Epidural analgesia in nulliparous women ≤ 4 cm vs. non-regional or epidural analgesia > 5 cm and mode of birth

Clinical question

Is the rate of cesarean section significantly different among nulliparous women who receive epidural analgesia during early labour (≤ 4 cm dilation) vs. those who receive non-regional or epidural analgesia > 5 cm?	
Population:	Term nulliparourous women in labour
Intervention:	Epidural analgesia ≤ 4 cm dilation
Comparison:	Non-regional or epidural analgesia > 5 cm dilation
Primary Outcome:	Cesarean section

Search strategy

- Time period: 1990-2010
- Search terms: Epidural, regional analgesia and labour, cesarean section
- Databases searched: MEDLINE (Ovid SP); EMBASE; Cochrane CDSR, CENTRAL, DARE, & Geneva Medical Foundation
- Inclusions: meta-analysis, systematic reviews, randomized controlled trials, cohort studies
- Exclusions: studies published as abstracts (Barry, 1997; Sharma, 2003; Muir, 1996)
- Findings: titles reviewed - 289; abstracts reviewed - 220; papers reviewed - 30; papers meeting eligibility for inclusion - 23

Synthesis of the evidence

The evidence from 4 meta-analyses, 17 RCTs, and 2 cohort studies indicate that the use of epidural versus non-regional analgesia during labour or timing of epidural analgesia

during labour is not associated with significantly increased rates of cesarean section in term, nulliparous women (rate difference < 3%).

Limitations

1. Studies are not blinded.
2. High rates of protocol violation, drop-outs (no analgesia), and cross-over. Reported cross-over rates from non-regional to epidural analgesia ranged from 2% to 62%, and cross-over rates from epidural to non-regional ranged from 0% to 34%. Drop-out rates ranged from 0 to 35%.
3. Findings were not consistently stratified on spontaneous versus induced labour
4. Use of high dose oxytocin protocols for induction and augmentation limit external validity to jurisdictions with low-dose protocols, such as BC.
5. Variance in management protocols for labour dystocia.
6. Time limit for second stage prior to the decision for caesarean section was less in early studies (2 hours) than what is currently accepted (4 hours).
7. 53% of RCTs were conducted in institutions where primary non-elective CS rates are lower (≤10%) than current rates (BC 28%, 2008).
8. Numerous studies enrolled racial/ethnic subjects not representative of the Canadian population.
9. Epidural analgesia used in earlier studies was associated with more motor blockade due to higher doses/concentrations of anaesthetic agent.
10. Many studies administered epidural at <3.0 cervical dilatation, prior to the onset of established labour.

Conclusions

While the studies overwhelmingly agree that the use and/or timing of epidural analgesia during labour in nulliparous women does not appear to affect cesarean section rates, the validity of randomized controlled trials and meta-analyses is severely limited by high crossover and drop-out rates. In contrast, cohort studies undertaken “as treated” analysis with control of confounding factors demonstrate a 2-3 fold increase in cesarean section. In addition, the generalizability of included studies is limited because the majority of these studies occurred in settings where primary, non-elective cesarean section rates were <10%. A randomized controlled trial that could evaluate the impact of epidural on cesarean section would require use of analgesia in the control group that was as effective as epidural to avoid cross over, but that was not in itself associated with cesarean section.

