ANNOTATIONS: "The physicians performing the circumcisions were not blinded to the anesthesia status." COMMENTS: Unblinded, but this is unlikely to influence reporting of outcome
Blinding of outcome assessment (detection bias)	Low risk	COMMENTS: Unblinded, but this is unlikely to influence reporting of outcome
Incomplete outcome data (attrition bias)	Unclear risk	COMMENTS: Insufficient information on incomplete outcome data
Selective reporting (reporting bias)	Low risk	COMMENTS: No reference to study protocol, but appears to report on all outcomes of interest
Other bias	Low risk	COMMENTS: The study appears to be free from other sources of bias

Lander 1997

Methods	RCT
Participants	54 male NB; FT; AGA; 1-3 d age
Interventions	2g LP cream (n=15) placebo cream (n=12) 0.8 ml 1% lidocaine DPNB (n=14) 0.8 ml 1% lidocaine RB (n=13) - penile blocks 8 min WT; creams applied 90 min prior and covered with occlusive dressing
Outcomes	HR; time cry; O2 sat, RR, palmar sweat, metHgb level
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information about sequence generation procedure
Allocation concealment (selection bias)	Unclear risk	No information about allocation concealment procedure
Blinding of participants and personnel (performance bias)	Low risk	Likely personnel were blinded. Type of topical were blinded for all personnel.
Blinding of outcome assessment (detection bias)	Low risk	Type of topical were blinded for all personnel. Outcome assessors were likely blinded.
Incomplete outcome data (attrition bias)	Low risk	Two infants were withdrawn due to reasons unrelated to study procedure.
Selective reporting (reporting bias)	Low risk	No protocol registered. Apparently comprehensive outcome reporting.
Other bias	Low risk	No other sources of bias is suspected

Lehr 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 39.2 (0.9) gestational age ● *Duration of surgery*: ● *Anesthesia duration*: Intervention 2 ● *Age*: 39.1 (1.3) ● *Duration of surgery*: ● *Anesthesia duration*: Control 1 ● *Age*: 39.1 (1.2) ● *Duration of surgery*: ● *Anesthesia duration*: Control 2 ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: Overall ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: **Included criteria:** Healthy, term males (n = 54), younger than 1 week old undergoing circumcision. **Excluded criteria:** **Pretreatment:** Infants in the LMX group were heavier and longer than infants in the to other groups.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: lidocaine 4% cream (LMX4) ● *Dose*: 4% ● *Follow-up time*: 72 hour Intervention 2 ● *Description*: lidocaine 2.5% and prilocaine 2.5% (EMLA) ● *Dose*: lidocaine 2.5% and prilocaine 2.5% ● *Follow-up time*: 72 hour Control 1 ● *Description*: DPNB ● *Dose*: ● *Follow-up time*: 72 hour

	Control 2 ● *Description*: ● *Dose*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Extern service conducted a computer-generated block randomization
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: The study states they used open label AND as a consequence all study personnel were blinded. This is conflicting information.
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Unlikely the study nurses or the parents evaluating AE were blinded. Not feasible to blind, but is unlikely to influence reported outcomes
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: AE data is reported for all groups. few dropouts in each group
Selective reporting (reporting bias)	Low risk	Judgement Comment: No pre-specified protocol. No reasons to expect selective outcome reporting bias.
Other bias	Low risk	Judgement Comment: No reasons to expect other sources of bias.

Lunn 1979

Methods	RCT
Participants	40 boys aged 2-12 years selected for day-case circumcision for surgical reasons. Exclusion criteria: unfused sacral vertebrae. Setting: UK
Interventions	CAUDAL versus PARENTERAL Caudal (n = 20): 0.5% bupivacaine, 1.5 mg/kg. Patient semi-prone - no other technique details described. Parenteral analgesia (n = 20): IM morphine 0.15 mg/kg administered leL deltoid as surgery started.
Outcomes	10-cm linear analogue scale labelled asleep at one end and restless at the other were marked by independent experienced stal nurse every 5 minutes for 30 minutes. Need for rescue analgesia (in recovery room) Incidence of vomiting (in recovery room) Incidence of later vomiting - partial results only (not able to be used) Duration of stay in day unit Time to standing unaided Complications assessed by community nurse in first 24 hours and at Surgical Outpatients at one week.
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers were used to allocate patients into two groups.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	No member of staff in the recovery room knew which technique of analgesia had been used.All the patients were treated in the same manner by the same anaesthetist.Those who were to receive intra- muscular morphine did so as surgery started: 0.15 mg/kg was given into the left deltoid muscle. Those who were to receive caudal analgesia were turned into the semi-prone position and received 1.5 mg/kg bupivacaine (0.5% without adrenaline). As soon as the injection was completed, a dressing was applied and the child was taken into theatre. Likely the parent and surgeon were blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Observations about later recovery at home were recorded by the Community Nurse who visited the patients twice in the next 24 hr. Final healing and overall results were noted at the subsequent visit to Surgical Outpatients one week later. Some months later measurement of the length of the analogue line were made by the author before the nature of the analgesia was again known.An independent experienced staff nurse made special notes of the child's behaviour.COMMENTSUnclear if the nurses were blinded. Likely the author were blinded.
Incomplete outcome data (attrition bias)	Unclear risk	Not all the records about vomiting were complete. Three out of 13 boys who received caudals (23%) and 8 out of 12 (80%) who received morphine, vomited (,yz 7.26: P <0.01).COMMENTSNo information about attrition. Likely all participants were included in

		follow up and hence in analysis.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcomes
Other bias	Low risk	Only one author/investigator who also assessed outcome and performed analysis.

Macke 2001

Methods	RCT
Participants	60 male NB; FT; Apgar >/= 8
Interventions	acetaminophen 10 mg/kg (n=29) placebo (n=31) given 1 hr prior to circumcision
Outcomes	HR , Nursing Child Assessment Feeding Scale, cry time, infant state
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Groups were compared, and no significant differences were found (see Table 1). Most mothers in the study were white: 93% in the analgesia group and 90% in the placebo group. Groups also were compared on variables related to the circumcision; no significant differences were found except for type of physicianA pretest-posttest experimental design with random-ized group assignment was used. The pharmacy staff determined group assignments.COMMENTSUnclear sequence generation
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Physicians, mothers, nurses, and the investigator were blind to participant groups. Participants were recruited at the convenience of the investigator, who explained the study and obtained consent.
Blinding of outcome assessment (detection bias)	Unclear risk	The investigator conducted all the observations to ensure uniform routine care for the newborns.The investigator analyzed the taped crying, and to ensure reliability, after every 20 newborn cry tapes, another investigator analyzed the tape.The investigator, certi- fied in the use of the NCAST tools, observed all the feeding interactions.COMMENTSUnclear how the investigator/assessor remained blinded.
Incomplete outcome data (attrition bias)	Low risk	No information about attrition. Likely no missin data.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcome.
Other bias	Low risk	The main (only) author is also the primary investigator.

Mak 2001

Methods	RCT
Participants	187 (185) boys aged between 1 and 12 years, admitted for elective day-surgery circumcision. Setting: Hong Kong
Interventions	CAUDAL versus DNPB versus RECTAL/IV Caudal (n = 61 (63)): 0.25% bupivacaine 0.5 ml/kg, maximum 20 ml - following induction, caudal blocks were given aseptically to the boys lying in a leL lateral position. DNPB (n = 63): 0.5% bupivacaine, < 15 kg - 2ml, 15-24 kg - 2.5 ml, 25-30 kg - 3 ml, 31-40 kg - 3.5 ml, > 40 kg - 4 ml; via intrapubic approach as described by Yeoman. RD/IVFENT (n = 61): Rectal diclofenac (1 mg/kg) and intravenous fentanyl 0.5 g/kg. Anaesthesia was induced by inhalation of sevoflurane and oxygen or intravenous propofol; maintained with nitrous oxide in oxygen and isoflurane.
Outcomes	Rescue analgesia (failed block) Other analgesia (no analgesia was given in the recovery ward, nurses gave oral paracetamol in day surgery ward if the boys complained of moderate or severe pain, or cried even in their parents' presence, or thrashed in beds, or were refrained from movement) Duration of analgesia Bleeding Haematoma/bruising of needle site Vomiting Hospital stay
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "There were no significant differences found among the three groups in terms of age and weight.Post-circumcision analgesia in children 147 allocated randomly to one of three groups by drawing cards. Informed parental consents were obtained."
Allocation concealment (selection bias)	Unclear risk	Comments: No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	SUPPORTING ANNOTATIONS: "Anaesthesia was induced by inhalation of sevoflu- rane and oxygen or intravenous propofol. Following inductions, caudal blocks were given aseptically to patients lying in a left lateral position and dorsal penile nerve blocks were given via an infrapubic approach as described by Yeoman et al. 5 All caudal blocks were given by the Hong Kong Buddhist Hospital's special- ist anaesthetist. Intravenous fentanyl was adminis- tered by anaesthetists while rectal diclofenac was administered by nursing staff." COMMENTS: No information about blinding of the personnel performing the procedure. The parents were likely blinded
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "Just before discharge, a medical staff member inspected the patient for wound bleeding and, for those boys who had received caudal block, instructed parents to remove the sacral dressings the following morning." "After returning to the day surgery ward, nursing staff, who were unaware of the type of analgesia given, started to record the pain response with respect to verbal complaints (mild, moderate or severe pain), crying and signs of distress. Thereafter, the boys were assessed at hourly intervals or earlier if complaints from the boys or parents arose between intervals." "Parents were allowed to come into the recovery ward to alleviate their child's fear. After returning to the day surgery ward, nursing staff, who were unaware of the type of analgesia given, started to record the pain response with respect to verbal complaints (mild, moderate or severe pain), crying and signs of distress. Thereafter, the boys were assessed at hourly intervals or earlier if complaints from the boys or parents arose between intervals." Comments: Nurses but not the patients were blinded.
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "Two boys had caudal blocks abandoned because of technical difficulties and these two boys were excluded from the study"
Selective reporting (reporting bias)	Unclear risk	COMMENTS: No protocol and no reporting of the pain responses assessed - stated in the methods section
Other bias	Low risk	COMMENTS: No reasons to suspect other sources of bias.

Marchette 1989

Methods	RCT
Participants	103 male NB; Apgar >/= 8
Interventions	classical music (n=25) intrauterine sounds (n=15) control (no nurse present) (n=18)
Outcomes	HR; heart rhythm; BP; TcpO2; MDFMCS; BNAS
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Marchette 1991

Methods	RCT
Participants	121 male NB; Apgar =/> 6; normal delivery; 2 - 9 days age
Interventions	taped music (n=20) intrauterine sounds (n=20) pacifier (n=20) music and pacifier (n=20) intrauterine sounds and pacifier (n=20) control - no treatment (n=21)
Outcomes	HR, rhythm, BP; tcPO2; rate pressure product, BNAS; crying

Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Martin 1982

Methods	RCT
Participants	60 inpatient boys admitted consecutively to hospital for circumcision. No age range given but mean age 5.6-6.5 in the three groups. Exclusion criteria: none reported. Setting: UK
Interventions	CAUDAL (CAUDAL or CAUDAL+OPIOID) versus PARENTERAL OPIOID Caudal: 0.5% bupivacaine, 0.5 ml/kg (n=20). Caudal: 0.5% bupivacaine and morphine 0.2 mg/ml, 0.5 ml/kg (n=20). Diamorphine 0.07 mg/kg, 0.05 mg/kg given IV during early part of operation and 0.02 mg/kg given IM when surgery completed (n = 20).
Outcomes	Pain: No criteria for rescue analgesia although paracetamol elixir said to be given by mouth if required. However diamorphine was given in the ward for two patients in the bupivacaine only caudal group due to block failures. 10-cm linear analogue scale of "anaesthetised child" at one end and "screaming and uncontrollable" at the other. Completed every 5 minutes for 1st hour, every 15 minutes for second hour then hourly for 4 more hours. Assessed by paediatric ward sister and a small number of stal nurses under her supervision. Number of patients vomiting.
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The characteristics of the three groups are shown in table I and it will be seen that they are comparable.Sixty boys admitted consecutively to hospital from the waiting list for circumcision were randomly allocated to one of three groups.COMMENTSLikely random allocation however unclear sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	No information on blinding
Blinding of outcome assessment (detection bias)	Unclear risk	After the operation children were assessed on a linear analogue scale by the paediatric ward sister and a small number of staff nurses under her super- vision.COMMENTSNo information about blinding of the ward sister or the staff nurses.
Incomplete outcome data (attrition bias)	Low risk	The results were different in the group receiving the caudal injection with bupivacaine alone. There were two complete failures in this group and diamorphine had to be given in the ward because of distress. One was a technical failure occasioned by anatomical abnormality and the other occurred in a small child in whom there was emotional distur- bance.COMMENTSTwo patients were excluded from the caudal injection with bupivacaine alone group. Per protocol analysis.
Selective reporting (reporting bias)	Low risk	No protocol however, thorough reporting of stated outcome pain/behaviour.
Other bias	Unclear risk	No reasons to suspect other sources of bias.

Masciello 1990

Methods	RCT
Participants	30 male NB, healthy, FT
Interventions	0.8 ml 1% lidocaine DPNB (n=10) 0.8 ml 1% lidocaine local block (n=10) no treatment control (n=10) 5 min WT

Outcomes	plasma cortisol, HR, O2sat, cry
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear how sequence generation were performed
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Personnel not blinded. - All anesthetic procedures and circumcisions were performed in an identical manner by the principal investigator.
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Low risk	One infant from each group were excluded from analysis on cortisol levels because of improper handling.
Selective reporting (reporting bias)	Unclear risk	No protocol. However, all relevant outcomes seem to be reported. Report on relevant outcomes
Other bias	Low risk	The study seems free of other bias

Maxwell 1987

Methods	RCT
Participants	30 male NB; FT; healthy
Interventions	0.8 ml 1% lidocaine DPNB (n=20) no treatment control (n=10) 5 min WT
Outcomes	HR, O2sat, BP, plasma lidocaine
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization by drawing cards. No baseline imbalances between groups
Allocation concealment (selection bias)	Unclear risk	No information about allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Surgeon was blinded to the procedure. No information about blinding of other personnel.
Blinding of outcome assessment (detection bias)	Unclear risk	No information about blinding of outcome assessors.
Incomplete outcome data (attrition bias)	Unclear risk	No information about missing data nor drop outs. 4 children had insufficient blocks
Selective reporting (reporting bias)	Low risk	No protocol however, all outcomes were relevant and thorough reported.
Other bias	Low risk	No reasons to suspect other sources of bias.

May 1982

Methods	RCT
Participants	44 healthy boys aged 9 months to 9 years, presenting for circumcision as day cases. Setting: UK
Interventions	CAUDAL versus PARENTERAL Caudal (n = 21): 0.25% bupivacaine, 0.5 ml/kg. Control (n = 23): buprenorphine 3 ug/kg IM.
Outcomes	postop. 3 further assessments by parents over next 24 hours with results via returned questionnaire. No record of how many questionnaires returned. Need for additional analgesia (aspirin) both in and out of hospital noted. Complications: not formally studied. Nausea and vomiting: noted in recovery and by returned questionnaire.
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Random numbers were used to allocate the patients into two groups." COMMENTS: Random numbers
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation concealment

Blinding of participants and personnel (performance bias)	Unclear risk	SUPPORTING ANNOTATIONS: "Both groups had Elastoplast dressings placed over the lateral aspect of the thigh and also over the sacral hiatus so that the injection site was not visible to the person making the postoperative assessment." COMMENTS: Blinding of personnel is not described. It is unclear whether the operating surgeon was aware of the type of anasthesia given.
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: aspirin (10 mg/kg) orally. All <b>the observations were made by one of the authors (A.M), who was unaware of the analgesic techniques used. Further assessments were made by the child's parents" "Both groups had Elastoplast dressings placed over the lateral aspect of the thigh and also over the sacral hiatus so that the injection site was not visible to the person making the postoperative assessment." COMMENTS: Outcome assessor blinded
Incomplete outcome data (attrition bias)	Low risk	COMMENTS: It seems there is no drop out
Selective reporting (reporting bias)	Low risk	COMMENTS: No protocol available. The study has not included heart rate or oxygen saturation
Other bias	Low risk	COMMENTS: The study seems to be free from other sources of bias

Mohan 1998

Methods	RCT
Participants	60 male NB; FT; BW>/= 2500 g; 5 min Apgar >/= 7; < 5 days age
Interventions	5 g LP cream + 2 ml 24% sucrose via pacifier (n=19) 5 g LP cream + water via pacifier (n=20) 2 ml 24% sucrose via pacifier (n=21) water via pacifier (n=19) - non-randomized control cream applied 45-60 min prior, covered with occlusive dressing
Outcomes	HR; O2sat; BP; cry duration
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not clear how participants were randomly assigned
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	The person performing the procedure was blinded as to the analgesic agent or agents used.
Blinding of outcome assessment (detection bias)	Unclear risk	unclear if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	One infant from the control group was eliminated.
Selective reporting (reporting bias)	Low risk	No protocol. However, all relevant outcomes seem to be included.
Other bias	Unclear risk	The control group was not randomly assigned.

Mudge 1989

Methods	RCT
Participants	44 male NB; 5 min Apgar > 7; BW 2.5 - 4.5 kg; FT; age 12 - 72 h
Interventions	4% lidocaine cream (n=20) placebo cream (n=24) cream applied 2 hr prior covered with occlusive dressing
Outcomes	HR, RR, O2sat, cry time, behavior
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "The groups were compared as to the variables of weight, Apgar scores, blood pressure, gestational age, chronological age, and time since eating. T-tests were performed to test differences, and no differences were found." COMMENTS: Unclear how the random sequence was generated but no differences at baseline.
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "The pharmacist kept the randomized list, and it was not given to the investigator until after the study. " COMMENTS: Likely the allocation was concealed
Blinding of participants and personnel (performance bias)	Unclear risk	SUPPORTING ANNOTATIONSThis was done by the institutional pharmacist, who prepared packets of either 4% lido- Caine mixed with acid mantle or acid mantle cream only.The cream was covered with an occlusive dressing of Saran wrap and secured with tape."

		COMMENTS: Unclear if the personnel were blinded throughout the procedure.
Blinding of outcome assessment (detection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "Throughout the procedure, the investigator and the physician carefully observed the infant' s reaction to the circumcision." "the severity of the overt response of the infant was dichotomously cate- gorized as distressed or not distressed, by joint agreement of the in- vestigator and the physician." "The pharmacist kept the randomized list, and it was not given to the investigator until after the study." COMMENTS: Likely the investigator were blinded. Unclear if the physician were blinded.
Incomplete outcome data (attrition bias)	Unclear risk	COMMENTS: Seems that all children are included in analysis.
Selective reporting (reporting bias)	Low risk	COMMENTS: Not reffering to a protocol but report on relevant outcomes No protocol. Clearly stated purposes, hypothesis and outcomes to measure. Reporting lacking variance.
Other bias	Low risk	COMMENTS: The study seems free of other bias

Mujeep 2013

Methods	RCT
Participants	Age: 2 months (range: 1-6 months)
Interventions	EMLA (n=50): "1-2 gm of EMLA cream was applied over the glans and prepuce. An occlusive Opsite (Smith & Nephew, Inc USA) dressing was applied, one hour prior to the procedure. " DPNB (n=50): "injection was given by infiltrating 1ml of 1% (plain) lignocaine at penile base."
Outcomes	HR, RR, and oxygen saturation. Neonatal infant Pain Scale (NIPS).
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	here was no statistically significant difference in base line parameters in both the groups except for the respiratory rate, which was significantly raised in DPNB group (<.01).Health Karachi, from May 2008 to October 2008. Patients under six month of age were randomized in to two groups (EMLA and DPNB) of fifty patients each. The effectiveness of pain control was assessed by measuring. For assigning into each group balloting was used on operation day. COMMENTSLikely sequence generation was random but unclear. No baseline group differences.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	No information on blnding
Blinding of outcome assessment (detection bias)	Unclear risk	Annotation: "An assessor recorded the physiological parameters and pain by using NIPS score during each standard step of the procedure." COMMENTS: Unclear if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Unclear risk	No information about attrition.
Selective reporting (reporting bias)	Low risk	No protocol. Apparently thorugh outcome reporting.
Other bias	Low risk	No other sources of bias suspected

Naja 2011

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Newton 1999

Methods	RCT
Participants	194 male NB; healthy
Interventions	0.8 ml 1% lidocaine DPNB (n=92) 0.8 ml 1% buffered lidocaine (n=102)
Outcomes	HR (primary outcome variable); O2sat; number crying/phase; modified BNAS
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Panda 2011

Methods	RCT
Participants	Sixty children between the age of 1-10 years belonging to American Society of Anesthesiologists (ASA) grades I and II were enrolled in the present study in a randomized manner and divided equally into two groups of 30 each.
Interventions	Intervention: Children in group G underwent a standard general anaesthetic. Induction of anaesthesia was achieved with a gas mixture of oxygen, nitrous oxide (50:50), sevoflurane (2-4%) and fentanyl 1-2 μg/kg body weight. Oral endotracheal intubation was performed with appropriately sized polyvinyl chloride (PVC) endotracheal tubes, facilitated by succinylcholine in a dose of 1 mg/kg body weight. Maintenance of anaesthesia was done with oxygen, nitrous oxide (40:60) and sevoflurane (1-1.5%), and vecuronium bromide 0.1 mg/kg body weight was utilized for neuromuscular blockade. Ventilation was controlled with a closed circuit system connected to a paediatric anaesthetic ventilator (PENLON AV 900). During peri-operative period, any increase of heart rate or mean arterial pressure (MAP) >20% of the baseline was managed by 25% of the initial dose of fentanyl as and when required. At the end of the procedure, the residual neuromuscular block was reversed with neostigmine 0.05 mg/kg body weight and atropine 0.02 mg/kg body weight and patients were extubated after clinical assessment and thorough orophanyngeal suction. Control: In group B, the penile block was administered by the anaesthesiologist using 0.25% bupivacaine without adrenaline in a dose of 0.5 mg/kg body weight and it was used as an isolated local block. Taking all antiseptic precautions, a 30 mm 23 G needle was inserted in the midline after gently pulling down the base of the penis by the index finger and directed below the symphysis pubis through the Scarpa's fascia and into the sub-pubic space. After a negative aspiration for blood, 25% of the calculated volume of drug was injected. The needle was withdrawn by 1-2 mm and redirected to 11:00 O' clock and 1:00 O' clock positions and 25% of the calculated volume of drug was injected on either side of midline to block the two dorsal nerves. Entry of the needle through the Scarpa's fascia was appreciated as a 'give'. An additional puncture was made on the raphe line at the borderline between the penis and scrotum and the remaining 25% of the calculated drug volume was injected to alleviate possible pain arising from the skin innervated by the perineal nerves. All these injections were made very slowly, taking 100-120 seconds to reduce pain during injection.
Outcomes	Intra-operatively, HR, ECG, NIBP (systolic and diastolic) and SpOwer recorded at 5 minute intervals for the first 60 min and then at 15 minute intervals till the end of procedure. The presence or absence of tears and sweating was also noted at the similar intervals.Post operatively, HR, NIBP, SpO2 and pain were assessed and recorded at 15 minutes, 1 hour, 4 hours and 8 hours. The pain relief or absence was assessed for the children by their mother based on cry, irritability or restlessness of the child on a smiley faces score which had five faces corresponding to 0, 25, 50, 75 and 100% analgesia.
Notes	18 ud af de 30 i hver gruppe blev omskåret

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Coded envelopes. The randomisation process was carried out by the central station staff.
Blinding of participants and personnel (performance bias)	High risk	Personnel could not be blinded
Blinding of outcome assessment (detection bias)	High risk	Several outcomes were recorded intra-operatively. It is not stated that the outcome assessors were blinded. Pain and crying observed by mothers
Incomplete outcome data (attrition bias)	Low risk	Two patients were excluded from Group B due to a failed block.
Selective reporting (reporting bias)	Low risk	Not reffereing to a protocol, but report on relevant outcomes

Other bias	Low risk	The study seem to free from other sources of bias

Sharara Chami 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 38.50 (1.35) wk ● *Duration of surgey*: 5.63 (0.78) min ● *Anesthesia duration* : intervention 2 ● *Age*: 38.45 (1.14) wk ● *Duration of surgey*: 6.59 (1.13) min ● *Anesthesia duration* : kontrol 1 ● *Age*: 38.65 (0.98) wk ● *Duration of surgey*: 6.31 (0.94) min ● *Anesthesia duration* : kontrol 2 ● *Age*: 38.26 (1.6) wk ● *Duration of surgey*: 6.35 (1.24) min ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** All healthy, late preterm and term (36-41 weeks' gestation) newborn boys admitted to the normal nursery at the American University of Beirut Medical Center whose parents requested circumcision were eligible for recruitment. After an infant's first void and clearance for circumcision by the nursery p **Excluded criteria:** **Pretreatment:** Similar in baseline characteristics
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: The control group received the traditional anesthetic that is, topical cream EMLA, whereas the combination groups received additional anesthetic agents. ● *Dose*: 1 g (eutectic mixture of 2.5% lidocaine and 2.5% prilocaine that is used as a topical anesthetic to diminish pain from cutaneous procedures) ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: EMLA cream is a eutectic mixture of 2.5 % lidocaine and 2.5% prilocaine that is used as a topical anesthetic to diminish pain from cutaneous procedures. Sixty minutes before the circumcision, 1 g of EMLA cream was . Sixty minutes before the circumcision, 1 g of EMLA cream was applied by the nurse to the penis of the newborn and wrapped with Tegaderm dressing (Johnson & Johnson, Inc, Arlington, TX). The cream and dressing were removed before the procedure. There is sufficient evidence to support the administration of sucrose, often in conjunction with additional pharmacologic and nonpharmacologic interventions, for relief of procedural pain.13 It is the neonate's detection of a sweet substance, not the volume, that produces the analgesic effect. As a result, studies report that 0.05 to 0.5 mL is an adequate volume of 24% to 25% sucrose or glucose for reducing procedural pain in neonates.14 For this study, 2 mL of 25% sucrose was administered orally and intermittently via a syringe throughout the circumcision procedure by an assisting nurse. ● *Dose*: 2 ML of 25% sucrose ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: The placement of EMLA and the administration of sucrose were the same as described for the EMLA + sucrose group. DPNB is an anesthetic technique that has been extensively used and evaluated in the management of pain during circumcision since the late 1970s. The pediatric urologist administered the DPNB (2 mg/kg of 1% lidocaine without epinephrine) in equal aliquots in milliliters at the 2 and 10 o'clock positions at the base of the penis 5 minutes before the cirumcision. ● *Dose*: 2 ML of 25% sucrose +2 mg/kg of 1% lidocaine without epinephrine ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: The placement of EMLA and the administration of sucrose were the same as described for the EMLA + sucrose group. RB is an anesthetic technique first described in the 1990s,2,16 which has also been examined for pain control during circumcision. The pediatric urologist administered the RB (2 mg/kg of 1% lidocaine without epinephrine) in a band around the penis 5 minutes before the circumcision. ● *Dose*: 2 ML of 25% sucrose +2 mg/kg of 1% lidocaine without epinephrine ● *Duration*: ● *Follow-up time*:

Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the control. Randomization and blinding Randomization by blocks of 6 and 9 was used. The allocation ratio of intervention to control was 2:1. An independent statistician not involved in the study" Judgement Comment: An independent statistician not involved in the study conducted the random assignment process.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: The random list was held by the research fellow. It is not clear whether this list was concealed or if he could foresee the next allocation.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: The surgeon was aware of group assignment
Blinding of outcome assessment (detection bias)	Low risk	Quote: "random assignment immediately before circumcision. The nurses scoring each infants' pain after the procedure were blinded to the type of analgesia administered, as were the 2 pediatricians who" Judgement Comment: Nurses and pediatricians were blinded to the analgesia used.
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: All randomized children were included in the analysis.
Selective reporting (reporting bias)	Low risk	Quote: "American University of Beirut approved the protocol and the trial is registered on clinicaltrials.gov (identifier NCT02990364). All healthy, late" Judgement Comment: Protocol at clinicaltrials.gov. All stated outcomes are reported
Other bias	Low risk	Judgement Comment: The study seem to be free from other sources of bias

South 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 39.4 (38.9-40) gestational week ● *Duration of surgery*: 11.75 (11.58-12.12) min ● *Anesthesia duration*: Intervention 2 ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: Control 1 ● *Age*: 39.7 (38.6-40.6) gestational week ● *Duration of surgery*: 11.98 (11.33-12.38) min ● *Anesthesia duration*: Control 2 ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: Overall ● *Age*: ● *Duration of surgery*: ● *Anesthesia duration*: **Included criteria:** The inclusion criteria included all term healthy infants delivered via vaginal or cesarean birth, including operative delivery (ie, forceps/vacuum) **Excluded criteria:** We excluded any infant born lessthan 37 weeks' gestation, any comorbid illness (ie, anymajor congenital anomalies or infectious diseases),babies born with an Apgar score less than 7 at 1 minuteand NICU infants (except if only for a short observational period of %6 hours). In addition, infants wereexcluded if they received more than routine neonatalmedications, were breastfed by mothers taking sulfonamides or salicylates, and if the parents declined informedconsent. Any other contraindications to circumcisionbased on current standards of care were also used toexclude infants from the study. **Pretreatment:** No differences
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Finger group. All infants received oral Tylenol and a dorsal penile nerve block (DPNB) before thecircumcision. ● *Dose*:

	● *Follow-up time*: Intervention 2 ● *Description*: ● *Dose*: ● *Follow-up time*: Control 1 ● *Description*: Control. All infants received oral Tylenol and a dorsal penile nerve block (DPNB) before thecircumcision. ● *Dose*: ● *Follow-up time*: Control 2 ● *Description*: ● *Dose*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Block randomization using STATA
Allocation concealment (selection bias)	Low risk	Judgement Comment: Allocation concealed from the physician using concealed envelope.
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Allocation concealed from the physician using concealed envelopes.Likely participants/parents were unblinded.
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Standardized assessment of HR, pain (PIPP) and crying time using nurses blinded to the nature of the study.
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No reasons to suspect bias from incomplete outcome data however, one participant from the control group excluded from analysis without stated explanations ("secondary to missing data").
Selective reporting (reporting bias)	Low risk	Judgement Comment: No protocol however no reasons to suspect selective outcome reporting.
Other bias	Low risk	Judgement Comment: Seems free of other potential biases

Spencer 1992

Methods	RCT
Participants	75 male NB; BW 2500 - 4500 g; >12 hr age; 5 min Apgar > 6; normal exam
Interventions	lidocaine DPNB - 5 min WT (n=15) lidocaine DPNB with 2 min WT (n=15) 1% chloroprocaine DPNB with 3 min WT (n=15) 1% chloroprocaine DPNB with 5 min WT (n=15) no treatment control (n=15)
Outcomes	cry duration, O2Sat, HR, BNAS
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Seventy-five neonates born in a private teaching hospital were screened and randomly assigned to series of five groups. COMMENTSNo information about sequence generation and no informaton about baseline imbalances between groups.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Unclear if personnel was blinded No information about blinding.
Blinding of outcome assessment (detection bias)	Unclear risk	Il re- search data were recorded on subject data entry sheets and transferred by one keypunch operator into an IBM computer using ABSTAT software to determine the descriptive and inferential statistics.Trained recorders logged highest or lowest heart rate and tissue oxygenation for six circumcision events: anesthetic infusion, lateral clamping, prob- ing, dorsal cutting, Gomco bell and platform place- ment, and foreskin cutting. Values were obtained using a pulse oximeter (Nellcor N-100) attached to each subjects right great toe. COMMENTSNo information about blinding of outcome assessors.

Incomplete outcome data (attrition bias)	Unclear risk	No information about missing data or drop outs.
Selective reporting (reporting bias)	Low risk	No protocol. All relevant outcomes where reported.
Other bias	Low risk	No reasons to suspect other sources of bias.

Stang 1988 A

Methods	RCT
Participants	60 male NB; > 24 hr age; BW > 3000 g; 5 min Apgar > 7; uncomplicated delivery
Interventions	0.8 ml 1% lidocaine DPNB (n=20) saline DPNB (n=20) no treatment control (n=20) 5 min WT *comparison is DPNB versus no treatment
Outcomes	% time cry, modal behavior state, plasma cortisol
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear how the sequence generation was performed
Allocation concealment (selection bias)	Unclear risk	Unclear if the allocation was concealed
Blinding of participants and personnel (performance bias)	Low risk	Stated: Observer assessing newborns behavioral state was blinded. The physicians and attendant was blinded.
Blinding of outcome assessment (detection bias)	Low risk	Stated: Observer assessing newborns behavioral state was blinded. The physicians and attendant was blinded.
Incomplete outcome data (attrition bias)	Low risk	No information on attrition however, no complications ocurred. Likely complete outcome data.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcomes
Other bias	Low risk	No reasons to suspect other sources of bias.

Stang 1988 B

Methods	See Stang 1988 A
Participants	See Stang 1988 A
Interventions	See Stang 1988 A
Outcomes	See Stang 1988 A
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	See Stang 1988 A
Allocation concealment (selection bias)	Unclear risk	See Stang 1988 A
Blinding of participants and personnel (performance bias)	Low risk	See Stang 1988 A
Blinding of outcome assessment (detection bias)	Low risk	See Stang 1988 A
Incomplete outcome data (attrition bias)	Low risk	See Stang 1988 A
Selective reporting (reporting bias)	Low risk	See Stang 1988 A
Other bias	Low risk	See Stang 1988 A

Stang 1997

Methods	RCT
Participants	83 male NB, > 20 hr age; BW 3000 - 4000 gm; 5 min Apgar >/= 8; FT
Interventions	group 1 = 0.8 ml 1% lidocaine DPNB, padded restraint , water via pacifier (n=20) group 2 = 0.8 ml 1% lidocaine DPNB, regular restraint, 24% sucrose via pacifier (n=20) group 3 = 0.8 ml 1% buffered lidocaine DPNB, regular restraint, water via pacifier (n=20) group 4 = 0.8 ml 1% lidocaine DPNB, regular restraint, water via pacifier (n=20) (control) 5 min WT
Outcomes	behavioral distress scale, plasma cortisol 30 min post-circ
Notes	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Allocation concealment (selection bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of participants and personnel (performance bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Blinding of outcome assessment (detection bias)	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Incomplete outcome data (attrition bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Selective reporting (reporting bias)	Unclear risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.
Other bias	Low risk	Please see Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD001069. DOI: 10.1002/14651858.CD001069.pub5.

Taddio 1997

Methods	RCT
Participants	68 male NB, BW >/= 2500 g; FT; no jaundice or metHgb
Interventions	1 g (1ml) LP cream (n=38) 1 g (1ml) placebo cream (n=30) creams covered with occlusive dressing for 60 - 80 min prior
Outcomes	HR, time cry, NFCS, systolic/diastolic BP, metHgb
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The neonates were randomly assigned to receive lidocaine– prilocaine or placebo cream.The characteristics of the 68 neonates, 38 in the lidocaine–prilocaine group and 30 in the placebo group, were similar. COMMENTSNo information about sequence generation. No baseline imbalances between groups.
Allocation concealment (selection bias)	Unclear risk	No infomation on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Circumcisions were performed by one of three study-team pe- diatricians in the nursery treatment room. COMMENTSStated double blind study however, unclear how personnel and parents were blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Assessment of Pain The facial activity of the neonates, which reflects the amount of pain experienced, was assessed by a research assistant unaware of the treatment assignments who was trained to use the Neona- tal Facial Coding System reliably (kappa, 0.93; P 0.001). 10-12 The presence or absence. COMMENTSresearch assistant unaware of allocation Pain assessment were likely blidned. Stated double blind study however, unclear how other outcome assessors were blinded.
Incomplete outcome data (attrition bias)	High risk	Eight neonates were treated with lidocaine–prilocaine cream in an un-only in the safety analysis. Fifty-nine neonates were included in the ef- ficacy analysis: 29 in the lidocaine–prilocaine group and 30 in the placebo group. One neonate in the li- docaine–prilocaine group was excluded because he was not circumcised on the day the cream was ap- plied. Fifty-five of the neonates were circumcised. COMMENTSHigh exclusion from intervention group (n=9), also compared to the control (n=0). No analysis (ITT) of the impact of not analyzing participants in the group they were allocated.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcome
Other bias	Low risk	Supported by Astra Pharma Inc., Canada, and by a grant from the Med- ical Research Council of Canada–Pharmaceutical Manufacturers Associa- tion of Canada.COMMENTSNo reasons to suspect other sources of bias.

Teunkens 2018

Methods	RCT
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	patients were ran- domly allocated to one of the 2 study groups receiving either a land- mark DPNB or an ultrasound DPNB, using a computer-generated random table.
Allocation concealment (selection bias)	Low risk	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 arri- val of the patient in the operating theater by the investigator.
Blinding of participants and personnel (performance bias)	High risk	Personnel could not be blinded.
Blinding of outcome assessment (detection bias)	Low risk	Anesthesiologists and nurses who were at any time responsible for the follow-up of the study-patients were blinded for the technique used, as were the patients and their parents.Study outcomes were assessed postoperatively by blinded nurses and anesthesiologists
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow up was evenly distributed between the two groups however rather substantial. Landmark lost 29 and ultrasound 33.
Selective reporting (reporting bias)	Low risk	Refer to a protocol. (I was not able to locate it).EUDRACT 2012-001217- 16).
Other bias	Low risk	The study seems to be free from other sources of bias

Tutuncu 2018

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 44.1 ± 23.9 month ● *Duration of surgey*: ● *Anesthesia duration* : intervention 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 1 ● *Age*: 46.2 ± 32.7 month ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** The study enrolled 85 children with ASA (American Society of Anesthesiologist Physical Status) I-II and in the age range of 1-10 years, planned to undergo cir-cumcision. **Excluded criteria:** Children with neurological or neuromuscular disorders, a history of hemorrhage or coagulation disorders were not included in the study. **Pretreatment:** There were not signifi-cant differences between groups with respect to age and body weight.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: In pudendal nerve block group (PDB group) Pudendal nerve block was performed by same two anesthesiolo-gists a in the lithotomy position, after the appropriate skin sterilization. The nerve stimulator was adjusted to 3mA and 2Hz, and the stimulator needle (22-24 G Stimuplex A, 50-100mm, B. Braun, Melsungen, Ger-many) was inserted from the inferomedial of ischial tuberosities while palpating the tuberosities located at position of 3 and 9 o'clock of the anus (Figure 1). Bu-pivacaine administered as a 0.25 % mixture at 0.3 ml/kg volume. Injection was performed bilaterally after the perineal muscle contraction and the up-down penile movements. ● *Dose*: 0.3 ml/kg 0.25 % bupivacaine ● *Duration*:

	● *Follow-up time*: 24 hours after operation intervention 2 ● *Description*: In pudendal nerve block group (PDB group) Pudendal nerve block was performed by same two anesthesiolo-gists a in the lithotomy position, after the appropriate skin sterilization. The nerve stimulator was adjusted to 3mA and 2Hz, and the stimulator needle (22-24 G Stimuplex A, 50-100mm, B. Braun, Melsungen, Ger-many) was inserted from the inferomedial of ischial tuberosities while palpating the tuberosities located at position of 3 and 9 o'clock of the anus (Figure 1). Bu-pivacaine administered as a 0.25 % mixture at 0.3 ml/kg volume. Injection was performed bilaterally after the perineal muscle contraction and the up-down penile movements. ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: In penile nerve block group (PNB group), dorsal pe-nile block was achieved by two surgeons in the supine position, after skin sterilization, by palpating the sym-physis pubis and perforating the Scarpa's fascia with a pop feeling by 25 G needle and injecting 0.25 % bu-pivacaine mixture of 0.3 ml/kg volume on the midline into the dorsal base of penis, between the pubis and the penis under Scarpa's fascia ● *Dose*: 0.3 ml/kg bupivacaine was applied with nerve stimulator at a concentration of 0.25 % ● *Duration*: ● *Follow-up time*: 24 hours after operation kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients' randomization was performed with sealed enveloped techniques (based on computer-generated random numbers), and they were randomly divided into two groups," Judgement Comment: computer-generated random numbers
Allocation concealment (selection bias)	Low risk	Quote: "sealed enveloped techniques (based" Judgement Comment: Sealed envelopes
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Patients are blinded but unclear if personnel are blinded. Surgeons could not be blinded
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The families, blind to the type of nerve block performed on the patient, were previously instructed on the postoperative pain evaluation which was made easy by the selective use of the Faces Pain" Quote: "All patients were evaluated in the pediatric recovery room by two different anesthesiologists who did not know which technique was performed for anal- gesia during the surgery. The secondary outcome was to evaluate the hemodynamic response of the blocks during surgery." Judgement Comment: The postoperative pain evaluation and the analgesic applications were carried out by the recovery unit anasthetists who were blinded to the type of nerve block technique. The families later reported pain evaluations. They were also blindedOBS sekundære outcomes blev assessed under operationen. Her er det ikke beskrevet om det er af en blinded person.
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: dropout balanced between groups and with same reason. two patients were loss to follow up from each group. Reason for exclusion were the same in both groups.
Selective reporting (reporting bias)	Low risk	Quote: "Clinical trial no: NCT03258255)" Judgement Comment: Protocol at clinicaltrials. Stated outcomes are reported.
Other bias	Low risk	Quote: "Authors declare that they have no conflict of interest." Judgement Comment: The study seem to be free from other sources of bias

Vater 1985

Methods	RCT
Participants	50 boys aged 1-13 years, admitted to day ward. Setting: UK
Interventions	CAUDAL versus DNPB Caudal (n = 25): 0.25% bupivacaine 0.5 ml/kg. DBPB (n = 25): 0.5% bupivacaine 3 ml (1-5 years) or 4 ml (5-13 years) via 23G needle.

Outcomes	Pain: scored on 3-point scale (good, fair, poor) at 2 and 4 hours. Rescue analgesia administered if pain relief deemed "poor" (required IM morphine sulphate within 1 hour of surgery). Time to first micturition, standing unaided, and oral fluids requested by child. After discharge questionnaire at 6,8,and 24 hours regarding pain (verbal rating score) and analgesic use, vomiting, micturition at home and mobilization.
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "allocated randomly" COMMENTS: unclear how sequence generation was performed
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	SUPPORTING ANNOTATIONS: "order to permit unbiased assessment, a dressing was applied to each of the two possible puncture sites in every child." COMMENTS: It is not described if the operating surgeon was blinded or not.
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "n order to permit unbiased assessment, a dressing was applied to each of the two possible puncture sites in every child." COMMENTS: One anasthetist, ignorant of the local technique employed, performed all assessments. Parents assessed the child 6 and 8 hours following surgery
Incomplete outcome data (attrition bias)	Low risk	COMMENTS: Two patients from the DNB group were excluded and one patient from the caudal group was excluded. equal distriution of dropout
Selective reporting (reporting bias)	Low risk	COMMENTS: No protocol available. The study seems to report on all relevant outcomes, however, they have not included heart rate or oxygen saturation
Other bias	Low risk	COMMENTS: The study seems to be free from other sources of bias

Wang 2019

Methods	RCT
Participants	110 ASA physical statuses I to II boys, aged 7 to 14 years old with normal cognition. Caudal block (n=43): age 12.5 (SD: 2.6) DPNB (n=47): age 11.7 (SD: 2.9)
Interventions	Caudal block: A caudal block was performed in the patients of Group CB with the lateral position followed by the loss of consciousness. A single injection of 0.25% ropivacaine (Naropina, AstraZeneca AB, Sweden) plus 0.8% lidocaine (Lidocaine Hydrochloride Injection, Shanghai Chaohui Pharmaceutical Group, China), a total of 0.5ml/kg, was administered using a standard anatomical landmark technique. DPNB: The patients in Group DPNB received dorsal penile nerve blocks via perineal approach, under the direction of a realtime ultrasonography. A single injection of 0.25% ropivacaine plus 0.8% lidocaine, a total volume of 3-5ml, was given
Outcomes	Continuous noninvasive monitoring items including noninvasive blood pressure (NIBP), electrocardiograph (ECG), peripheral oxygen saturation (SPO2), and respiratory rate were obtained by the monitors. Postoperative pain score (NRS) using two pain rating scales by an anesthesia nurse blinded to this trial. Adverse efects such as nausea, vomiting, numbness of the lower limbs, and other postoperative complications within the 2 days afer the surgeries were also recorded and compared.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "The patients were randomly and evenly divided into two parallel groups, Group DPNB, and Group CB, with the random number generated by the Excel software (Microsoft Office, 2007 edition). No difference was found in the mean age, weight, height, and BMI between the two groups (all P values were more than 0.05)."
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	SUPPORTING ANNOTATIONS: "Caudal blocks and dorsal penile nerve blocks were performed by wellexperienced pediatric anesthesiologists blinded to the study. All circumcisions were performed using the same surgical technique by senior pediatric surgeons. All information on surgeries was recorded." COMMENTS: Unclear if and how parents were blinded
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "leaving the PACU, all patients were evaluated on the postoperative pain score using two pain rating scales by an anesthesia nurse blinded to this trial"
Incomplete outcome data (attrition bias)	Unclear risk	SUPPORTING ANNOTATIONS: "With 14 dropouts, 90 patients were recruited and finally analyzed, with 47 in Group DPNB and 43 in Group CB (Figure 3). All patients completed surgeries under general anesthesia with a caudal block or a dorsal penile nerve block." COMMENTS: Per protocol analysis. No analysis of the impact of the failure to analyze

		particpants in the group they were allocated.
Selective reporting (reporting bias)	High risk	SUPPORTING ANNOTATIONS: "(registration No.: ChiCTR-IPR- 15006670, Principal investigator: Xiaowei Qian)" COMMENTS: Protocol available. Primary outcome Body movement during surgery not reported at all in study. Postoperative pain score (other primary outcome) reported as stated. Postoperative restlessness, nausea, vomiting, urinary retention, itching and other adverse reactions (other primary outcome) reported as stated. Respiratory depression during surgery (secondary outcome) not reported in article. Pulse oximetry not reported either.
Other bias	Low risk	SUPPORTING ANNOTATIONS: "This work was supported by grants funded from Zhejiang Medical and Health Science Technology Program (no. 2017185647) and Wenzhou Public Welfare Science and Technology Pro- gram (no. Y20160381)." COMMENTSThe study seems free of other sources of bias

Weatherstone 1993

Methods	RCT
Participants	30 male NB; BW >/= 2500 g; FT; Apgar >/= 7; 6-72 hr age
Interventions	0.5 g 30% lidocaine cream (n=15) placebo cream (n=15) applied 20 min prior to circumcision and covered with occlusive dressing
Outcomes	HR, RR, O2 sat, BP, Newborn Pain Behavior Scale, serum B-endophin (15 min post), serum lidocaine
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	By computer-generated randomization,parental consent was ob- tamed. By computer-generated randomization, 15 subjects were assigned to receive a topical application of 30% lidocaine in acid mantle cream (treatment group) 20 minutes prior to circumcision and 15 subjects were assigned to receive the acid mantle cream alone (placebo group). Both pharmaceutical preparations were compounded.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	the placebo or lidocaine cream (approximately 0.5 g) was applied to the penis using gloved hands to avoid detection of the anesthetic by the investigator. A small piece of plastic wrap was then applied over the cream to form an occlusive dressing and the diaper was secured. The newborn was monitored forCOMMENTSPersonnel were likely blinded.
Blinding of outcome assessment (detection bias)	Low risk	the newborn was scored for behavioral state, leg movement, arm movement, facial expression, torso movement, respiratory pattern, soothability re- sponse to distress by caregivers, and tactile stimulation. The tapes were viewed in 30-second intervals (15 seconds of observation and 15 seconds of recording scores) by blinded observers. Interobserver reliabifity of scoring onCOMMENTSLikely outcome assessors were blinded.
Incomplete outcome data (attrition bias)	Unclear risk	twelve subjects in the lidocaine group and 13 in the placebo group had complete analysis of the video recordingsCOMMENTSNo analysis of the impact of not analysing the patients in the group they were allocated.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcomes
Other bias	Low risk	No reasons to suspect other sources of bias.