Meta-analysis	Inclusion	Intervention/Findings	Comments
Marucci M, et al. Anesthesiology 2007;106 (5):1035–45. **Patient-requested neuraxial analgesia for labor: Impact on rates of caesarean and instrumental vaginal delivery**	5 RCTs and 4 retrospective cohort studies, 1994-2006 N=3,320 mixed parity N=2,980 nulliparous (All study populations nulliparous except for Ohel, 1994 which is mixed parity). **RCTs** Ohel, 2006, Israel n=449 Wong, 2005, US n=728 Luxman, 1998, Israel n=60 Chestnut, 1994, US n=149 Chestnut, 1994, US n=334 **Prospective Cohort** Vahratian, 2004, US n=501 **Retrospective Cohort** Sharma, 2003, US* n=504 Rogers, 1999, US n=255 Ohel, 1994, Israel n=340 Inclusion: • epidural or combined spinal–epidural analgesia initiated before the cervix is dilated to 4–5 cm • > 36 weeks, singleton • spontaneous and induced labour Exclusion: • studies that defined “early labor” relative to fetal station rather than cervical dilation	**Early neuraxial vs.** **a) early parenteral opioid** **b) late epidural analgesia** **c) both early parenteral opioid and late epidural analgesia** **Cesarean section (nulliparous)** 15.3% vs. 15.3%, OR 1.0 (0.82-1.23) **Cesarean section (nulliparous, RCTs only)** 14.5% vs. 15.2% OR 0.95 (0.72-1.24) **Cesarean section (individual studies, nulliparous)** Ohel ’06 17.6% vs. 18.7% OR 0.93 (0.40-2.14) Wong 17.7% vs. 21.0% OR 0.83 (0.57-1.2) Luxman 6.7% vs. 10.0% OR 0.64 (0.10-4.15) Chestnut 17.6% vs. 18.7% OR 0.93 (0.40-2.14) Chestnut 9.9% vs. 8.0% OR 1.26 (0.59-2.68) Sharma 15.5% vs. 15.4% OR 1.0 (0.62-1.63) Rogers 14.5% vs. 7.9% OR 1.98 (0.78-5.03) Vahratian 17.9% vs. 17.2% OR 1.0 (0.63-1.59)	* Abstract only . Early neuraxial defined as epidural or combined spinal-epidural analgesia initiated ≤ 4.0 cm cervical dilation. No significant heterogeneity among studies. Oxytocin protocols: Included studies with both high and low dose protocols and studies where the dose was not reported. Crossover and dropout rates not provided.

Meta-analysis	Inclusion	Intervention/Findings	Comments
Sharma, SK et al. Anesthesiology 2004; 100:142–8. **Labour analgesia and caesarean delivery. An individual patient meta-analysis of nulliparous women**	5 RCTs at Parkland Hospital, Dallas, US, 1993-2000 N=2703 nulliparous Ramin, 1995, US n=693 Sharma, 1997, US n=386 Gambling, 1998, US n=650 Lucas, 2001, US n=515 Sharma, 2002, US n=459 Inclusion: • healthy term nulliparous (n=2188) • pregnancy induced hypertension (n= 515) • spontaneous labour	**Epidural vs. Intravenous meperidine** **Cesarean section (5 RCTs)** 10.5% vs. 10.3%, OR 1.04 (0.81-1.34) **Cesarean section odds ratios (individual studies)** Ramin OR 1.20 (0.73-1.97) Sharma OR 1.77 (0.31-1.91) Gambling OR 1.13 (0.65-1.97) Lucas OR 1.05 (0.68-1.63) Sharma OR 0.81 (0.41-1.61)	Epidural: Initiated with bupivacaine or intrathecal sufentanil and maintained with low dose (0.0625% or 0.125%) bupivacaine with fentanyl Intravenous opioid: Initiated with 50 mg meperidine and 25 mg promethazine hydrochloride and maintained with intravenous boluses of meperidine as needed. No significant heterogeneity among studies. For all trials combined: Oxytocin protocols: Not provided. 48% of epidural group and 40% intravenous meperidine group received oxytocin. Epidural group: No analgesia: 14.1% Cross-over: 3.7% IV meperidine group: No analgesia: 11.8% Cross-over: 13.6%