Weksler 2005

Methods	RCT
Participants	100 ASA I and II boys aged 3 to 8 years undergoing circumcision for religious reasons; day surgery. Setting: hospital in Israel
Interventions	CAUDAL versus DNPB Caudal (n = 50): 1 ml/kg body weight of 0.25% bupivacaine (up to 20 ml), in lateral position. DNBP (n = 50): bupivacaine (0.5% 0.2 ml/kg) injected into the two compartments of the subpubic space, with an additional ventral infiltration of a small volume of bupivacaine (0.1 ml/kg) along the raphe of the penis.
Outcomes	Pain (five point face pain assessment - excruciating, severe, moderate, some, no pain) - 10-cm VAS. Analgesia (15 mg/kg of oral paracetamol given as postoperative pain relief for severe or excruciating pain). Rescue analgesia (paracetamol in recovery room). Any analgesia (assumed that 2 boys who had rescue analgesia (in the caudal group) were different boys from the 10 who had paracetamol at home). Induction-incision time (time interval from the beginning of the halothane administration until the beginning of surgery). Complications: haematoma at base of penis motor block

	tachycardia phonation movement Nausea and vomiting Time to discharge Parental satisfaction (10-cm VAS: 0 = not satisfied at all to 10 = extraordinarily satisfied).
Notes	Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "One hundred consecutive ASA I and II children aged from 3 to 8 years undergoing circumcision for religious reasons were enrolled in this study and allocated to two groups of 50 patients each by a lottery of closed envelopes.allocated to two groups of 50 patients each by a lottery of closed envelopes." COMMENTS: Lottery of closed envelopes.
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "study and allocated to two groups of 50 patients each by a lottery of closed envelopes." COMMENTS: Closed envelops
Blinding of participants and personnel (performance bias)	Unclear risk	COMMENTS: Blinding not feasable and not described.
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "Immediately after surgery, the children were trans- ferred to the recovery room where a nurse who was unaware of the study protocol applied the five-point Faces Pain Assessment Ruler [9] (Fig. 1) when the child was fully awake for pain intensity self-assessment." COMMENTS: Parents also reported the need for paracetamol at home (it is not clear if they were blinded or not).
Incomplete outcome data (attrition bias)	Low risk	COMMENTS: Seems that all children are included in analysis
Selective reporting (reporting bias)	Low risk	COMMENTS: No protocol available. It seems that the study report on all relevant outcomes (not heart rate or oxygen saturation)
Other bias	Low risk	COMMENTS: The study seems to be free from other sources of bias.

White 1983

Methods	RCT
Participants	50 boys aged 2-12 years undergoing circumcision for medical indications as day patients. Exclusion criteria: none noted. Setting: UK
Interventions	CAUDAL versus DNPB Caudal (n = 23): 0.5% bupivacaine 0.5 ml/year of age. DNPB: bupivacaine 0.5% 0.2 ml/kg.
Outcomes	Pain: Need for rescue analgesia assessed by anaesthetist in recovery. Criteria for rescue analgesia not stated. Time to first evidence of pain. Need for paracetamol after discharge, quality of night's sleep (questionnaire returned by patient's family). Other Outcomes: Incidence of leg weakness and haematoma.
Notes	Abstract. Please see Cyna AM, Middleton P. Caudal epidural block versus other methods of postoperative pain relief for circumcision in boys. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD003005

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	SUPPORTING ANNOTATIONS: "They were randomly allocated to one of two groups to receive caudal or penile block immediately before surgery." COMMENTSLikely random allocation however unclear sequence generation
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information about allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	SUPPORTING ANNOTATIONS: "analgesia was assessed continuously for five hours by the anaesthetist (JW) who had conducted the preoperative interview and induced anaesthesia; she had then left the anaesthetic room so that she did not know which type of analgesia had been used." COMMENTS: Participants/parents likely blinded due to procedure and JW likely blinded. Participants/parents likely blinded due to procedure and JW likely blinded
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "analgesia was assessed continuously for five hours by the anaesthetist (JW) who had conducted the preoperative interview and induced anaesthesia; she had then left the anaesthetic room so that she did not know which type of analgesia had been used. Before the child left hospital his parents received a form for assessment of

		analgesia at home and some paracetamol. The table shows the results. The time from administration of the block to first evidence of pain was assessed by the anaesthetist (in hospital) or parent (at home), the need for supplemental analgesia in hospital (papa- veretum) by the anaesthetist, and the quality of the night's sleep and need for paracetamol after discharge by the parents. Statistical analysis was per- formed using a single tailed t test and x2 tests with Yates's correction."
Incomplete outcome data (attrition bias)	Unclear risk	COMMENTS: No information about attrition. Likely no missing data nor drop outs. No information about attrition. Likely no missing data nor drop outs
Selective reporting (reporting bias)	Low risk	COMMENTS: Not reffering to a protocol but report relevant outcomes No protocol however, relevant outcomes reported. No information about how outcomes (pain and quality of sleep) were monitored.
Other bias	Low risk	COMMENTS: No reasons to suspect other sources of bias

Williamson 1983

Methods	RCT
Participants	30 male NB; BW = 2500 - 4000 g; 24 - 72 hr age; FT; Apgar score > 7; systolic BP > 40 mm Hg
Interventions	0.6 to 0.8 1% ml lidocaine DPNB (n=20) no treatment control (n=10) 4 min WT
Outcomes	TcpO2, time cry; HR, RR
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	RTICLES 37 domly assigned to the test group and ten to the control group, by the assignment of each eligible cluster of three in the order: control, anesthetized, and anesthetized. Ten unanesthetized infants had previously been studied during circumcision by Rawlings et al5; therefore, only ten additional con- trol infants were included. The mean values for each of the screening criteria by group are shown in Table 1. There was no significant difference be- tween groups for any of the entry data categories. Each infant studied was continuouslyCOMMENTSsequence generation not described
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	No information about blinding
Blinding of outcome assessment (detection bias)	Unclear risk	ontinuous changes from the five-minute base line in the transcutaneous Po2, heart rate, respira- tory rate, and crying were recorded for each infant in 30-second intervals. Group means were compared byCOMMENTSNo information about blinding of outcome assessors Objective measures
Incomplete outcome data (attrition bias)	Low risk	No information about missing data. Likely no drop outs.
Selective reporting (reporting bias)	Low risk	Not reffering to a portocol but report on relevant outcomes No protocol. Apparently thorough outcome reporting of PO2, HR, respiration and crying.
Other bias	Low risk	each eligible cluster of three in the order: control, anesthetized, and anesthetized. Ten unanesthetized infants had previously been studied during circumcision by Rawlings et al5; therefore, only ten additional con- trol infants were included. The mean values for each of the screening criteria by group are shown in Table 1. There was no significant difference be- tween groups for any of the entry data categories. Each infant studied was continuously monitored

Williamson 1986

Methods	RCT
Participants	24 male NB; Apgar > 7; BW 2500 - 4500 g; FT; 24 - 72 hr age; normal physical exam
Interventions	lidocaine DPNB (n= 11) no treatment control (n=13) 5 min WT
Outcomes	plasma cortisol pre and 30 min post circumcision
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "13 infants were assigned by a random numbers table to Group A, controls who were circumcised 13 infants were assigned by a random numbers table to Group A, controls who were circumcised in the usual manner without anesthesia. Eleven were assigned toare listed in Table 1. There was no difference between the four baseline means (ANOVA, F = 0.39, df = 3, p = >0.05), indicating the infants started in equivalent adrenal states. Both Groups A and B
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	SUPPORTING ANNOTATIONS: "All operations were performed by the principal investigator in an identical manner at approximately the same hour of the afternoon." "The DPNB of Kirya and Werthmann5 5 was administered in Group B at a dose of 2 mg of lidocaine per kilogram of body weight, approximately 5 minutes prior to operation. Both Groups A and B were circumcised in the usual manner by the bloodless circumcision clamp (Gomco) method. All operations were performed by the principal investigator in an identical manner at approximately the same hour of the afternoon."
Blinding of outcome assessment (detection bias)	Low risk	COMMENTS: No information on outcome assessors but report objective measures.
Incomplete outcome data (attrition bias)	Unclear risk	COMMENTS: Unclear if all are inlcuded in analysis. No information. Likely no drop outs and complete data
Selective reporting (reporting bias)	Low risk	COMMENTS: Not reffering to a protocol but report on relevant outcomes
Other bias	Low risk	COMMENTS: No reasons to suspect other sources of bias.

Williamson 1997

Methods	RCT
Participants	30 male NB; FT; >/= 24 hr age; BW 2500- 4500g; Apgar > 7
Interventions	lidocaine DPNB (n=20) no treatment control (n=10)
Outcomes	TcPO2, RR, HR, cardiac rhythm, cry time and type
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Woodman 1999

Methods	RCT
Participants	61 male NB; Apgar > 7; FT; BW > 2500 g; 6-72 hr age
Interventions	1 g (1 ml) LP cream (n=20) 30% lidocaine cream (n=20) placebo cream (n=21) creams applied 1 hr prior and covered with occlusive dressing
Outcomes	HR; time crying; O2sat
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sample characteristics were similar for each study group (Table 1). Differences before the procedure were controlled by randomization. The three groups were not significantly different in birth weight, age, baseline pulse, baseline PO 2, baseline BP, time to complete the procedure, and type of delivery. Apgar scores at 1 and 5 minutes were similar across groups (P .57).The 61 infants were assigned to one of three groups using a computer-generated random list:
Allocation concealment (selection bias)	Unclear risk	No information allocation concealment

Blinding of participants and personnel (performance bias)	Low risk	control), and C (5% lidocaine-prilocaine). The investigator was blinded to the contents of each vial until completion of statistical analysis. Enrollment criteria were listed onAll circumcisions were done by the same operator.COMMENTSInvestigator likely blinded throughout the study.
Blinding of outcome assessment (detection bias)	Low risk	All procedures were coded by the same operator, who was blinded to the analgesics.COMMENTSOperator and investigator likely blinded throughout the study
Incomplete outcome data (attrition bias)	Unclear risk	Isolated data points missed because of gaps in pulse oximeter readouts were excluded.COMMENTSNo information on the proportion of excluded data or the handling of missing data. Likely no drop outs.
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol, but report on relevant outcomes.
Other bias	Low risk	The study seems free of other sources of bias.

Zahorodny 1998

Methods	RCT
Participants	53 healthy male NB
Interventions	1g LP cream + 2 ml 50% sucrose 1g LP cream + 2 ml H2O 1g placebo cream + 2 ml 50% sucrose 1g placebo cream + 2mL H2O creams applied 1 hr prior; sucrose or H2O oral 2 min prior total n=53, allocation not clear
Outcomes	time cry
Notes	abstract only - not possible to assess Risk of Bias. Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	A randomized, double-blind, placebo control trial. Randomization method not described
Allocation concealment (selection bias)	Unclear risk	EMLA or placebo cream was applied 1 hour prior to procedure; sucrose or sterile water was given orally, 2 minutes prior to procedure.
Blinding of participants and personnel (performance bias)	Unclear risk	Only abstract with no information
Blinding of outcome assessment (detection bias)	Unclear risk	Only abstract with no information. Duration of crying during baseline, antiseptic, incision, clamping and dressing phases was determined from videotapes of the procedure and compared
Incomplete outcome data (attrition bias)	Unclear risk	Only abstract with no information
Selective reporting (reporting bias)	Low risk	Not reffering to a protocol but report on relevant outcomes.
Other bias	Low risk	No reason to suspect other bias

Zahorodny 1999

Methods	RCT
Participants	61; healthy male NB
Interventions	10 ml 50% sucrose via pacifier 10 ml H2O via pacifier no treatment control total n=61, allocation not clear
Outcomes	HR, time cry
Notes	Abstract. Not possible to assess RoB. Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	

Zavras 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age*: 7.15 (2.47) years ● *Duration of surgey*: 18.74 (1.24) min ● *Anesthesia duration* : 27.02 (1.1) min intervention 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : kontrol 1 ● *Age*: 6.43 (2.27) years ● *Duration of surgey*: 18.32 (1.25) min ● *Anesthesia duration* : 26.6 (1.2) min kontrol 2 ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : Overall ● *Age*: ● *Duration of surgey*: ● *Anesthesia duration* : **Included criteria:** we enrolled 106 ASA Grade I-II boys in the study, all of whom were scheduled for elective circumcision (ages ranging from 2 to12 years) **Excluded criteria:** Exclusion criteria included a severe systemic disease, neurological and bleeding diseases, and a previous unsuccessful circumcision. **Pretreatment:** No differences between groups at baseline
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Group A (53 patients) received SCRB with 0.25% levobupivacaine (0.5% levobupivacaine diluted in normal saline, Chirocaine®, Abbott Laboratories, Ltd) with a dose of 0.1 ml/kg (total dose 0.5 mg/kg) injected around the base of the penis[7] plus rectal paracetamol of 30 mg/kg ● *Dose*: ● *Duration*: ● *Follow-up time*: intervention 2 ● *Description*: group B (53 patients, control group) received a paracetamol suppository of 30 mg/kg. ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 1 ● *Description*: group B (53 patients, control group) received a paracetamol suppository of 30 mg/kg. ● *Dose*: ● *Duration*: ● *Follow-up time*: kontrol 2 ● *Description*: ● *Dose*: ● *Duration*: ● *Follow-up time*:
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Sequence generation not described
Allocation concealment (selection bias)	Low risk	Judgement Comment: Following induction of anesthesia and before the start of surgery, the children were randomized into two groups, by the closed-envelope technique.

Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Not clear how patients og personnel were blinded to the intervention. Personnel could not be blinded
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: A nurse blinded to group allocation observed the children and assessed outcomes: Pain scores, need for analgesia, post-anesthetic, and surgical complications.
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: It seems all included participants were included in the analysis
Selective reporting (reporting bias)	Low risk	Judgement Comment: Not reffering to a protocol. However, reports on relevant outcomes.
Other bias	Low risk	Judgement Comment: No other sources of bias. Conflict of Interest: None.Der bliver også udført forskellige operationsteknikker.

Zolnoski 1993

Methods	RCT
Participants	20 male NB, 8 - 120 hr age, FT; no maternal medication, BW > 2700 g, 5 min Apgar >/= 7
Interventions	2.4 ml 24% sucrose (n=10) 2.4 ml water via syringe (n=10) given 3 min prior
Outcomes	Cry time; HR
Notes	Please see Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004217.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "infants received sucrose via syringe. Random assignment to groups was accomplished by a lottery-type selection. The numbers 1 15" COMMENTS: randomly assigned to either the treatment group or the control group. Random assignment to groups was accomplished by a lottery-type selection
Allocation concealment (selection bias)	Unclear risk	COMMENTS: No information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	COMMENTS: Both the sucrose and sterile water were placed in the buccal mucosa to prevent aspiration
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "The tapes were later evaluated for the duration of crying in minutes and seconds by a coder who was unaware of 11nvasive" COMMENTS: All data information was collected on a data collection form developed by the researcher .Crying means any audible crying vocalizations exclusive of fussing or whimpering sounds. The tapes were later evaluated for the duration of crying in minutes and seconds by a coder who was unaware of group assignments. The coder was a senior nursing student who had agreed to participate
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "and 3 infants were bottle-fed. All infants who participated in the study were able to complete the study without being eliminated or excluded. Hypotheses Testing The hypotheses were" COMMENTS: all children included in analysis
Selective reporting (reporting bias)	Low risk	Comments: Not reffering to a protocol but report relevant outcomes
Other bias	Low risk	COMMENTS: Master thesis, one author/investigator, pilot study.

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

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Unpublished data only

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Data and analyses

1 DPNB versus no treatment or sham

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Pain score	3	135	Std. Mean Difference (IV, Random, 95% CI)	-1.76 [-2.31, -1.21]
1.1.1 infant irritability score	1	49	Std. Mean Difference (IV, Random, 95% CI)	-1.70 [-2.36, -1.03]
1.1.2 modified behavioral pain scale (MBPS)	1	48	Std. Mean Difference (IV, Random, 95% CI)	-1.37 [-2.00, -0.74]
1.1.3 author-created behavioural score	1	38	Std. Mean Difference (IV, Random, 95% CI)	-2.40 [-3.25, -1.54]
1.2 Cry time (by unit)	7	249	Std. Mean Difference (IV, Random, 95% CI)	-1.76 [-2.06, -1.46]
1.2.1 in %	5	163	Std. Mean Difference (IV, Random, 95% CI)	-1.67 [-2.04, -1.29]
1.2.2 in seconds	1	48	Std. Mean Difference (IV, Random, 95% CI)	-1.97 [-2.67, -1.27]
1.2.3 Crying component of behavioural score	1	38	Std. Mean Difference (IV, Random, 95% CI)	-1.92 [-2.70, -1.13]
1.3 Heart rate (by unit)	8	348	Std. Mean Difference (IV, Random, 95% CI)	-1.78 [-2.29, -1.27]
1.3.1 in bpm	3	135	Std. Mean Difference (IV, Random, 95% CI)	-1.60 [-2.00, -1.21]
1.3.2 in bpm change-from-baseline	3	135	Std. Mean Difference (IV, Random, 95% CI)	-1.46 [-2.05, -0.87]
1.3.3 in % change-from-baseline	2	78	Std. Mean Difference (IV, Random, 95% CI)	-3.38 [-7.04, 0.28]
1.4 Heart rate (by wait time)	7	299	Std. Mean Difference (IV, Random, 95% CI)	-1.87 [-2.50, -1.24]
1.4.1 wait time after anesthetic administration </= 5 min	3	158	Std. Mean Difference (IV, Random, 95% CI)	-1.64 [-2.01, -1.27]
1.4.2 wait time after anesthetic administration > 5 min	3	93	Std. Mean Difference (IV, Random, 95% CI)	-2.44 [-4.49, -0.40]
1.4.3 wait time after anesthetic administration - other wait time reported	1	48	Std. Mean Difference (IV, Random, 95% CI)	-1.98 [-2.69, -1.28]
1.5 Heart rate (by clamp)	9	348	Std. Mean Difference (IV, Random, 95% CI)	-1.84 [-2.39, -1.30]
1.5.1 Gomco	8	316	Std. Mean Difference (IV, Random, 95% CI)	-1.76 [-2.34, -1.19]
1.5.2 Mogen	1	32	Std. Mean Difference (IV, Random, 95% CI)	-2.51 [-3.46, -1.56]
1.6 Oxygen saturation (by unit)	6	293	Mean Difference (IV, Random, 95% CI)	3.38 [0.46, 6.30]
1.6.1 in %	4	165	Mean Difference (IV, Random, 95% CI)	4.44 [0.55, 8.34]
1.6.2 in % change-from-baseline	2	128	Mean Difference (IV, Random, 95% CI)	1.12 [0.40, 1.84]
1.7 Transcutaneous oxygen saturation - change from baseline	1	30	Mean Difference (IV, Random, 95% CI)	9.30 [1.75, 16.85]
1.7.1 torr (TcpO2)	1	30	Mean Difference (IV, Random, 95% CI)	9.30 [1.75, 16.85]
1.8 Respiratory rate (by unit)	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.83, 0.76]
1.8.1 rpm	1	38	Std. Mean Difference (IV, Random, 95% CI)	-0.66 [-1.32, -0.01]
1.8.2 in % change-from-baseline	2	48	Std. Mean Difference (IV, Random, 95% CI)	0.39 [-0.19, 0.96]
1.9 Systolic blood pressure (by unit)	2	68	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-2.96, 0.97]
1.9.1 in mmHg	1	38	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.66, 0.61]
1.9.2 in % change-from-baseline	1	30	Std. Mean Difference (IV, Random, 95% CI)	-2.03 [-2.97, -1.09]
1.10 Serum cortisol (nmol/dL) 30 min post	4	102	Mean Difference (IV, Random, 95% CI)	-70.11 [-142.12, 1.91]
1.11 Salivary cortisol increase (ug/dL) from baseline to 30 min post	1	48	Mean Difference (IV, Random, 95% CI)	-0.54 [-1.08, -0.00]
1.12 B-endorphin (pmol/L)	1	38	Mean Difference (IV, Random, 95% CI)	21.00 [-73.45, 115.45]
1.13 Adverse events	1	38	Risk Ratio (M-H, Random, 95% CI)	Not estimable

2 Ring block versus no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Cry time (by unit)	2	63	Std. Mean Difference (IV, Random, 95% CI)	-1.40 [-2.44, -0.36]
2.1.1 in %	1	23	Std. Mean Difference (IV, Random, 95% CI)	-2.01 [-3.05, -0.98]
2.1.2 in seconds	1	40	Std. Mean Difference (IV, Random, 95% CI)	-0.94 [-1.60, -0.29]
2.2 Heart rate (bpm) change-from-baseline	1	23	Mean Difference (IV, Random, 95% CI)	-29.27 [-52.94, -5.60]
2.3 Oxygen saturation (%) change-from-baseline	1	40	Mean Difference (IV, Random, 95% CI)	3.84 [-0.94, 8.62]
2.4 Respiratory rate (rpm) change-from-baseline	1	40	Mean Difference (IV, Random, 95% CI)	-5.69 [-16.02, 4.64]

3 EMLA versus placebo or no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Pain score	2	86	Std. Mean Difference (IV, Random, 95% CI)	-0.59 [-1.02, -0.16]
3.1.1 neonatal facial coding system (NFCS)	1	27	Std. Mean Difference (IV, Random, 95% CI)	-0.82 [-1.61, -0.03]
3.1.2 NFCS - author-devised summary score	1	59	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-1.01, 0.03]
3.2 Cry time (by unit)	6	189	Std. Mean Difference (IV, Random, 95% CI)	-0.78 [-1.08, -0.48]
3.2.1 in %	3	79	Std. Mean Difference (IV, Random, 95% CI)	-0.81 [-1.40, -0.23]
3.2.2 in minutes	2	51	Std. Mean Difference (IV, Random, 95% CI)	-0.57 [-1.13, -0.01]
3.2.3 percent increase in time crying	1	59	Std. Mean Difference (IV, Random, 95% CI)	-0.95 [-1.49, -0.41]
3.3 Heart rate (by unit)	5	143	Mean Difference (IV, Random, 95% CI)	-14.59 [-19.34, -9.84]
3.3.1 in bpm	3	78	Mean Difference (IV, Random, 95% CI)	-15.80 [-21.50, -10.10]
3.3.2 in bpm change-from-baseline	2	65	Mean Difference (IV, Random, 95% CI)	-13.46 [-26.41, -0.50]
3.4 Oxygen saturation (%)	3	78	Mean Difference (IV, Random, 95% CI)	2.63 [-1.26, 6.51]
3.5 Respiratory rate (rpm)	1	10	Mean Difference (IV, Random, 95% CI)	-4.31 [-20.79, 12.17]
3.6 Systolic blood pressure (mmHg) change-from-baseline	1	38	Mean Difference (IV, Random, 95% CI)	-3.00 [-15.50, 9.50]
3.7 Diastolic blood pressure (mmHg) change-from-baseline	1	38	Mean Difference (IV, Random, 95% CI)	-5.00 [-23.60, 13.60]

4 Topical lidocaine versus placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 Pain score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1.1 % change- from-baseline in time spent in Brazelton state 6 (full cry)	1	25	Mean Difference (IV, Random, 95% CI)	-8.00 [-22.90, 6.90]
4.2 Cry time (s)	2	85	Mean Difference (IV, Random, 95% CI)	-59.75 [-99.14, -20.36]
4.3 Heart rate (bpm)	2	85	Mean Difference (IV, Random, 95% CI)	-9.18 [-14.66, -3.71]
4.4 Oxygen saturation (%)	2	85	Mean Difference (IV, Random, 95% CI)	-0.50 [-1.75, 0.75]
4.5 Respiratory rate (rpm)	1		Mean Difference (IV, Random, 95% CI)	No totals
4.6 B-endorphin (pg/mL)	1	30	Mean Difference (IV, Random, 95% CI)	-49.00 [-88.73, -9.27]

5 Sucrose versus water or no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Pain score	2	87	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-1.46, 0.49]
5.1.1 behavioral distress score	1	40	Std. Mean Difference (IV, Random, 95% CI)	-1.00 [-1.66, -0.33]
5.1.2 modified behavioral pain scale (MBPS)	1	47	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.57, 0.57]
5.2 Cry time (by unit)	5	123	Std. Mean Difference (IV, Random, 95% CI)	-0.30 [-1.16, 0.57]
5.2.1 in %	3	56	Std. Mean Difference (IV, Random, 95% CI)	-1.03 [-2.39, 0.33]
5.2.2 in seconds	2	67	Std. Mean Difference (IV, Random, 95% CI)	0.56 [0.07, 1.04]
5.3 Heart rate (by unit)	3	146	Mean Difference (IV, Random, 95% CI)	-2.45 [-11.01, 6.11]
5.3.1 in bpm	2	67	Mean Difference (IV, Random, 95% CI)	2.16 [-5.45, 9.78]
5.3.2 in bpm change-from-baseline	1	79	Mean Difference (IV, Random, 95% CI)	-9.70 [-17.72, -1.68]

5.4 Oxygen saturation (by unit)	2	126	Mean Difference (IV, Random, 95% CI)	1.26 [-2.68, 5.21]
5.4.1 in %	1	47	Mean Difference (IV, Random, 95% CI)	-0.83 [-3.07, 1.41]
5.4.2 in % change-from-baseline	1	79	Mean Difference (IV, Random, 95% CI)	3.20 [1.59, 4.81]
5.5 Serum cortisol (nmol/dL) 30 min post	1	40	Mean Difference (IV, Random, 95% CI)	68.90 [-53.93, 191.73]

6 Acetaminophen versus placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 Pain / behavior score	2	104	Std. Mean Difference (IV, Random, 95% CI)	0.39 [-0.18, 0.95]
6.1.1 comfort score - change from baseline score at 30 min post	1	44	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.51, 0.67]
6.1.2 Nursing Child Assessment Feeding Scale (NCAFS) - total infant score	1	60	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.14, 1.18]
6.2 Cry time (%)	2	104	Mean Difference (IV, Random, 95% CI)	-2.03 [-9.80, 5.74]
6.3 Heart rate (bpm)	2	104	Mean Difference (IV, Random, 95% CI)	2.27 [-2.89, 7.44]
6.4 Respiratory rate (rpm)	1	44	Mean Difference (IV, Random, 95% CI)	-3.73 [-11.00, 3.54]

7 DPNB versus EMLA

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 Pain score	3	204	Std. Mean Difference (IV, Random, 95% CI)	-0.69 [-1.70, 0.31]
7.1.1 neonatal infant pain scale (NIPS)	2	144	Std. Mean Difference (IV, Random, 95% CI)	-0.79 [-2.66, 1.08]
7.1.2 behavioral distress score	1	60	Std. Mean Difference (IV, Random, 95% CI)	-0.56 [-1.08, -0.05]
7.2 Cry time (%)	1	29	Mean Difference (IV, Random, 95% CI)	-10.00 [-29.74, 9.74]
7.3 Heart rate (by unit)	3	133	Mean Difference (IV, Random, 95% CI)	-16.11 [-40.33, 8.10]
7.3.1 in bpm	1	60	Mean Difference (IV, Random, 95% CI)	-7.90 [-15.52, -0.28]
7.3.2 in bpm change-from-baseline	2	73	Mean Difference (IV, Random, 95% CI)	-20.06 [-60.47, 20.35]
7.4 Heart rate by wait time	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
7.4.1 wait time after anesthetic administration </= 5 min	2	104	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-3.04, 0.33]
7.4.2 wait time after anesthetic administration > 5 min	1	29	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.68, 0.78]
7.5 Respiratory rate (rpm)	1	60	Mean Difference (IV, Random, 95% CI)	-2.90 [-7.47, 1.67]
7.6 Adverse events	3	91	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.07, 18.05]

8 DPNB versus local block

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.1 Serum cortisol (nmol/dL) 30 min post	1	18	Mean Difference (IV, Random, 95% CI)	306.27 [141.33, 471.21]

9 DPNB versus ring block

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
9.1 Cry time (%)	1	26	Mean Difference (IV, Random, 95% CI)	6.33 [-15.94, 28.60]
9.2 Heart rate (bpm) change-from-baseline	1	26	Mean Difference (IV, Random, 95% CI)	4.43 [-14.42, 23.28]

10 DPNB versus sucrose

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
10.1 Pain score	1	47	Mean Difference (IV, Random, 95% CI)	-3.23 [-4.65, -1.81]
10.1.1 modified behavioral pain scale	1	47	Mean Difference (IV, Random, 95% CI)	-3.23 [-4.65, -1.81]
10.2 Cry time (s)	1	47	Mean Difference (IV, Random, 95% CI)	-166.00 [-210.54, -121.46]
10.3 Heart rate (by unit)	2	126	Mean Difference (IV, Random, 95% CI)	-32.85 [-63.89, -1.81]
10.3.1 in bpm	1	47	Mean Difference (IV, Random, 95% CI)	-49.08 [-61.72, -36.44]
10.3.2 in bpm change-from-baseline	1	79	Mean Difference (IV, Random, 95% CI)	-17.40 [-25.47, -9.33]

10.4 Oxygen saturation (by unit)	2	126	Mean Difference (IV, Random, 95% CI)	1.13 [-4.11, 6.38]
10.4.1 in %	1	47	Mean Difference (IV, Random, 95% CI)	3.85 [2.06, 5.64]
10.4.2 in % change-from-baseline	1	79	Mean Difference (IV, Random, 95% CI)	-1.50 [-2.75, -0.25]

11 Ring block versus EMLA

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
11.1 Heart rate (bpm) change-from-baseline	1	27	Mean Difference (IV, Random, 95% CI)	-3.17 [-20.84, 14.50]
11.2 Cry time (%)	1	27	Mean Difference (IV, Random, 95% CI)	-16.33 [-36.15, 3.49]

12 Buffered lidocaine DPNB versus plain lidocaine DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
12.1 Pain score	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1.1 behavioral distress score	1	40	Mean Difference (IV, Random, 95% CI)	0.10 [-0.30, 0.50]
12.2 Cry time (%)	1	194	Mean Difference (IV, Random, 95% CI)	9.00 [-11.71, 29.71]
12.3 Heart rate (bpm)	1	194	Mean Difference (IV, Random, 95% CI)	-4.20 [-10.51, 2.11]
12.4 Oxygen saturation (%)	1	194	Mean Difference (IV, Random, 95% CI)	0.50 [-0.87, 1.87]
12.5 Serum cortisol (nmol/dL) 30 min post	1	40	Mean Difference (IV, Random, 95% CI)	35.80 [-105.62, 177.22]

13 EMLA versus 30% topical lidocaine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
13.1 Cry time (s)	1	40	Mean Difference (IV, Random, 95% CI)	-17.00 [-75.00, 41.00]
13.2 Heart rate (bpm)	1	40	Mean Difference (IV, Random, 95% CI)	-11.88 [-19.40, -4.36]
13.3 Oxygen saturation (%)	1	40	Mean Difference (IV, Random, 95% CI)	-0.17 [-1.44, 1.10]

14 EMLA versus sucrose

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
14.1 Cry time (%)	1	26	Mean Difference (IV, Random, 95% CI)	-10.00 [-26.74, 6.74]
14.2 Heart rate (bpm)	2	101	Mean Difference (IV, Random, 95% CI)	-6.76 [-11.87, -1.65]
14.3 Oxygen saturation (%)	2	101	Mean Difference (IV, Random, 95% CI)	1.02 [-2.42, 4.47]
14.4 Systolic blood pressure (mmHg)	1	41	Mean Difference (IV, Random, 95% CI)	Not estimable
14.5 Diastolic blood pressure (mmHg)	1	41	Mean Difference (IV, Random, 95% CI)	Not estimable
14.6 Respiratory rate (cycles/min) during circumcision	1	60	Mean Difference (IV, Random, 95% CI)	-1.90 [-4.00, 0.20]
14.7 N-PASS score after 5 min	1	60	Mean Difference (IV, Random, 95% CI)	1.40 [0.74, 2.06]
14.8 N-PASS score during circumcision	1	60	Mean Difference (IV, Random, 95% CI)	2.40 [1.85, 2.95]

15 EMLA versus music

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
15.1 Cry time (min)	1	12	Mean Difference (IV, Random, 95% CI)	0.38 [-3.68, 4.44]
15.2 Heart rate (bpm)	1	12	Mean Difference (IV, Random, 95% CI)	2.31 [-15.99, 20.61]
15.3 Oxygen saturation (%)	1	12	Mean Difference (IV, Random, 95% CI)	0.19 [-3.56, 3.94]
15.4 Respiratory rate (rpm)	1	12	Mean Difference (IV, Random, 95% CI)	1.52 [-13.60, 16.64]

16 Music versus no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
16.1 Cry time (min)	1	12	Mean Difference (IV, Random, 95% CI)	-1.58 [-5.81, 2.65]
16.2 Heart rate (bpm)	1	12	Mean Difference (IV, Random, 95% CI)	-7.89 [-41.37, 25.59]
16.3 Oxygen saturation (%)	1	12	Mean Difference (IV, Random, 95% CI)	2.51 [-0.62, 5.64]
16.4 Respiratory rate (rpm)	1	12	Mean Difference (IV, Random, 95% CI)	-5.83 [-21.41, 9.75]

17 Caudal analgesia versus parenteral analgesia

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
17.1 Need for analgesia	4	235	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.12, 1.43]
17.2 Nausea or vomiting	4	235	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.17, 0.01]

18 Bupivacaine + clonidine vs. Bupivacaine (DPNB)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
18.1 Adverse events	1		Risk Difference (IV, Random, 95% CI)	No totals
18.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	-0.60 [-1.13, -0.07]
18.9 Need for analgesia	1	40	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.18, 0.96]

19 Caudal analgesia versus rectal or intravenous

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
19.1 Need for any analgesia (rescue or other)	2	164	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.51, 1.27]
19.2 Need for rescue analgesia	1	124	Risk Ratio (M-H, Random, 95% CI)	4.84 [0.24, 98.88]
19.3 Other analgesia	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
19.3.1 acetaminophen before discharge	1	40	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.35, 1.04]
19.3.2 paracetamol up to 2 hours postop	1	124	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.01, 3.96]
19.3.3 paracetamol on day of operation	1	124	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.75, 1.41]
19.4 Complications	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
19.4.1 nausea and vomiting	2	164	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.14, 5.53]
19.4.2 bleeding	1	124	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.06, 15.14]
19.4.3 bruising of skin/at needle site	1	124	Risk Ratio (M-H, Random, 95% CI)	2.91 [0.12, 69.99]
19.5 Hospital stay	1		Other data	No numeric data
19.5.1 recovery room stay	1		Other data	No numeric data

20 Caudal analgesia versus dorsal nerve penile block

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
20.1 Need for any analgesia (rescue or other)	4	336	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.64, 2.44]
20.2 Need for rescue analgesia	4	336	Risk Ratio (M-H, Random, 95% CI)	2.40 [0.60, 9.59]
20.3 Other analgesia	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.3.1 paracetamol up to 2 hours postop	1	126	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 8.03]
20.3.2 paracetamol on day of operation	1	126	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.68, 1.24]
20.3.3 paracetamol at home	1	100	Risk Ratio (M-H, Random, 95% CI)	1.67 [0.66, 4.24]
20.4 Time to first analgesia demand	3	211	Mean Difference (IV, Random, 95% CI)	2.95 [-73.98, 79.88]
20.5 Pain	6	441	Std. Mean Difference (IV, Random, 95% CI)	0.54 [-0.17, 1.25]
20.6 Complications	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.6.1 nausea and vomiting	6	443	Risk Ratio (M-H, Random, 95% CI)	1.68 [0.76, 3.70]
20.6.2 motor block	3	251	Risk Ratio (M-H, Random, 95% CI)	17.00 [1.01, 286.82]
20.6.3 motor/leg weakness	2	110	Risk Ratio (M-H, Random, 95% CI)	10.07 [1.25, 81.32]
20.6.4 bleeding	3	277	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.08, 2.70]
20.6.5 bruising of skin/at needle site	3	274	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.07, 1.82]
20.6.6 tachycardia	1	100	Risk Ratio (M-H, Random, 95% CI)	2.00 [0.53, 7.56]
20.6.7 phonation	1	100	Risk Ratio (M-H, Random, 95% CI)	3.00 [0.32, 27.87]
20.6.8 movement	1	100	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.06]
20.6.9 eating disturbance	1	57	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.27, 2.97]
20.6.10 sleep disturbance	1	57	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.73, 2.29]
20.6.11 behavioural disturbance	1	57	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.45, 1.85]
20.6.12 urinary retention	1	57	Risk Ratio (M-H, Random, 95% CI)	Not estimable
20.6.13 Aspiration of blood	1	47	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.01, 7.48]
20.6.14 Edema	2	151	Risk Ratio (M-H, Random, 95% CI)	Not estimable

20.6.15 Hematoma	3	241	Risk Ratio (M-H, Random, 95% CI)	Not estimable
20.6.16 uninary retention	3	191	Risk Ratio (M-H, Random, 95% CI)	3.00 [0.13, 69.52]
20.6.17 Postop agitation	3	211	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.05, 5.22]
20.6.18 Numbness of lower limbs	1	90	Risk Ratio (M-H, Random, 95% CI)	9.82 [0.54, 177.19]
20.11 SAE	3	241	Risk Ratio (M-H, Random, 95% CI)	Not estimable
20.12 Heart rate	2	130	Mean Difference (IV, Random, 95% CI)	-1.50 [-10.14, 7.13]

21 Topical vs injectable anaesthesia

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
21.2 Adverse events	1		Risk Ratio (IV, Random, 95% CI)	No totals
21.8 Pain	1	344	Mean Difference (IV, Random, 95% CI)	0.10 [-0.01, 0.21]

22 GA DPNB+bupivacaine vs.GA+morphine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
22.2 Adverse events	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
22.3 Heart rate	1	40	Mean Difference (IV, Random, 95% CI)	-6.80 [-18.00, 4.40]
22.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	-0.12 [-0.76, 0.52]

24 GA+morphine vs. GA+caudal block+bupivacaine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
24.2 Adverse events	0		Risk Ratio (IV, Random, 95% CI)	No totals
24.3 Heart rate	1	40	Mean Difference (IV, Random, 95% CI)	-10.85 [-21.44, -0.26]
24.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	-1.58 [-2.14, -1.02]

25 Caudal morphine 7.5 (with levobupivacaine) vs Caudal morphine 10.0 (with levobupivacaine)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
25.2 Adverse events	1		Risk Ratio (IV, Random, 95% CI)	No totals
25.9 Need for analgesia	1	160	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.78, 2.63]

26 Caudal morphine 7.5 (with levobupivacaine) vs Caudal morphine 15.0 (with levobupivacaine)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
26.2 Adverse events	1	160	Risk Ratio (IV, Random, 95% CI)	0.29 [0.10, 0.83]
26.9 Need for analgesia	1	160	Risk Ratio (M-H, Random, 95% CI)	2.50 [1.17, 5.34]

27 Caudal morphine 10 (with levobupivacaine) vs Caudal morphine 15.0 (with levobupivacaine)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
27.2 Adverse events	1	160	Risk Ratio (IV, Random, 95% CI)	0.71 [0.34, 1.51]
27.9 Need for analgesia	1	160	Risk Ratio (M-H, Random, 95% CI)	1.75 [0.78, 3.94]

28 Midazolam+ketamin vs. fentanyl+licaine+propofol

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
28.1 Serious adverse events	1		Risk Difference (IV, Random, 95% CI)	No totals

29 EMLA vs. EMLA+Sucrose

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
29.3 Heart rate	1	30	Mean Difference (IV, Random, 95% CI)	11.27 [0.39, 22.15]
29.5 Oxygen saturation %	1	30	Mean Difference (IV, Random, 95% CI)	1.15 [-1.15, 3.45]
29.8 Pain	1	30	Mean Difference (IV, Random, 95% CI)	2.40 [1.73, 3.07]
29.11 Crying time (s)	1	30	Mean Difference (IV, Random, 95% CI)	28.90 [18.91, 38.89]

30 EMLA vs EMLA+sucrose+DNPB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
30.2 Adverse events	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
30.3 Heart rate	1	30	Mean Difference (IV, Random, 95% CI)	16.75 [6.07, 27.43]
30.5 Oxygen saturation	1	30	Mean Difference (IV, Random, 95% CI)	2.56 [0.34, 4.78]
30.8 Pain	1	30	Mean Difference (IV, Random, 95% CI)	2.50 [1.83, 3.17]
30.11 Crying time	1	0	Mean Difference (IV, Random, 95% CI)	Not estimable

31 Circumcision: sucrose 50% solution on a premature nipple containing a 2 x 2 cm sterile gauze pad moistened by the fluid versus no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
31.1 Change from baseline in heart rate (beats/min)	1	56	Mean Difference (IV, Random, 95% CI)	-9.70 [-19.82, 0.42]

32 EMLA vs. EMLA+sucrose+ring block

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
32.3 Heart rate	1	30	Mean Difference (IV, Random, 95% CI)	24.03 [14.81, 33.25]
32.5 Oxygen saturation %	1	30	Mean Difference (IV, Random, 95% CI)	1.89 [-0.31, 4.09]
32.8 Pain	1	30	Mean Difference (IV, Random, 95% CI)	3.05 [2.40, 3.70]
32.11 Crying time (s)	1	0	Mean Difference (IV, Random, 95% CI)	Not estimable

33 Circumcision: sucrose (24%) versus EMLA + sucrose (24%)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
33.1 N-PASS score during circumcision	1	60	Mean Difference (IV, Random, 95% CI)	3.00 [2.42, 3.58]
33.2 N-PASS score after 5 min	1	60	Mean Difference (IV, Random, 95% CI)	1.20 [0.49, 1.91]
33.3 Heart rate (beats/min) during circumcision	1	60	Mean Difference (IV, Random, 95% CI)	12.00 [6.62, 17.38]
33.4 Respiratory rate (cycles/min)	1	60	Mean Difference (IV, Random, 95% CI)	0.60 [-1.77, 2.97]
33.5 Oxygen saturation (%) during circumcision	1	60	Mean Difference (IV, Random, 95% CI)	3.40 [2.41, 4.39]

34 Circumcision: sucrose solution (50%) on a premature nipple containing a 2 x 2 cm sterile gauze pad moistened by the fluid versus dorsal penile nerve block (DPNB)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
34.1 Change in heart rate (beats/min) from baseline	1	79	Mean Difference (IV, Random, 95% CI)	17.40 [11.16, 23.64]

35 Circumcision: pacifier dipped in sucrose (24%) + DPNB versus pacifier dipped in water + DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
35.1 Mean Behavioral Distress Scale scores during circumcision	1	40	Mean Difference (IV, Random, 95% CI)	-0.67 [-1.08, -0.26]
35.2 Mean plasma cortisol levels n mol/dL	1	40	Mean Difference (IV, Random, 95% CI)	68.90 [-53.93, 191.73]

36 EMLA+sucrose vs. EMLA+sucrose+DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
36.2 Adverse events	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
36.3 Heart rate	1	40	Mean Difference (IV, Random, 95% CI)	5.48 [-4.42, 15.38]
36.5 Oxygen saturation %	1	40	Mean Difference (IV, Random, 95% CI)	1.41 [0.19, 2.63]
36.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	0.10 [-0.72, 0.92]
36.11 Crying time (s)	1	40	Mean Difference (IV, Random, 95% CI)	4.94 [-3.24, 13.12]

37 EMLA+sucrose VS EMLA+sucrose+RB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate

37.2 Adverse events	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
37.3 Heart rate	1	40	Mean Difference (IV, Random, 95% CI)	12.76 [4.46, 21.06]
37.5 Oxygen saturation %	1	40	Mean Difference (IV, Random, 95% CI)	0.74 [-0.45, 1.93]
37.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	0.65 [-0.16, 1.46]
37.11 Crying time (s)	1	0	Mean Difference (IV, Random, 95% CI)	Not estimable

38 EMLA+sucrose+DPNB vs EMLA+sucrose+RB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
38.3 Heart rate	1	40	Mean Difference (IV, Random, 95% CI)	7.28 [-0.77, 15.33]
38.5 Oxygen saturation %	1	40	Mean Difference (IV, Random, 95% CI)	-0.67 [-1.70, 0.36]
38.8 Pain	1	40	Mean Difference (IV, Random, 95% CI)	0.55 [-0.26, 1.36]
38.11 Crying time (s)	1	0	Mean Difference (IV, Random, 95% CI)	Not estimable

39 Ring block+levobupivacaine+parcetamol vs. paracetamol

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
39.2 Adverse events	0		Risk Ratio (IV, Fixed, 95% CI)	No totals
39.3 Heart rate (bpm)	1	106	Mean Difference (IV, Random, 95% CI)	0.40 [-2.95, 3.75]
39.8 Pain	1	106	Mean Difference (IV, Random, 95% CI)	-0.19 [-0.55, 0.17]
39.9 Need for analgesia	1	106	Risk Ratio (M-H, Random, 95% CI)	Not estimable
39.10 Nausea and vomiting	1	106	Risk Ratio (M-H, Random, 95% CI)	2.00 [0.38, 10.46]

40 LMX4 versus EMLA

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
40.1 Adverse events	1	36	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.05, 5.04]

41 LMX4 versus DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
41.1 Adverse events	1	36	Risk Ratio (M-H, Random, 95% CI)	3.00 [0.13, 69.09]

42 DPNB+Non nutritive sucking VS. DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
42.1 Heart rate (bpm)	1	43	Mean Difference (IV, Random, 95% CI)	-13.00 [-18.49, -7.51]
42.2 Cortisol levels (saliva)	1	43	Mean Difference (IV, Random, 95% CI)	-28.00 [-43.29, -12.71]
42.3 Pain	1	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
42.4 Crying time	1	43	Mean Difference (IV, Random, 95% CI)	-2.10 [-3.58, -0.62]

43 GA versus Penile block

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
43.1 HR (intra-operative)	1	60	Mean Difference (IV, Random, 95% CI)	7.01 [4.56, 9.46]
43.2 Time to food intake	1	60	Mean Difference (IV, Random, 95% CI)	13.50 [-5.48, 32.48]
43.3 Time to rescure analgesia	1	60	Mean Difference (IV, Random, 95% CI)	-275.00 [-384.10, -165.90]
43.4 Adverse events	1	60	Risk Ratio (M-H, Random, 95% CI)	9.00 [0.51, 160.17]

44 Pudendal nerve block versus penile block

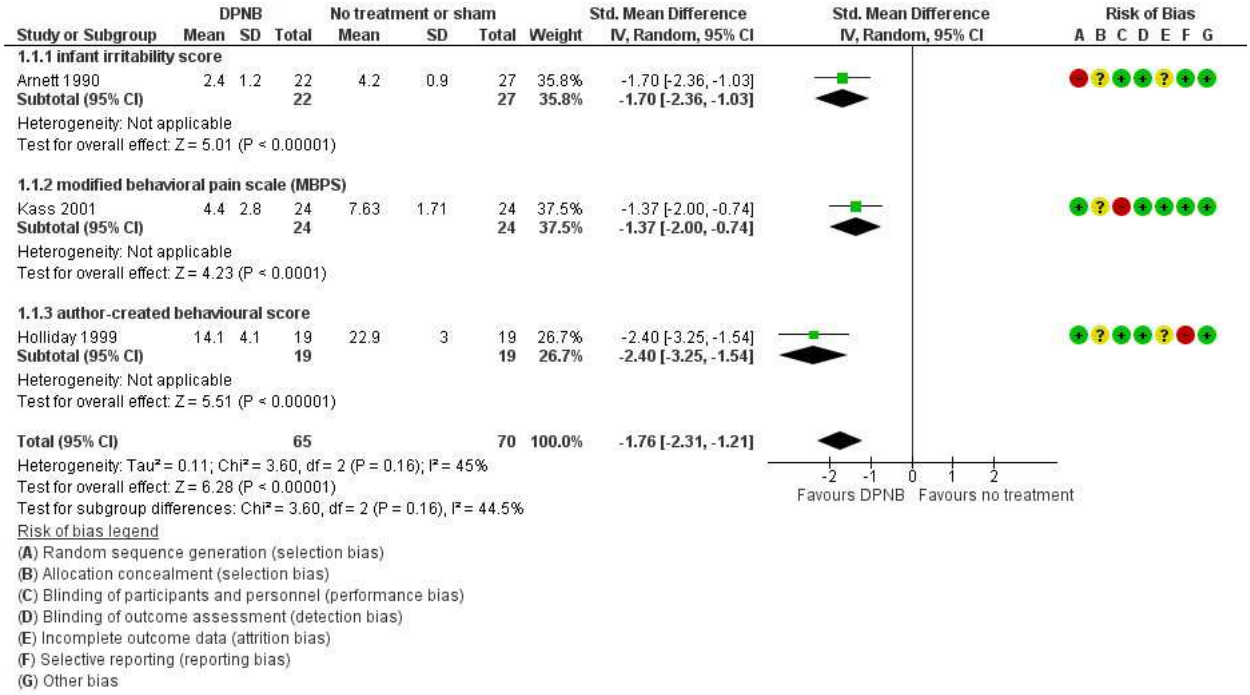
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
44.1 Pain	2	138	Std. Mean Difference (IV, Random, 95% CI)	-1.82 [-4.18, 0.54]
44.2 Additional Analgesia	2	138	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.00, 188.56]
44.3 HR	2	138	Mean Difference (IV, Random, 95% CI)	6.35 [-6.96, 19.67]
44.4 Adverse events	1	60	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.00]