Meta-analysis	Inclusion	Intervention/Findings	Comments
Liu E. et al. BMJ 2004; 328:1410–20 **Rates of caesarean section and instrumental vaginal delivery in nulliparous women after low concentration epidural infusions or opioid analgesia: Systematic review**.	7 RCTs, 1993-2002 N=2962 nulliparous Dickinson, 2002, Australia n=992 Sharma, 2002, US n=459 Loughnan, 2000, UK n=614 Clarke, 1998, US n=318 Bofill, 1997, US n=100 Sharma, 1997, US n=386 Thorpe, 1993, US n=93 Inclusion: • RCTs comparing low concentration bupivacaine (≤ 0.125%) with parenteral opioids • term, uncomplicated pregnancies • cephalic presentation • spontaneous and induced labour	**Epidural vs. parenteral opioids** **Cesarean section** 12.1% vs. 11.3% OR 1.03 (0.71-1.48) **Cesarean section (excluding Thorpe)** 11.7% vs. 11.6% OR 1.01 (0.80-1.28) **Cesarean section (individual studies)** Dickinson 17.2% vs.14.2% OR 1.26 (0.89-1.77) Sharma '02 7.1% vs. 8.6% OR 0.81 (0.41-1.61) Loughnan 11.8% vs.12.9% OR 0.91 (0.56-1.47) Clarke 9.6% vs. 13.6% OR 0.68 (0.34-1.36) Bofill 10.2% vs. 5.9% OR 1.82 (0.41-8.06) Sharma '97 4.6% vs. 5.8% OR 0.78 (0.31-1.91) Thorpe 25% vs. 2.2% OR 14.67 (1.82-118.22)	Heterogeneity attributed to Thorpe. When excluded from sensitivity analysis, there is no heterogeneity. Included studies with both high dose and low dose oxytocin protocols. Crossover rates among included studies ranged from 0 – 27.7% in the epidural group and 1.4 - 62.1% in the opioid group.