45 ultrasound-guided DPNB versus landmark-guided DPNB

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
45.1 Pain	1	310	Mean Difference (IV, Random, 95% CI)	0.20 [0.14, 0.26]
45.2 Adverse events	1	310	Risk Ratio (M-H, Random, 95% CI)	Not estimable
45.3 Resucures analgesia	1	310	Risk Ratio (M-H, Random, 95% CI)	1.34 [0.96, 1.88]

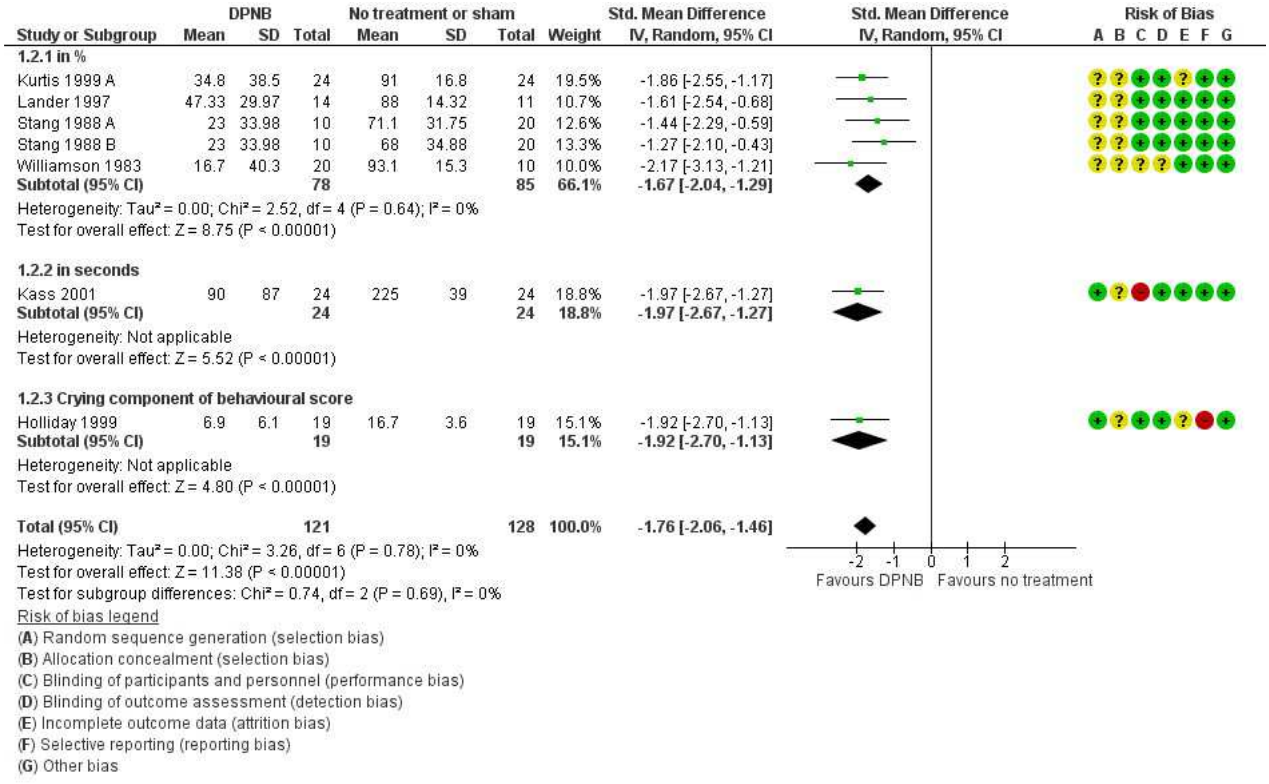
Figures

Figure 1 (Analysis 1.1)



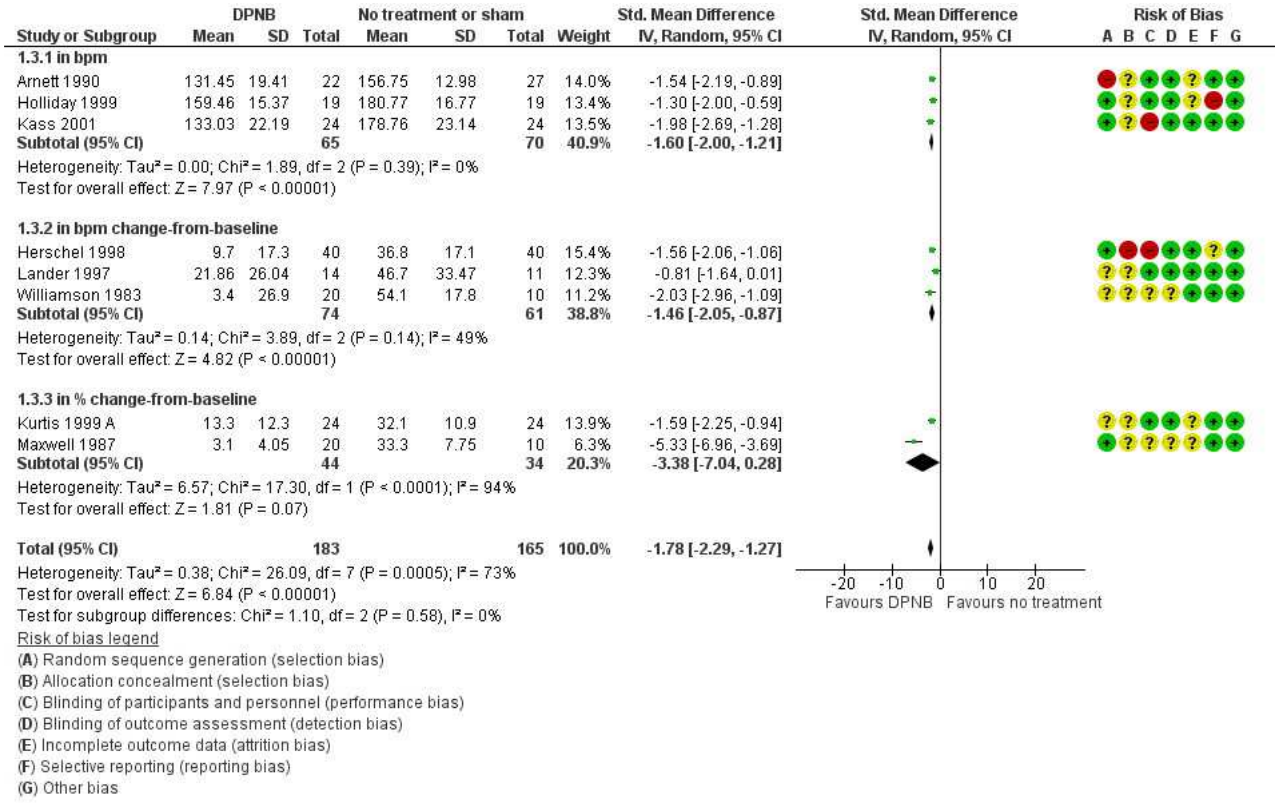
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.1 Pain score.

Figure 2 (Analysis 1.2)



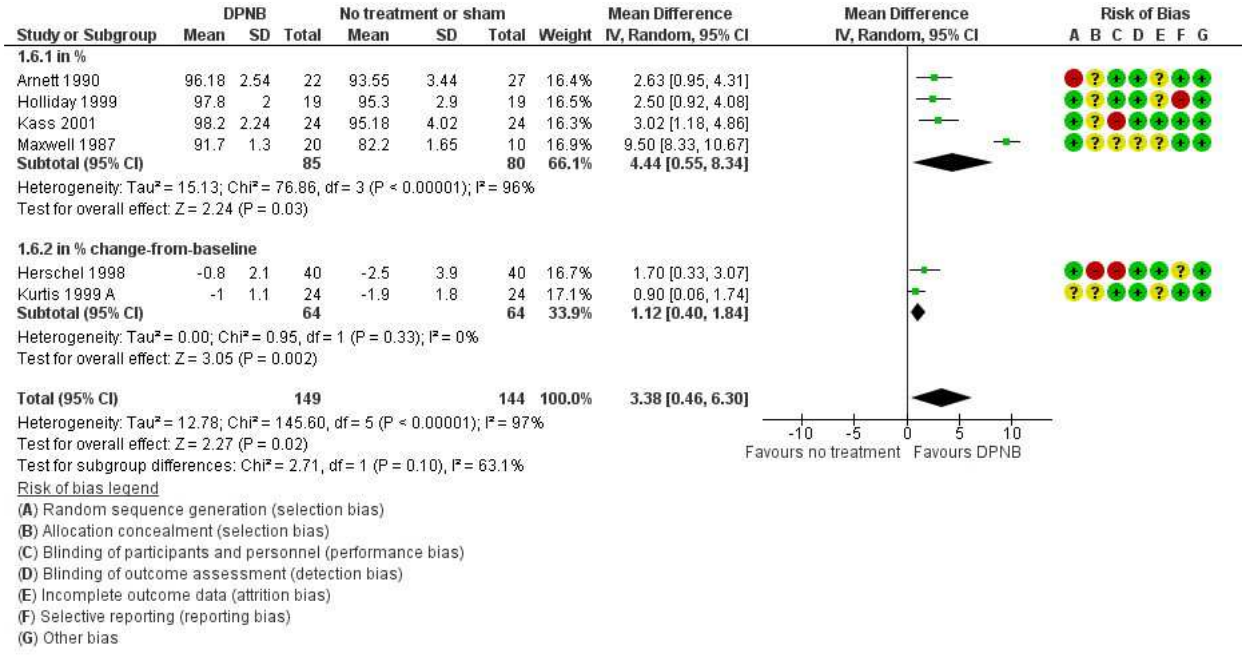
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.2 Cry time (by unit).

Figure 3 (Analysis 1.3)



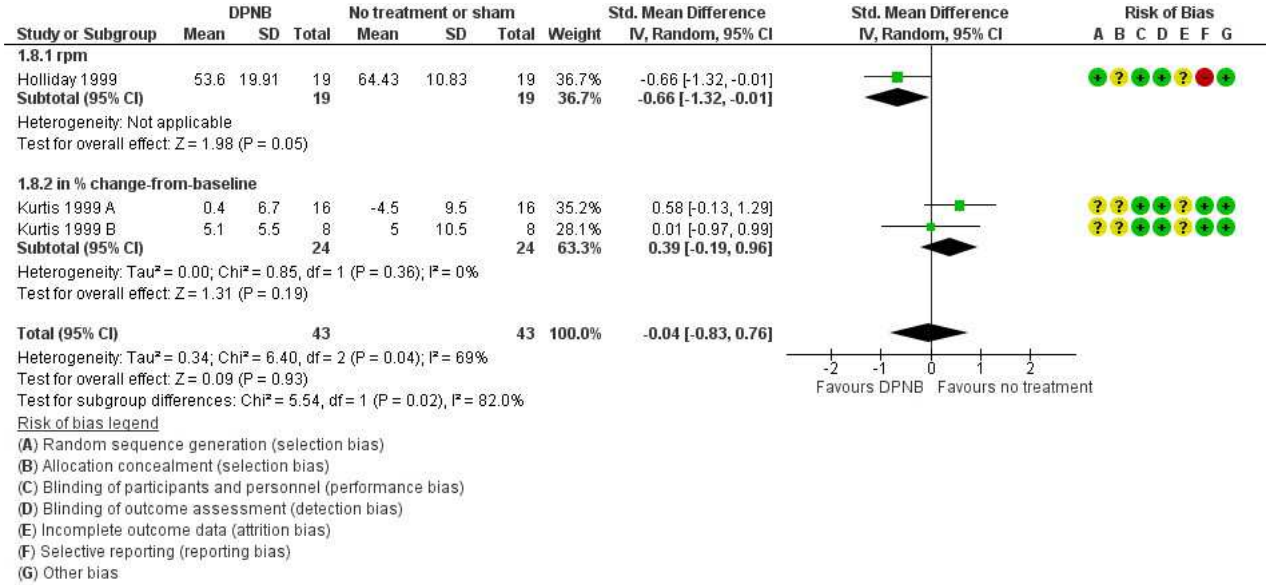
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.3 Heart rate (by unit).

Figure 4 (Analysis 1.6)



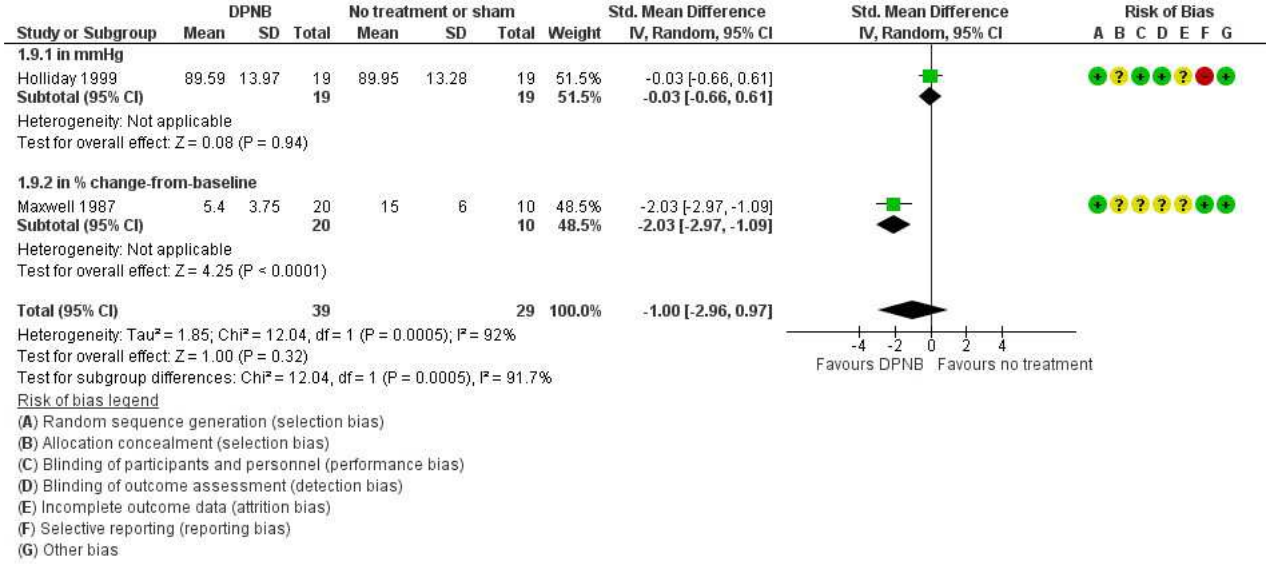
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.6 Oxygen saturation (by unit).

Figure 5 (Analysis 1.8)



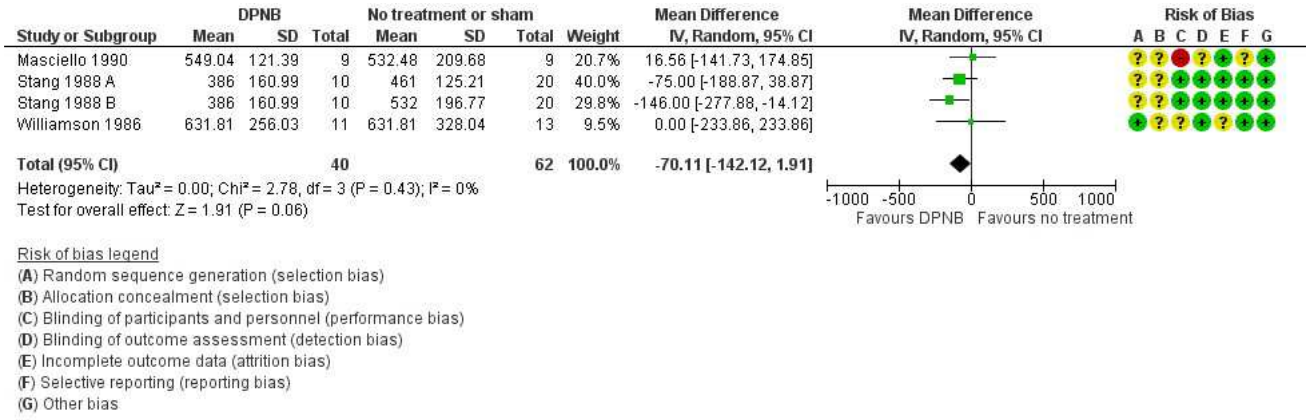
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.8 Respiratory rate (by unit).

Figure 6 (Analysis 1.9)



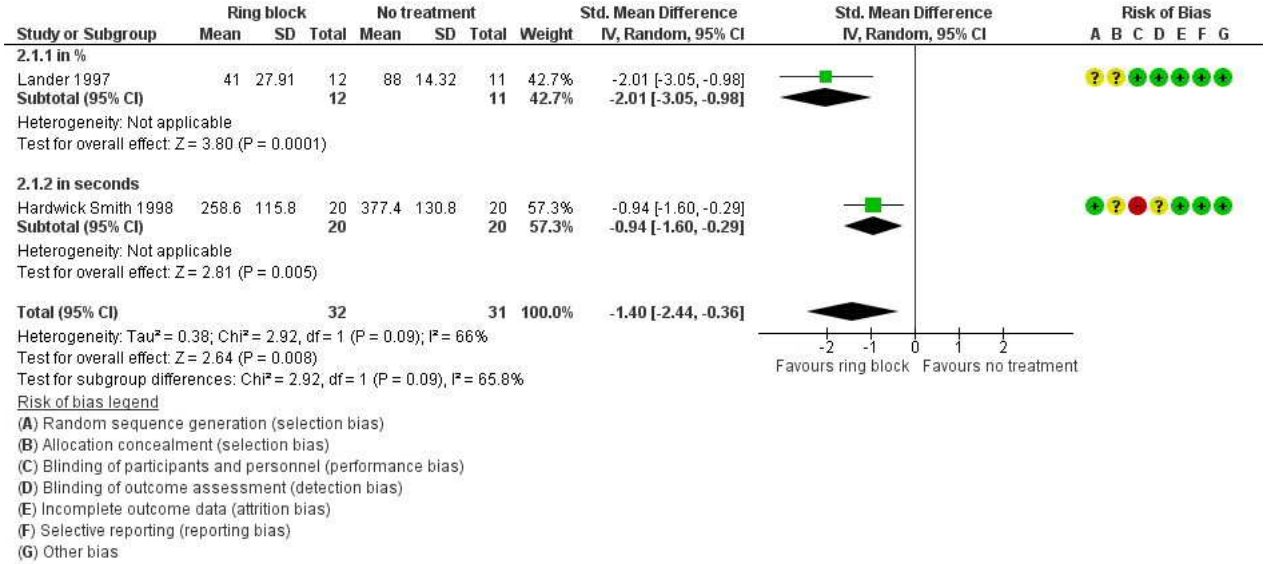
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.9 Systolic blood pressure (by unit).

Figure 7 (Analysis 1.10)



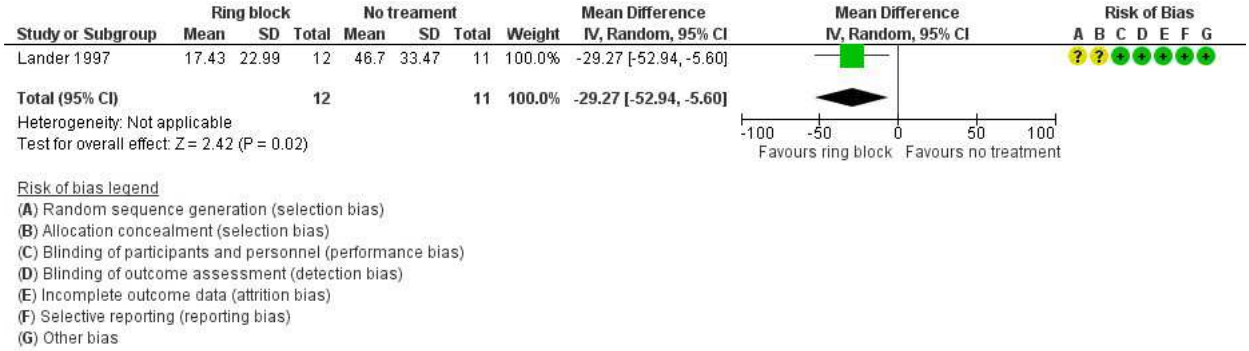
Forest plot of comparison: 1 DPNB versus no treatment or sham, outcome: 1.10 Serum cortisol (nmol/dL) 30 min post.

Figure 8 (Analysis 2.1)



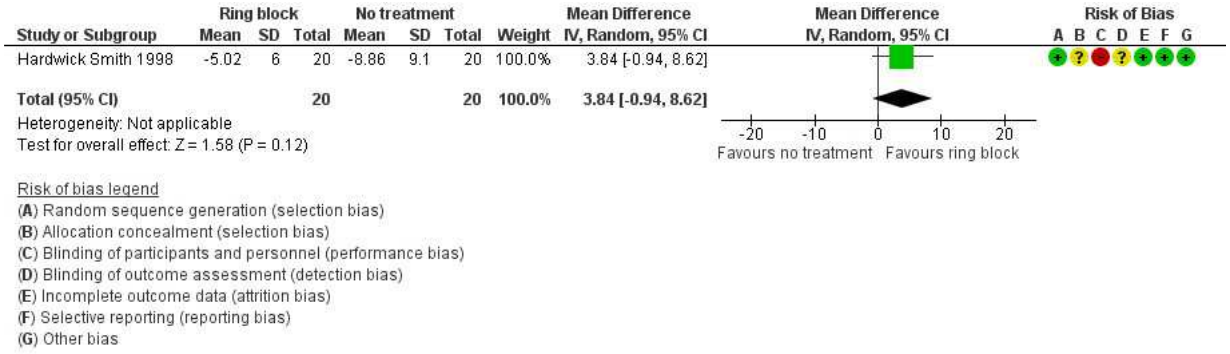
Forest plot of comparison: 2 Ring block versus no treatment, outcome: 2.1 Cry time (by unit).

Figure 9 (Analysis 2.2)



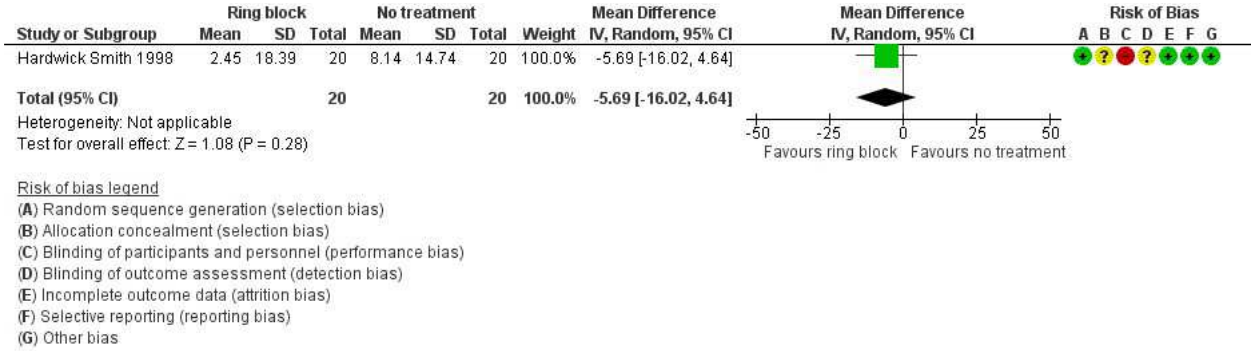
Forest plot of comparison: 2 Ring block versus no treatment, outcome: 2.2 Heart rate (bpm) change-from-baseline.