Meta-analysis	Inclusion	Intervention/Findings	Comments
Halpern S. et al. JAMA;1998 ;280 (24) 2 105-09. **Effect of Epidural vs Parenteral Opioid Analgesia on the Progress of Labor: A Meta-analysis**	10 RCTs, 1980-1997 N=2369 mixed parity nulliparous n = 1614 multiparous n = 755 7/10 RCTs nulliparous women Sharma, 1997, US n=386 Bofill, 1997, US n=100 Nikkola, 1997, Finland n=20 Barry, 1997, US n=318 Muir, 1996, Canada n=50 Ramin, 1995, US n=485 Robinson,1980, UK n=80 Inclusion: • spontaneous and induced labour healthy women with uncomplicated pregnancies	**Epidural vs. parenteral opioid** **Cesarean section (n=1025 nulliparous)** 8.5% vs. 7.7%, OR 1.28 (0.55-2.93) **Cesarean section (individual studies)** Sharma 3.6% vs. 4.5% OR 0.80 (0.38-1.70) Bofill 10.2% vs. 5.9% OR 1.82 (0.41-8.06) Barry 9.6% vs.13.6% OR 0.68 (0.34-1.36) Muir 10.7% vs. 9.1% OR 1.20 (0.18-7.89) Ramin 9.0% vs.3.9% OR 2.45 (1.36-4.41) Robinson CS not an outcome Nikkola CS not an outcome	Heterogeneity attributed to Thorpe. Sensitivity analysis not provided. 7/10 studies reported outcomes by intention-to-treat, 2 reported both intention-to-treat and protocol compliant, and one reported only protocol compliant. 2 studies included where CS not an outcome. Oxytocin protocols: Not provided. 9 studies enrolled women in spontaneous labour and one study included inductions. 7/10 studies included only nulliparous women. Crossover rates ranged from 2.2% - 3.2% in the epidural group and 2.2% 51.8% in the opioid group. Drop-out (no analgesia) rates ranged from 2% - 34.9% in the epidural group and 26.1% (one study reporting) in the opioid group.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Wang, F. et al. Anesthesiology; 2009;111:871-80. **Epidural analgesia in the latent phase of labor and the risk of caesarean delivery. A five-year randomized controlled trial.**	China N =12,793 Latent phase n = 6,394 Active phase n = 6,399 Inclusion: • nulliparous • spontaneous labour • term • vertex presentation • ≥ 1.0 cm dilation Exclusion: • allergy to opioids • history of centrally-acting drugs • alcohol or opioid dependency • chronic pain (cont) • psychiatric disease history • < 18 or > 45 years • non-vertex presentation • induction of labour • diabetes mellitus • hypertensive disorders of pregnancy • twin gestation	**Latent phase epidural ≥ 1.0 cm. vs. active labour epidural ≥ 4 cm.** **Cesarean section** 23.2% vs. 22.8% p = .51	Epidural protocol: 15 ml epidural analgesic mixture of 0.125% (1.25 mg/ml) ropivacaine plus 0.3 *u*g/ml sufentanil as single dose, followed by patient-controlled infusion with a 10-ml bolus without background infusion. Repeatable meperidine (25 mg IM) was rescue analgesic in active labour epidural group. Median cervical dilation at epidural placement: 1.6 cm in early group vs. 5.1 cm in delayed group P = < 0.0001. Oxytocin protocol: Not provided. Crossover: 1.5% of women in active labour assigned to the latent phase group and 0.7% of women assigned to active phase were in latent phase labour when epidural received. Did not compare epidural with other analgesia.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Ohel, G. et al. RCT. AJOG, 2006 194: 600-5. **Early vs. Late initiation of epidural analgesia in labour: Does it increase the risk of Cesarean?**	Israel N = 449 immediate epidural < 3 cm n = 221 delayed epidural ≥ 4 cm n = 228 Inclusion: • nulliparous • spontaneous or induced labour • ≥ 36 weeks • ≥ 2 painful contractions in 10 min. • Cx ≤ 3 cm dilated and 80% effaced Exclusion: • contraindication to epidural • cervical dilation > 3 cm at time of enrollment • estimated fetal weight > 4000 g. • medical complications of pregnancy • abnormal admission fetal heart tracing	**Early epidural < 3 cm (mean 2.4 cm) vs. delayed epidural ≥ 4 cm (mean 4.6 cm)** **Cesarean section** 13% vs. 11% p = .77	Enrolled at first request for analgesia. Early group – epidurals were started immediately. In delayed group, IV pethidine and promethazine provided, until epidural placement. Immediate epidural: mean cervical dilation 2.4 cm Delayed epidural: mean cervical dilation 4.6 cm Epidural bolus of 10 ml ropivacaine 0.2% and 50 *u*g fentanyl. Epidural maintained with continuous infusion of ropivacaine 0.1% with fentanyl 0.0002% at 10 ml/hr. Further bolus of ropivacaine 0.2% 5-10 ml provided upon request. Early epidural: 4.5% did not receive epidural. 47% received pethidine. Delayed epidural group: 13.6% did not receive an epidural. 80% received pethidine. Epidural not compared with other analgesia. Oxytocin protocol: Not provided. Oxytocin use 36% in early group vs. 37% in late group.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Wong CA, et al. New England Journal of Medicine 2005;352:655–65. **The risk of caesarean delivery with neuroaxial analgesia given early versus late in labour**.	