Figure 10 (Analysis 2.3)



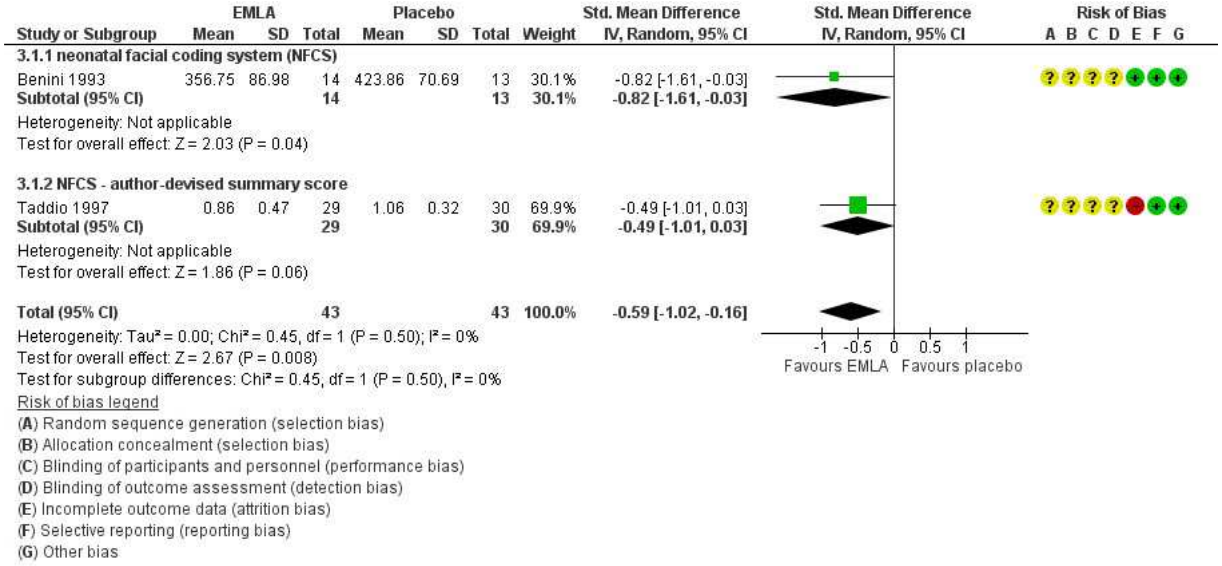
Forest plot of comparison: 2 Ring block versus no treatment, outcome: 2.3 Oxygen saturation (%) change-from-baseline.

Figure 11 (Analysis 2.4)



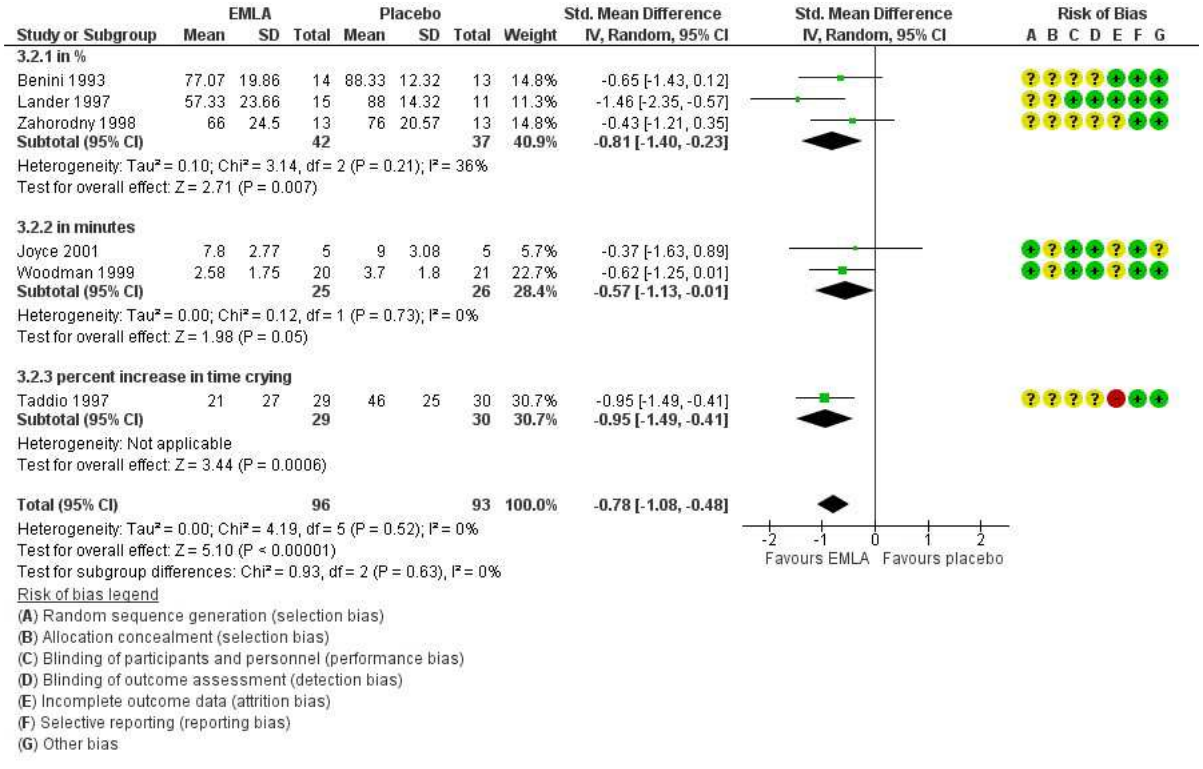
Forest plot of comparison: 2 Ring block versus no treatment, outcome: 2.4 Respiratory rate (rpm) change-from-baseline.

Figure 12 (Analysis 3.1)



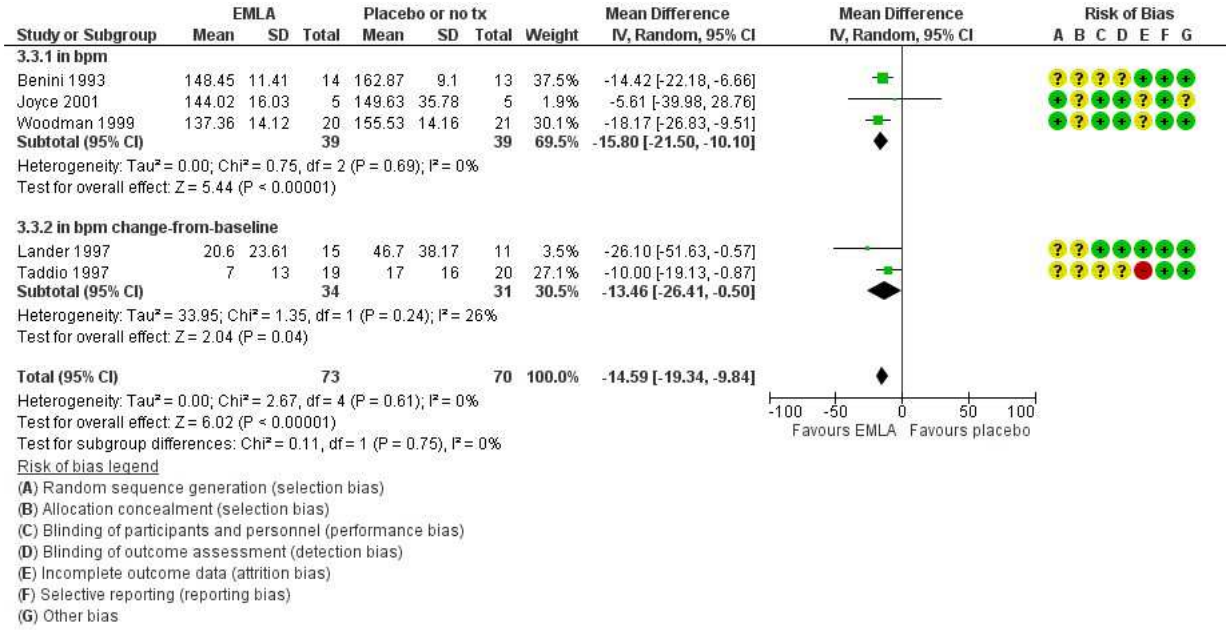
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.1 Pain score.

Figure 13 (Analysis 3.2)



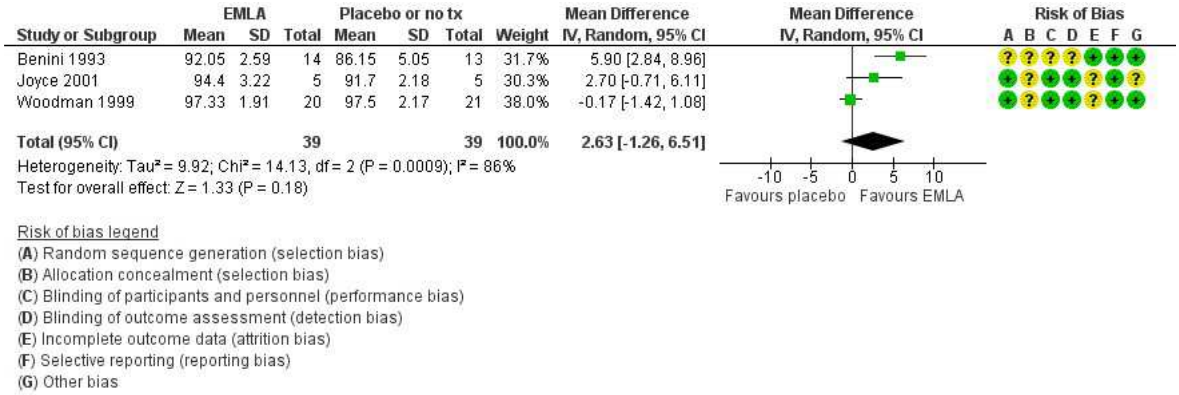
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.2 Cry time (by unit).

Figure 14 (Analysis 3.3)



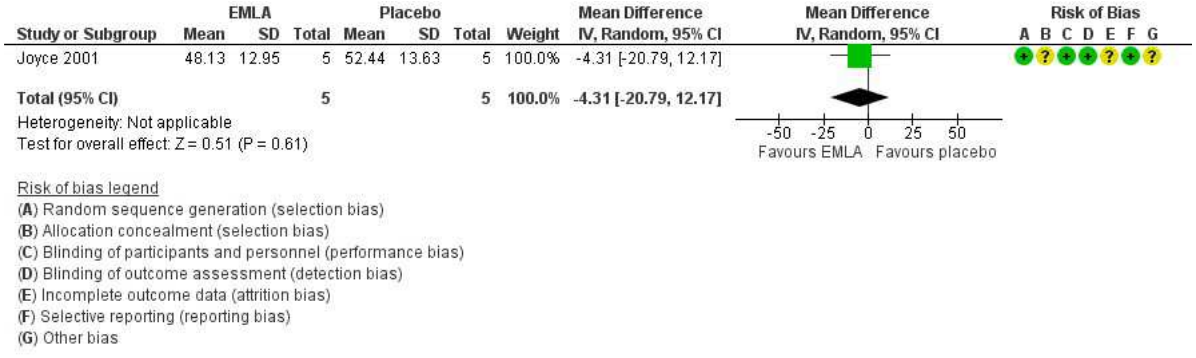
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.3 Heart rate (by unit).

Figure 15 (Analysis 3.4)



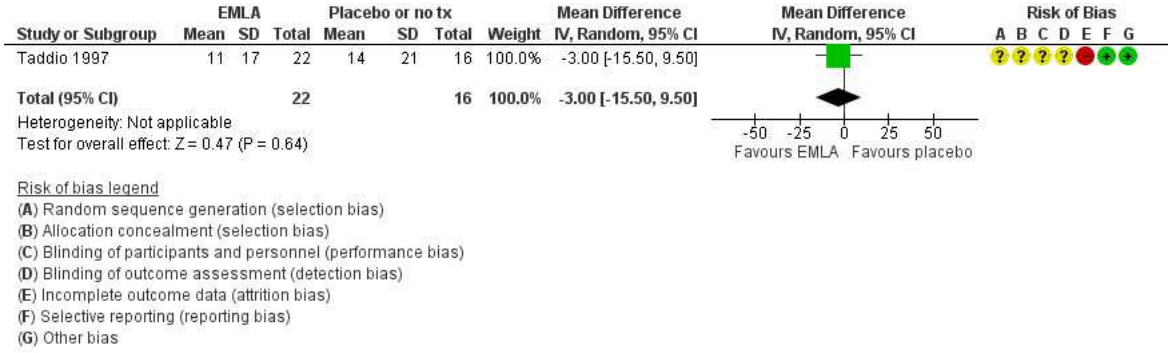
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.4 Oxygen saturation (%).

Figure 16 (Analysis 3.5)



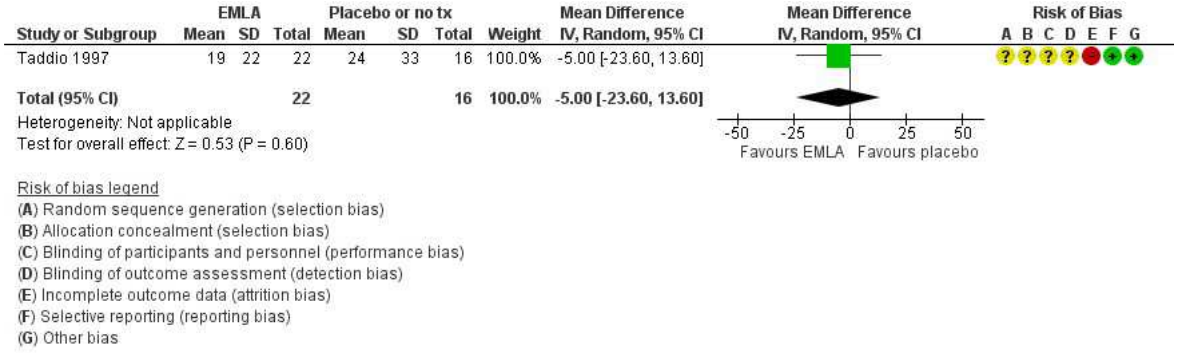
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.5 Respiratory rate (rpm).

Figure 17 (Analysis 3.6)



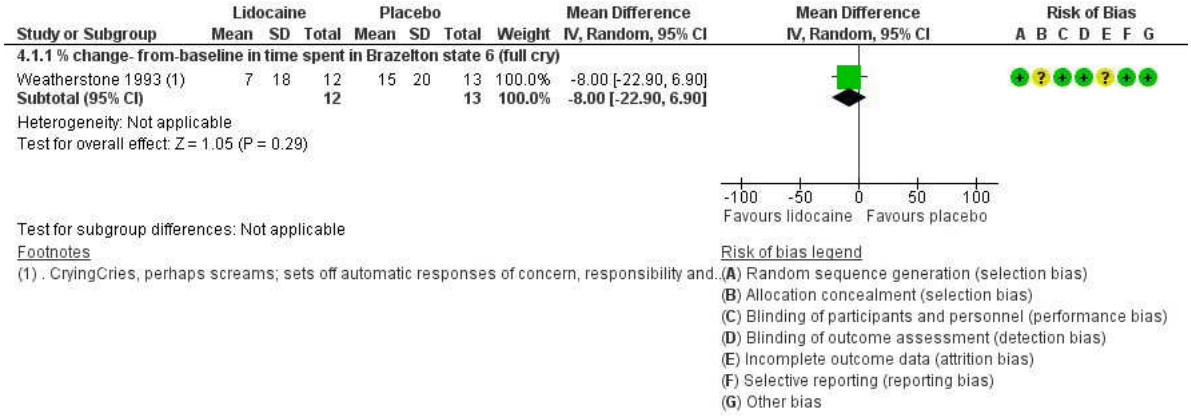
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.6 Systolic blood pressure (mmHg) change-from-baseline.

Figure 18 (Analysis 3.7)



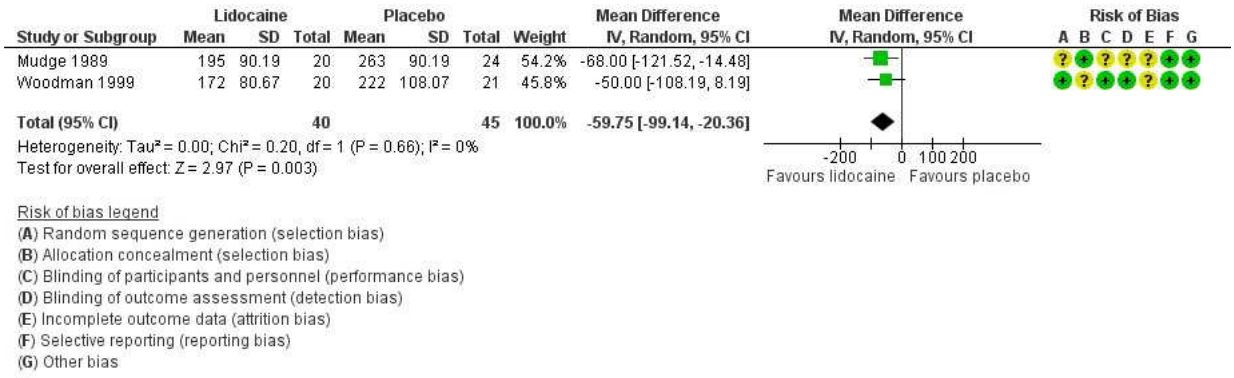
Forest plot of comparison: 3 EMLA versus placebo or no treatment, outcome: 3.7 Diastolic blood pressure (mmHg) change-from-baseline.

Figure 19 (Analysis 4.1)



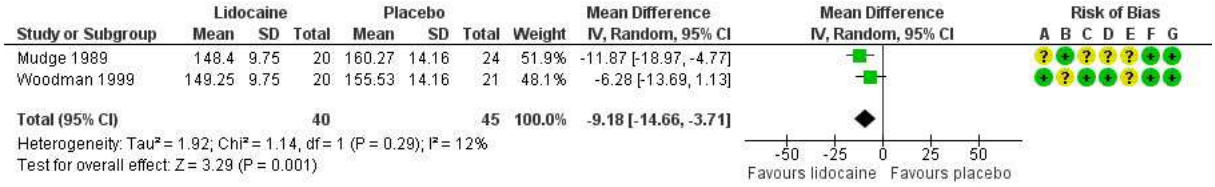
Forest plot of comparison: 4 Topical lidocaine versus placebo, outcome: 4.1 Pain score.

Figure 20 (Analysis 4.2)



Forest plot of comparison: 4 Topical lidocaine versus placebo, outcome: 4.2 Cry time (s).

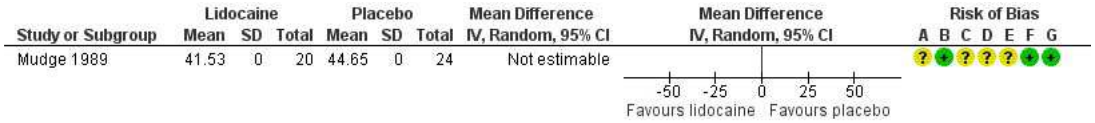
Figure 21 (Analysis 4.3)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 4 Topical lidocaine versus placebo, outcome: 4.3 Heart rate (bpm).

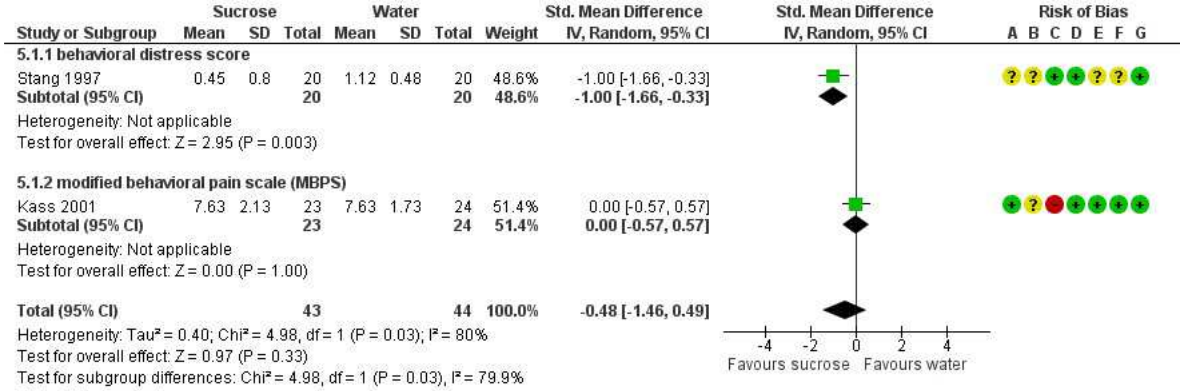
Figure 22 (Analysis 4.5)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 4 Topical lidocaine versus placebo, outcome: 4.5 Respiratory rate (rpm).

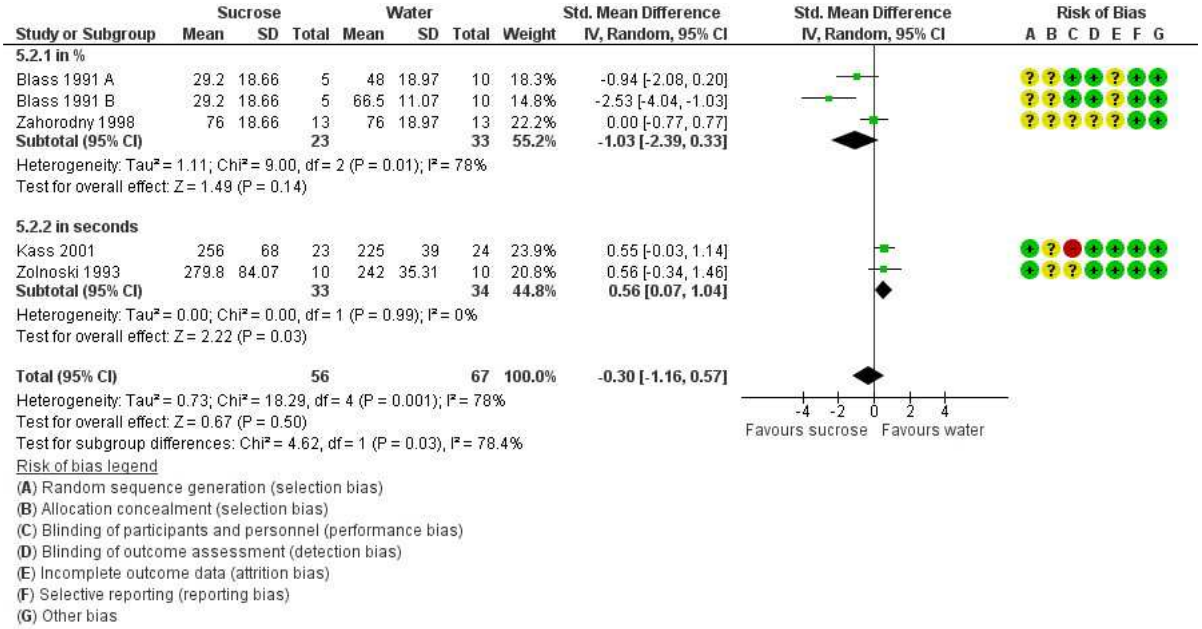
Figure 23 (Analysis 5.1)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

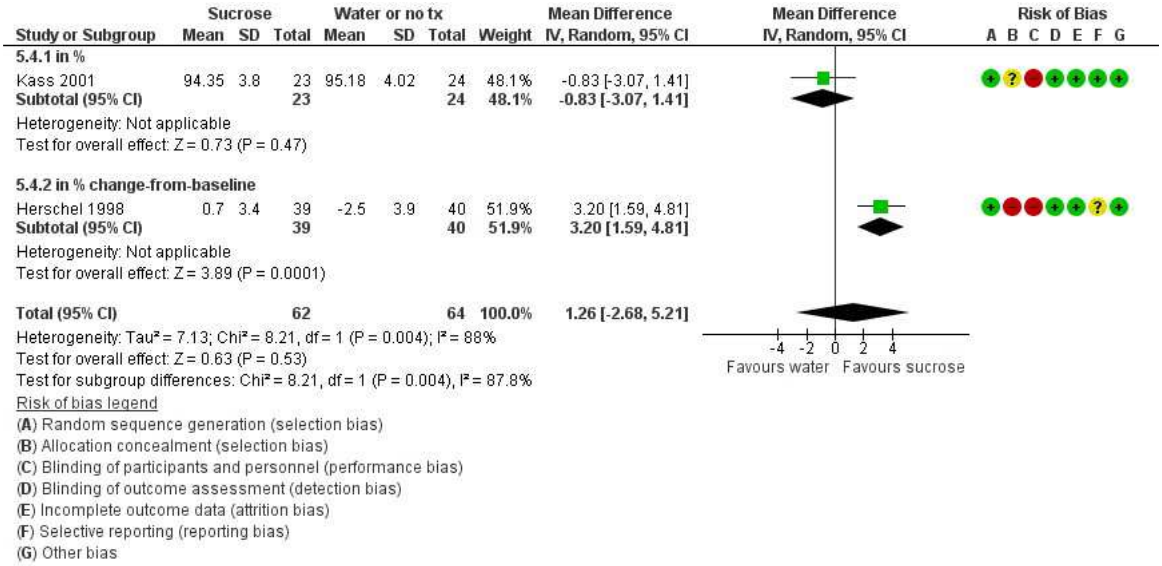
Forest plot of comparison: 5 Sucrose versus water or no treatment, outcome: 5.1 Pain score.

Figure 24 (Analysis 5.2)



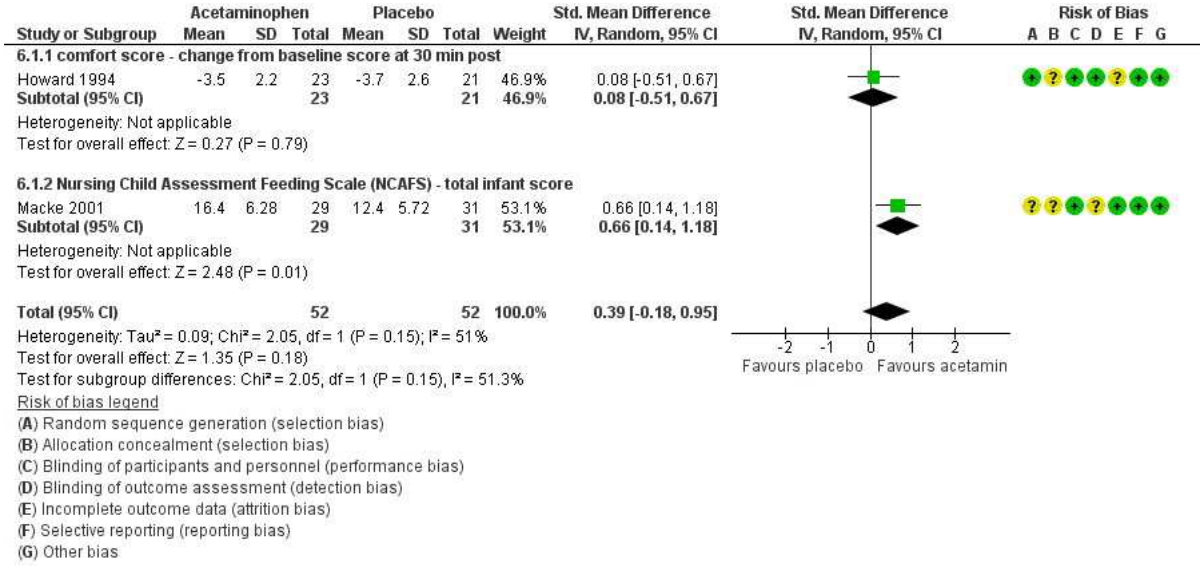
Forest plot of comparison: 5 Sucrose versus water or no treatment, outcome: 5.2 Cry time (by unit).

Figure 25 (Analysis 5.4)



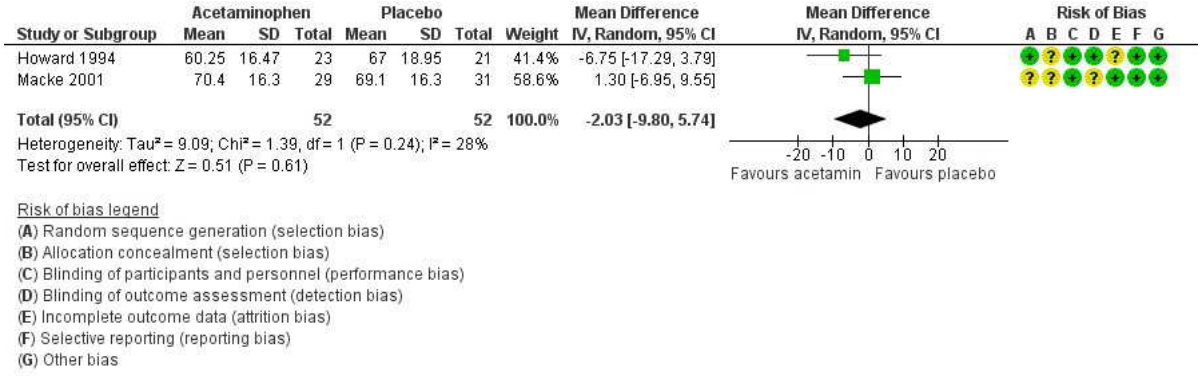
Forest plot of comparison: 5 Sucrose versus water or no treatment, outcome: 5.4 Oxygen saturation (by unit).

Figure 26 (Analysis 6.1)



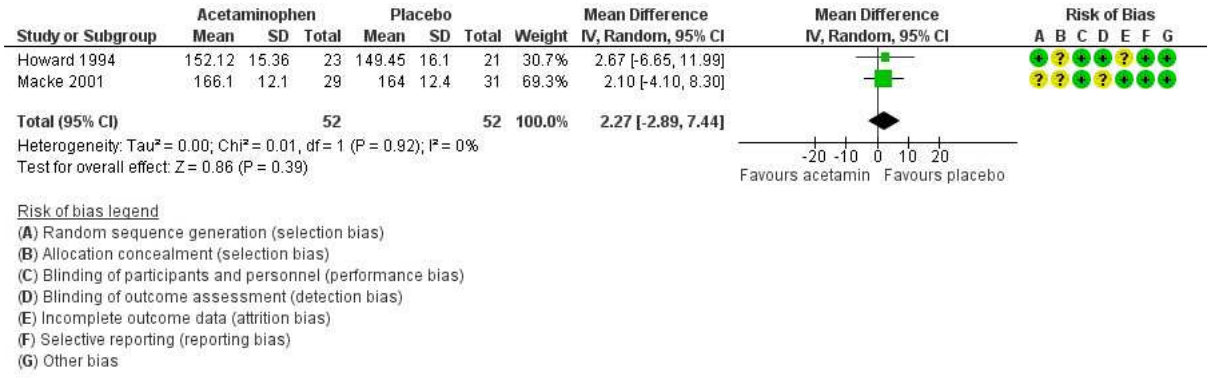
Forest plot of comparison: 6 Acetaminophen versus placebo, outcome: 6.1 Pain / behavior score.

Figure 27 (Analysis 6.2)



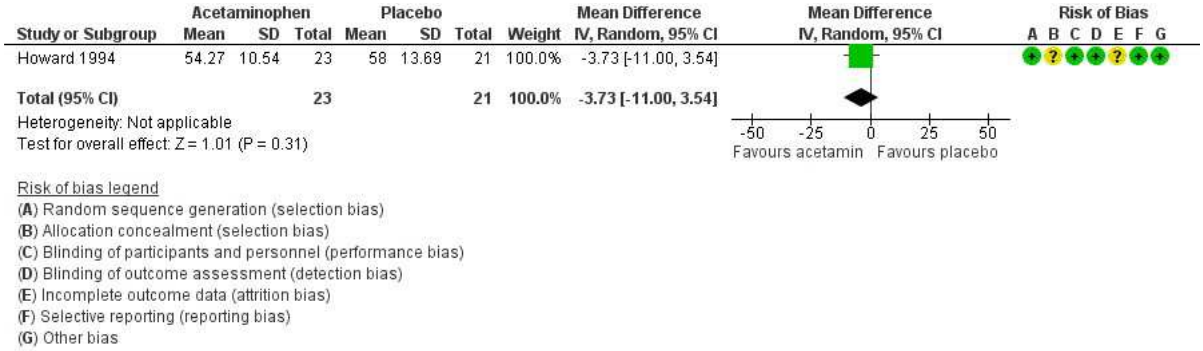
Forest plot of comparison: 6 Acetaminophen versus placebo, outcome: 6.2 Cry time (%).

Figure 28 (Analysis 6.3)



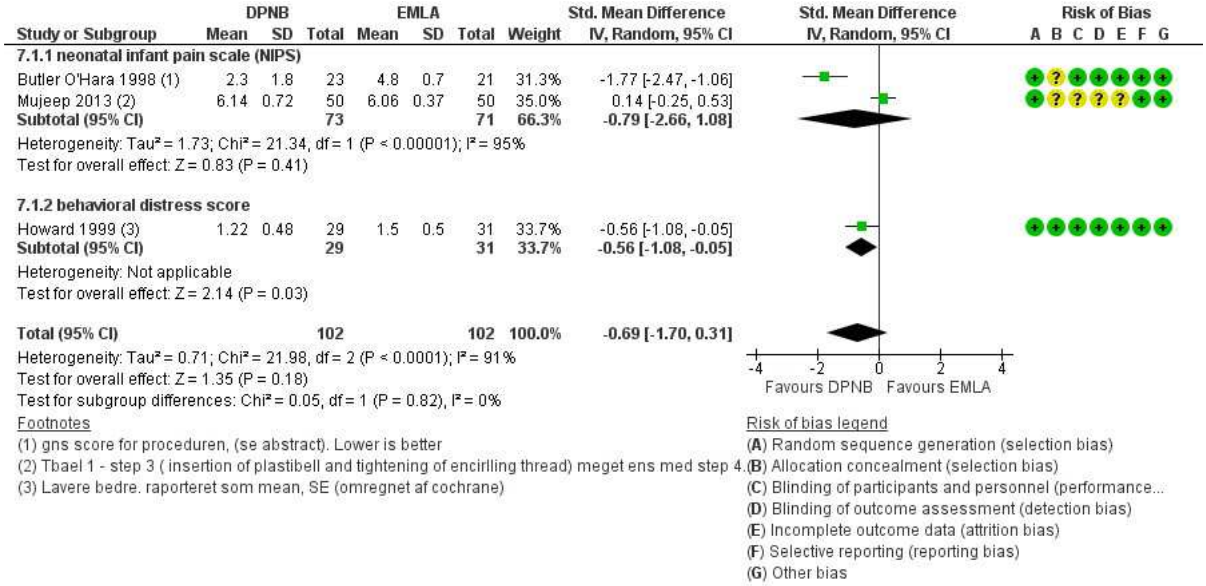
Forest plot of comparison: 6 Acetaminophen versus placebo, outcome: 6.3 Heart rate (bpm).

Figure 29 (Analysis 6.4)



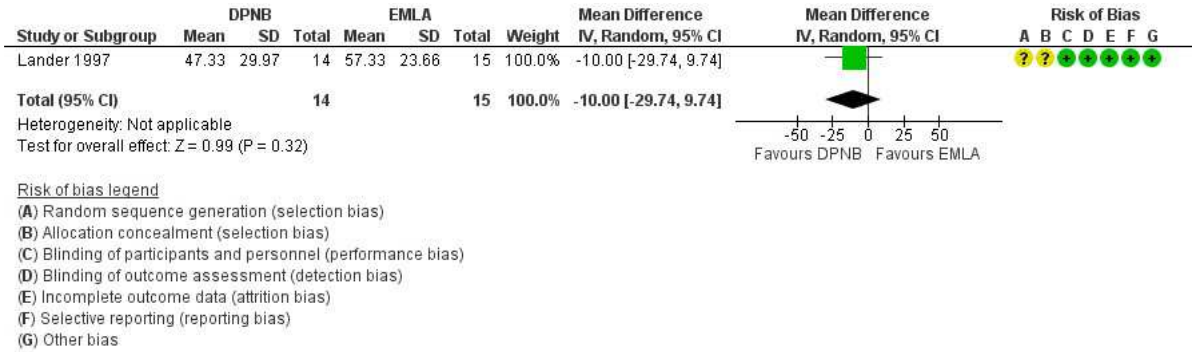
Forest plot of comparison: 6 Acetaminophen versus placebo, outcome: 6.4 Respiratory rate (rpm).

Figure 30 (Analysis 7.1)



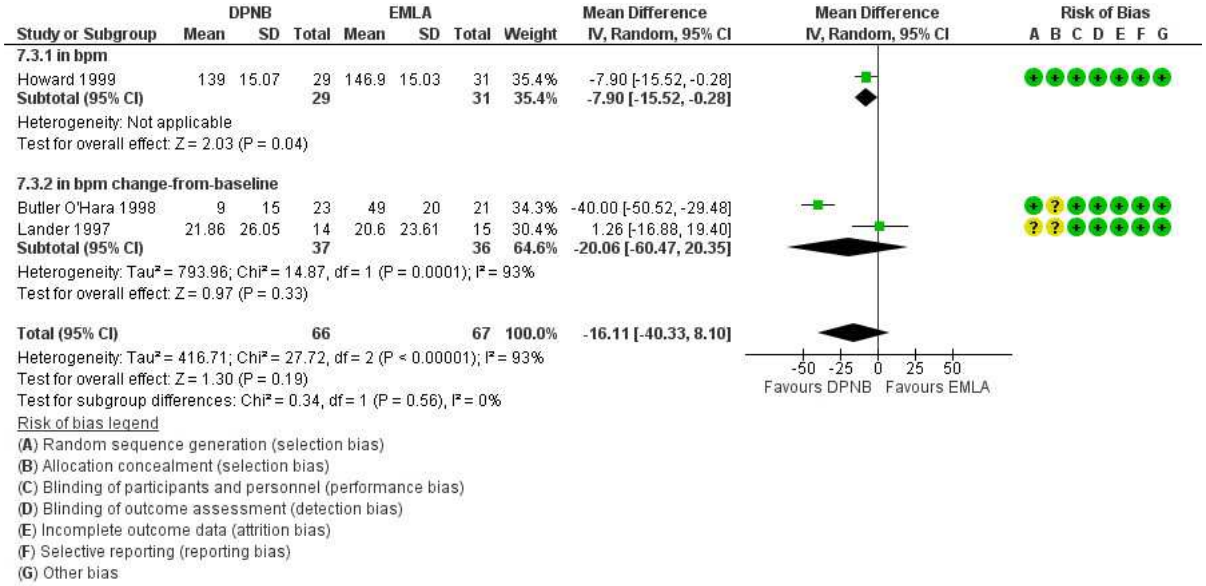
Forest plot of comparison: 7 DPNB versus EMLA, outcome: 7.1 Pain score.

Figure 31 (Analysis 7.2)



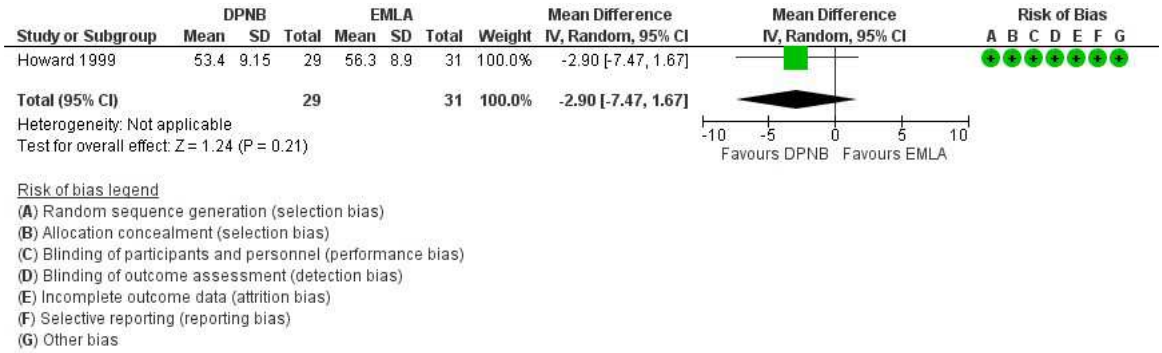
Forest plot of comparison: 7 DPNB versus EMLA, outcome: 7.2 Cry time (%).

Figure 32 (Analysis 7.3)



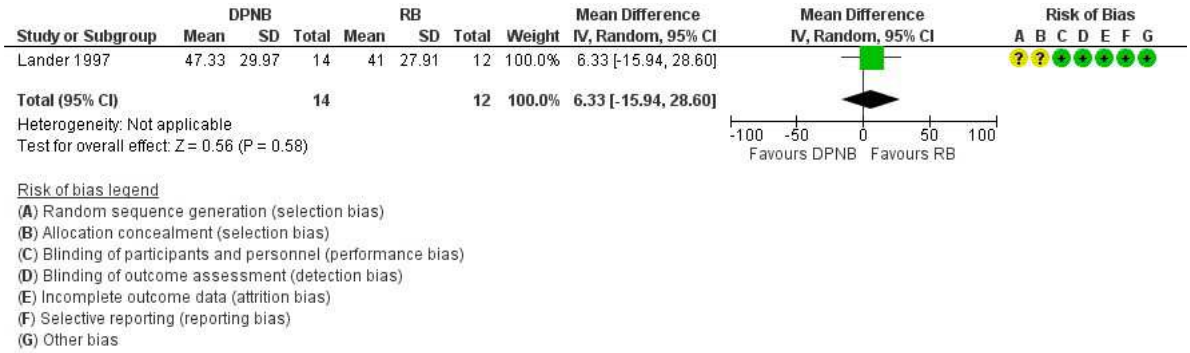
Forest plot of comparison: 7 DPNB versus EMLA, outcome: 7.3 Heart rate (by unit).

Figure 33 (Analysis 7.5)



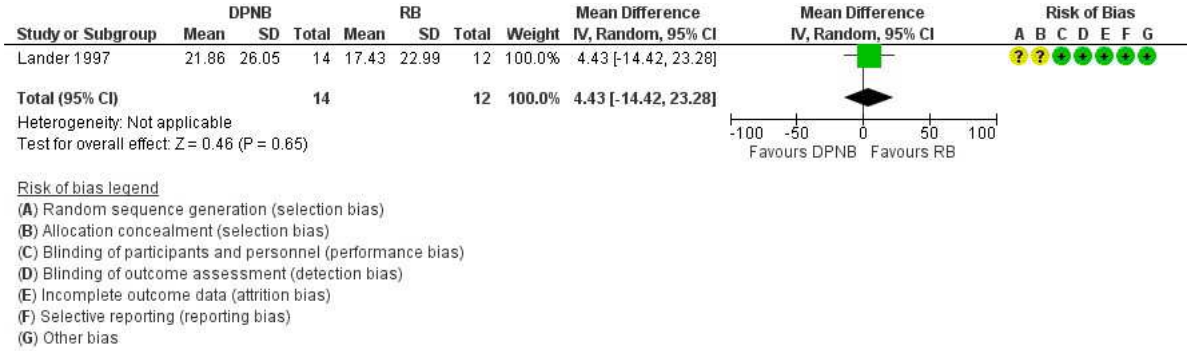
Forest plot of comparison: 7 DPNB versus EMLA, outcome: 7.5 Respiratory rate (rpm).

Figure 34 (Analysis 9.1)



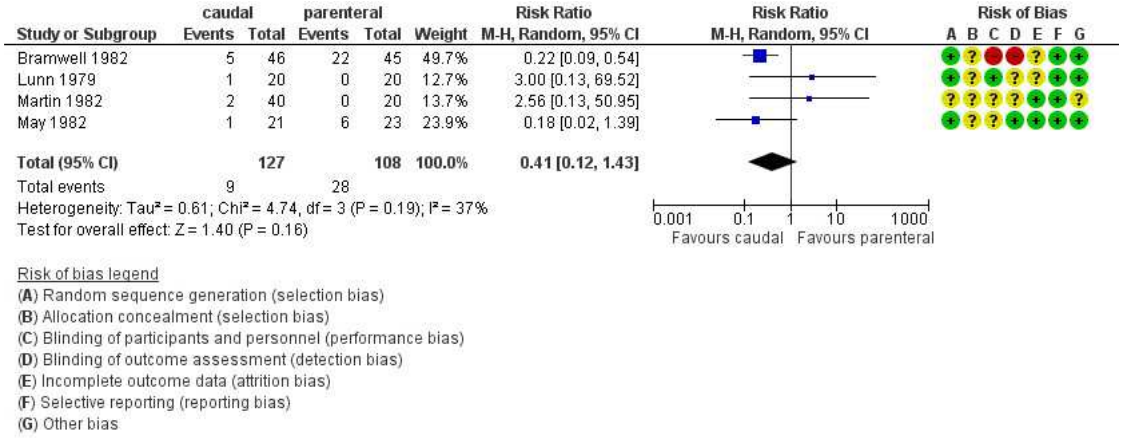
Forest plot of comparison: 9 DPNB versus ring block, outcome: 9.1 Cry time (%).

Figure 35 (Analysis 9.2)



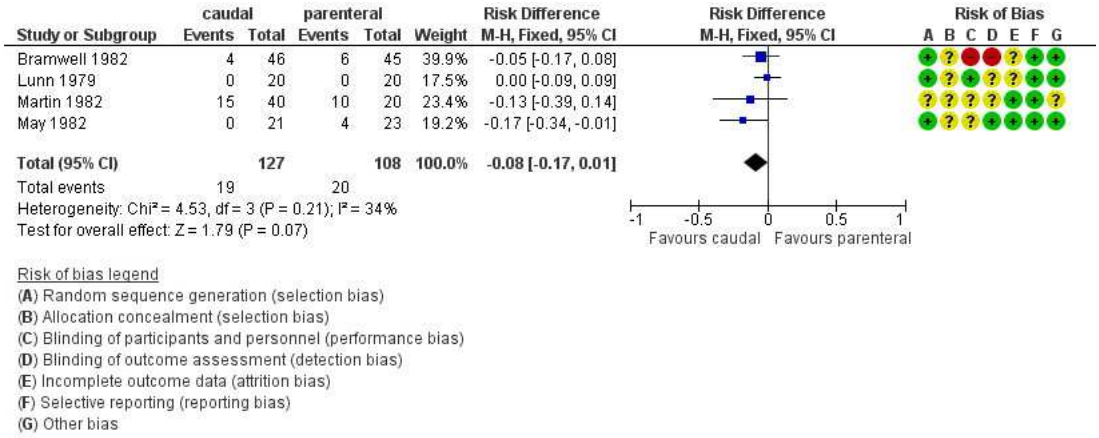
Forest plot of comparison: 9 DPNB versus ring block, outcome: 9.2 Heart rate (bpm) change-from-baseline.

Figure 36 (Analysis 17.1)



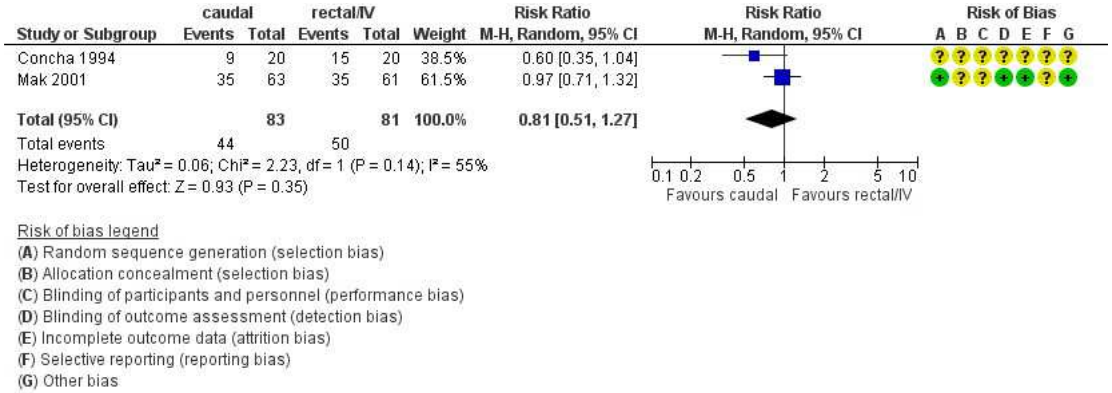
Forest plot of comparison: 17 Caudal analgesia versus parenteral analgesia, outcome: 17.1 Need for analgesia.

Figure 37 (Analysis 17.2)



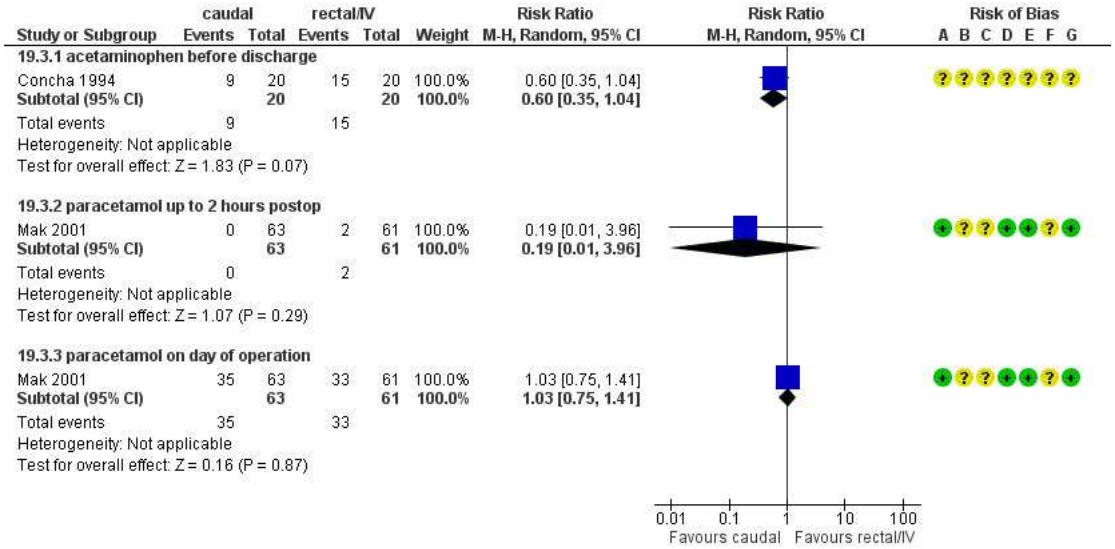
Forest plot of comparison: 17 Caudal analgesia versus parenteral analgesia, outcome: 17.2 Nausea or vomiting.

Figure 38 (Analysis 19.1)



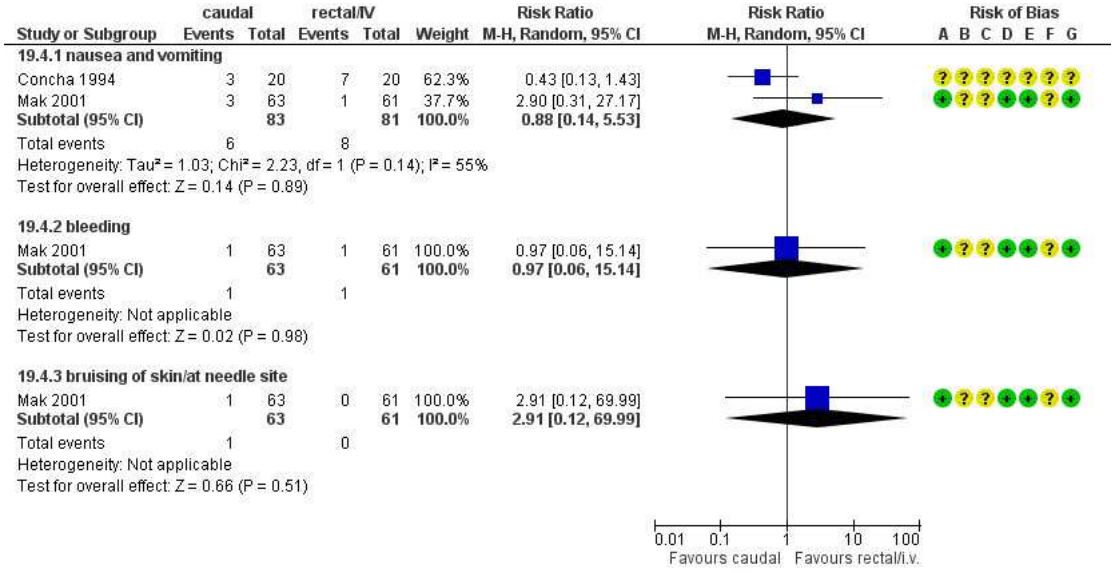
Forest plot of comparison: 19 Caudal analgesia versus rectal or intravenous, outcome: 19.1 Need for any analgesia (rescue or other).

Figure 39 (Analysis 19.3)



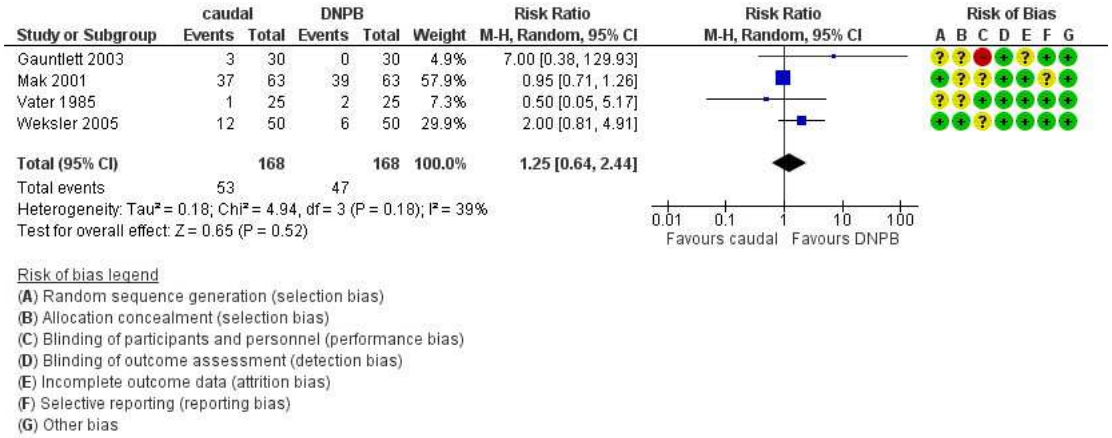
Forest plot of comparison: 19 Caudal analgesia versus rectal or intravenous, outcome: 19.3 Other analgesia.

Figure 40 (Analysis 19.4)



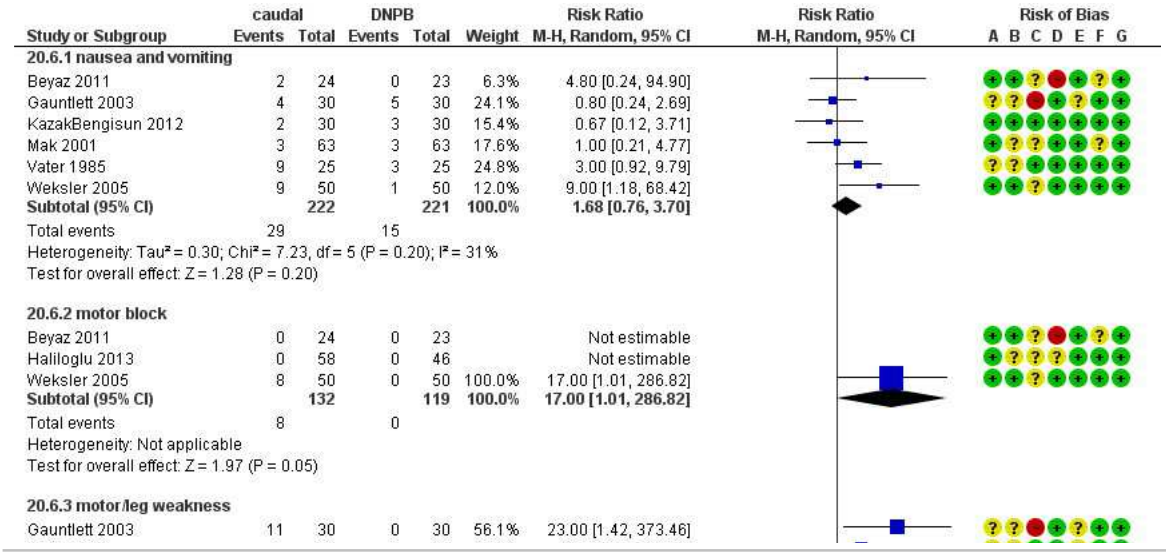
Forest plot of comparison: 19 Caudal analgesia versus rectal or intravenous, outcome: 19.4 Complications.

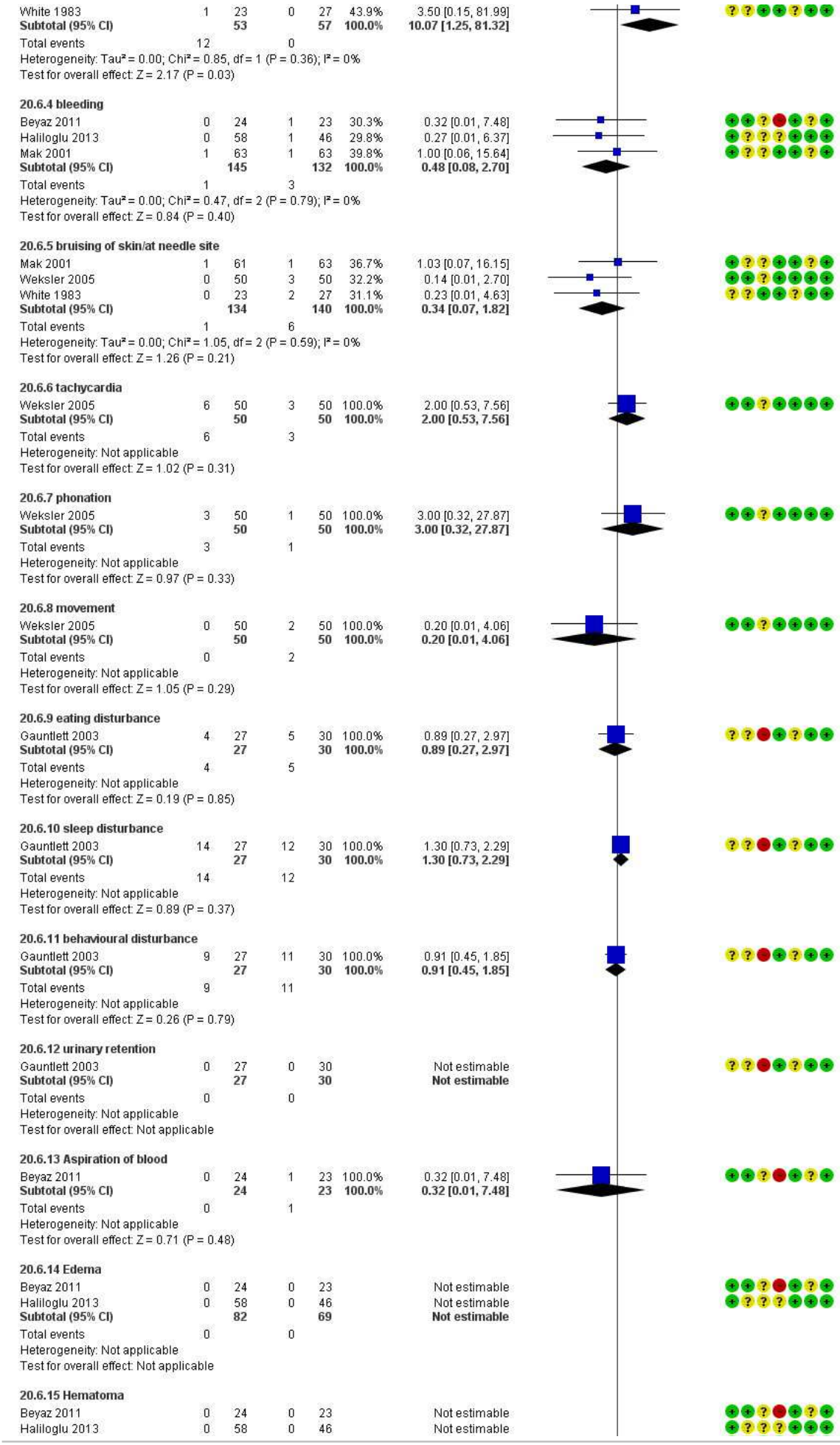
Figure 41 (Analysis 20.1)

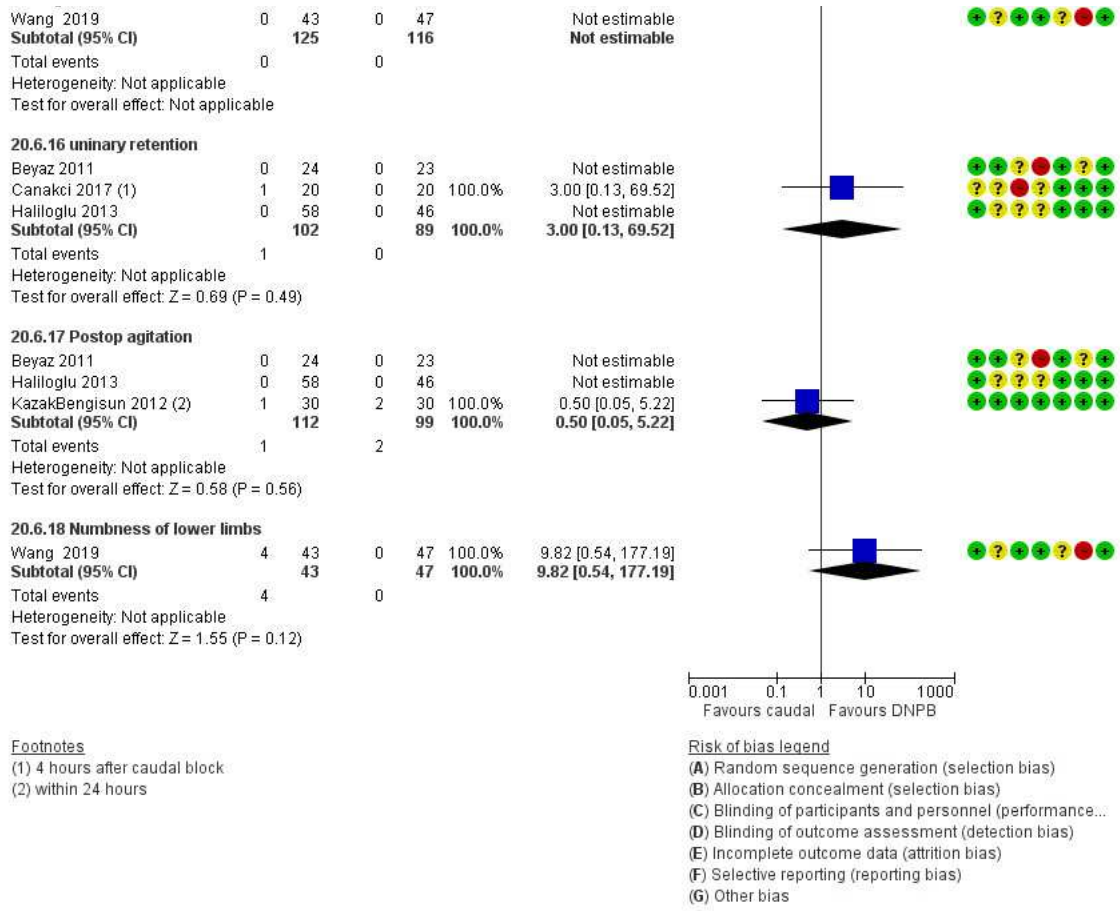


Forest plot of comparison: 20 Caudal analgesia versus dorsal nerve penile block, outcome: 20.1 Need for any analgesia (rescue or other).

Figure 43 (Analysis 20.6)

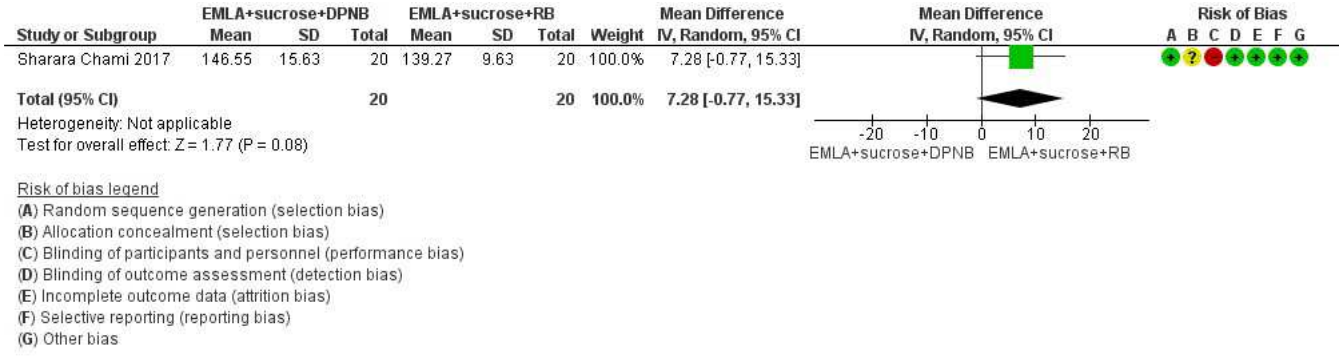



White 1983 1 23 0 27 43.9% 3.50 [0.15, 81.99]
Subtotal (95% CI) 53 57 100.0% 10.07 [1.25, 81.32]
Total events 12 0
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 2.17 (P = 0.03)
20.6.4 bleeding
Beyaz 2011 0 24 1 23 30.3% 0.32 [0.01, 7.48]
Haliloglu 2013 0 58 1 46 29.8% 0.27 [0.01, 6.37]
Mak 2001 1 63 1 63 39.8% 1.00 [0.06, 15.64]
Subtotal (95% CI) 145 132 100.0% 0.48 [0.08, 2.70]
Total events 1 3
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%
Test for overall effect: Z = 0.84 (P = 0.40)
20.6.5 bruising of skin/at needle site
Mak 2001 1 61 1 63 36.7% 1.03 [0.07, 16.15]
Weksler 2005 0 50 3 50 32.2% 0.14 [0.01, 2.70]
White 1983 0 23 2 27 31.1% 0.23 [0.01, 4.63]
Subtotal (95% CI) 134 140 100.0% 0.34 [0.07, 1.82]
Total events 1 6
Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.26 (P = 0.21)
20.6.6 tachycardia
Weksler 2005 6 50 3 50 100.0% 2.00 [0.53, 7.56]
Subtotal (95% CI) 50 50 100.0% 2.00 [0.53, 7.56]
Total events 6 3
Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)
20.6.7 phonation
Weksler 2005 3 50 1 50 100.0% 3.00 [0.32, 27.87]
Subtotal (95% CI) 50 50 100.0% 3.00 [0.32, 27.87]
Total events 3 1
Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)
20.6.8 movement
Weksler 2005 0 50 2 50 100.0% 0.20 [0.01, 4.06]
Subtotal (95% CI) 50 50 100.0% 0.20 [0.01, 4.06]
Total events 0 2
Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)
20.6.9 eating disturbance
Gauntlett 2003 4 27 5 30 100.0% 0.89 [0.27, 2.97]
Subtotal (95% CI) 27 30 100.0% 0.89 [0.27, 2.97]
Total events 4 5
Heterogeneity: Not applicable
Test for overall effect: Z = 0.19 (P = 0.85)
20.6.10 sleep disturbance
Gauntlett 2003 14 27 12 30 100.0% 1.30 [0.73, 2.29]
Subtotal (95% CI) 27 30 100.0% 1.30 [0.73, 2.29]
Total events 14 12
Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)
20.6.11 behavioural disturbance
Gauntlett 2003 9 27 11 30 100.0% 0.91 [0.45, 1.85]
Subtotal (95% CI) 27 30 100.0% 0.91 [0.45, 1.85]
Total events 9 11
Heterogeneity: Not applicable
Test for overall effect: Z = 0.26 (P = 0.79)
20.6.12 urinary retention
Gauntlett 2003 0 27 0 30 Not estimable
Subtotal (95% CI) 27 30 Not estimable
Total events 0 0
Heterogeneity: Not applicable
Test for overall effect: Not applicable
20.6.13 Aspiration of blood
Beyaz 2011 0 24 1 23 100.0% 0.32 [0.01, 7.48]
Subtotal (95% CI) 24 23 100.0% 0.32 [0.01, 7.48]
Total events 0 1
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)
20.6.14 Edema
Beyaz 2011 0 24 0 23 Not estimable
Haliloglu 2013 0 58 0 46 Not estimable
Subtotal (95% CI) 82 69 Not estimable
Total events 0 0
Heterogeneity: Not applicable
Test for overall effect: Not applicable
20.6.15 Hematoma
Beyaz 2011 0 24 0 23 Not estimable
Haliloglu 2013 0 58 0 46 Not estimable



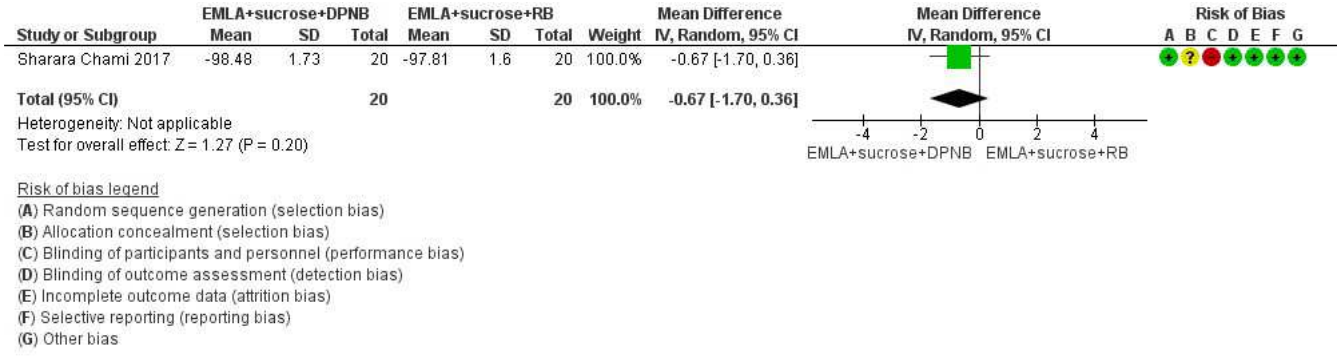
Forest plot of comparison: 20 Caudal analgesia versus dorsal nerve penile block, outcome: 20.6 Complications.

Figure 44 (Analysis 38.3)



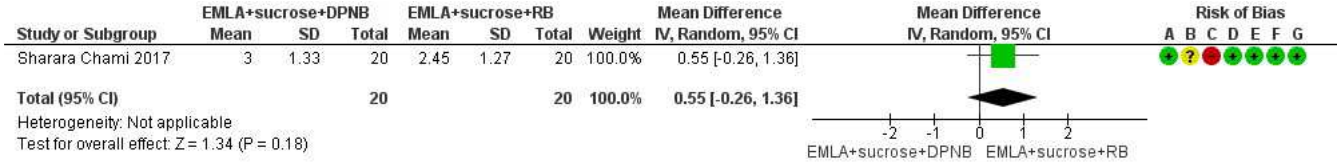
Forest plot of comparison: 38 EMLA+sucrose+DPNB vs EMLA+sucrose+RB, outcome: 38.3 Heart rate.

Figure 45 (Analysis 38.5)



Forest plot of comparison: 38 EMLA+sucrose+DPNB vs EMLA+sucrose+RB, outcome: 38.5 Oxygen saturation %.

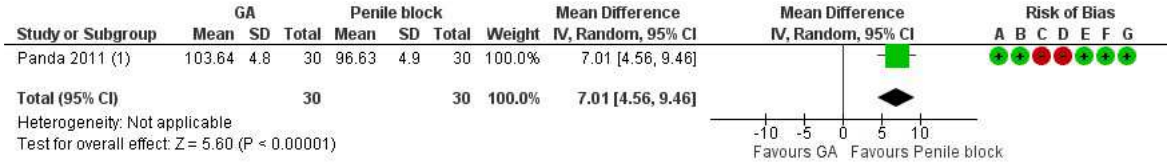
Figure 46 (Analysis 38.8)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 38 EMLA+sucrose+DPNB vs EMLA+sucrose+RB, outcome: 38.8 Pain.

Figure 47 (Analysis 43.1)

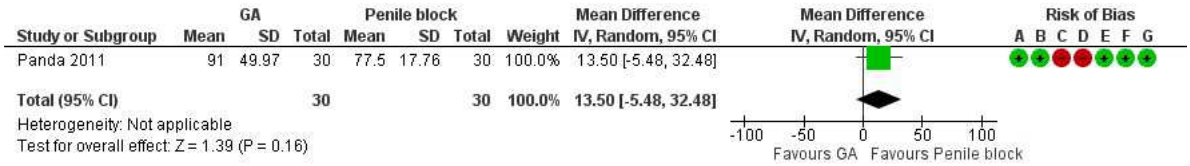


Footnotes
(1) HR ved 45 min ud af 90 min

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance...
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 43 GA versus Penile block, outcome: 43.1 HR (intra-operative).

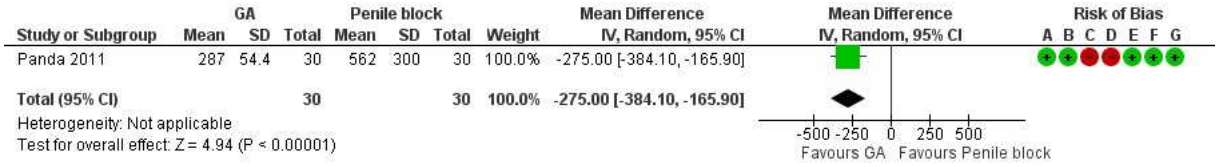
Figure 48 (Analysis 43.2)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 43 GA versus Penile block, outcome: 43.2 Time to food intake.

Figure 49 (Analysis 43.3)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 43 GA versus Penile block, outcome: 43.3 Time to rescure analgesia.