United States N=728 Early intrathecal analgesia n = 366 Late systemic analgesia n = 362 Inclusion: • healthy, low risk women • term (37– 42 weeks) • nulliparous • spontaneous labour or spontaneous rupture of membranes • cervical dilation <4 cm Exclusion: • non-vertex presentation • scheduled induction of labour • contraindication to opioid analgesia	**Early (< 4 cm) Intrathecal vs. late (> 4 cm) systemic (IV & IM) hydromorphone** **Cesarean section** 17.8% vs. 20.7% Risk difference: -2.9% (95%CI -9.0 – 3.0) p = .31	Systemic-analgesia: At first request for analgesia – 25 ug fentanyl intrathecally (early group) vs. hydromorphine 1 mg IM and I mg IV (late group). At second request Early group: if the cervix < 4.0 cm dilated, a 15-ml epidural bolus of bupivacaine (0.625 mg per milliliter) with fentanyl (2 µg per milliliter) was given, and if the cervix ≥ 4.0 cm dilated, a 15-ml epidural bolus of bupivacaine (1.25 mg per milliliter) was given. Both groups had patient controlled epidural analgesia. Late group: hydromorphone repeated if cervix < 4cm otherwise, patient controlled epidural analgesia was initiated. Epidural analgesia was given at the third analgesia request, regardless of cervical dilatation. Drop out (no analgesia) and crossover rates not given. Oxytocin protocol: Not provided. Oxytocin use > 92% in both trial arms.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Halpern et al. Anesth Analg. 2004. 99:1532-8. **A multicenter randomized controlled trial comparing patient-controlled epidural with intravenous analgesia for pain relief in labor**.	Canada N=242 PCIA n = 118 PCEA n = 124 Inclusion: • healthy, low risk women • term (37– 42 weeks) • nulliparous • spontaneous labour Exclusion: • preeclampsia • antenatal hemorrhage • BMI >35 • multiple gestation • malpresentation • known fetal anomalies • fetal distress	**Patient-controlled intravenous opioid (PCIA) vs. patient-controlled epidural (PCEA) for labor at ≥ 3 cm dilation.** **Cesarean Section** 10.2% vs. 9.7% Risk difference: 0.5% (95% CI -7% to 8 %) p = .9	PCIA: 100 *u*g fentanyl initially, and 50 *u*g q 5 min until adequate pain relief. Aliquots of 25 to 50 *u*g fentanyl q 10 min. PCEA: 3-5 ml aliquots 0.1% bupivacaine, then maximum 25 mL with 100 *u*g fentanyl; followed by PCEA pump 0.08% bupivacaine with fentanyl 1.6 *u*g/mL q 10 min. prn. Oxytocin protocol: Not provided. 52% PCIA group and 44% PCEA group received oxytocin. CS performed for dystocia after giving a trial of oxytocin therapy of at least 2 h. PCIA group: 51/118 (43%) requested epidural – actual proportion who received it not clearly stated; 36% received analgesia before randomization. PCEA group: no crossover; 44% received analgesia before randomization.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Dickinson JE, et al. Australian and New Zealand Journal of Obstetrics & Gynaecology 2002;42:65–72. **The impact of intrapartum analgesia on labour and delivery outcomes in nulliparous women.**	Australia N = 992 Epidural n = 493 CMS n = 499 Inclusion: • healthy, low risk women • term (37– 41 6/7 weeks) • nulliparous • spontaneous and induced labour • cervical dilation < 5 cm • cephalic presentation • absence of contraindication for epidural analgesia	**Epidural vs. continuous midwifery support (CMS) and attempt to avoid epidural** **Cesarean Section** 17.2% vs. 14.2% p = 0.22	Epidural analgesia: combined spinal-epidural technique, with patient-controlled epidural analgesia. Continuous midwifery support: 1:1 midwife-patient ratio throughout labour, intramuscular pethidine (1.5 mg/kg maternal body weight), nitrous oxide inhalation or non-pharmacological methods of pain relief. Oxytocin protocol: 2 mU/min if cervix dilation <1 cm/h, increased by 2 mU/min at 30 minute intervals to maximum 36 mU/min. 45% CMS group and 46% epidural group induced. Crossover rates: Epidural to CMS: 27.8% CMS to epidural: 61.3%
Sharma. SK., Anesthesiology 2002;96(3):546–51 **Cesarean delivery: a randomized trial of epidural analgesia versus intravenous meperidine analgesia during labor in nulliparous women.**	United States N=459 Epidural n= 226 IV meperidine n= 233 Inclusion: • healthy, low risk women • term • nulliparous • spontaneous laobur • cephalic presentation	**Epidural vs. IV meperidine** **Cesarean Section** 7% vs. 9% p =0.61	Epidural: initiated with 0.25% bupivacaine and maintained with 0.0625% bupivacaine and fentanyl 2 g/ml at 6 ml/h with 5-ml bolus doses every 15 min prn using a patient-controlled pump. IV meperidine: 50 mg meperidine with 25 mg promethazine hydrochloride as an initial bolus, followed by 15 mg meperidine every 10 min prn, using a patient-controlled pump. cont.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Sharma. SK., Anesthesiology 2002;96(3):546–51 cont.			Oxytocin protocol: 6 mU/min if cervix dilation <1 cm/h, increased by 6 mU/min every 40 minutes up to 42 mU/min. 45% epidural group and 34% IV meperidine group received oxytocin. IV meperidine: Cross-over to epidural: 6% Refusal of allocated analgesia and received other analgesia: 10% Epidural: refused epidural and had a different (unspecified) analgesic: 5.3%
Howell C. et al. BJOG;2001:08, 27-33. **A randomised controlled trial of epidural compared with non-epidural analgesia in labour.**	United Kingdom N = 369 nulliparous Epidural n = 184 Non-epidural n = 185 Inclusion: • primigravida women • term • spontaneous labour • normal obstetric and medical history	**Epidural vs. non-epidural** **Cesarean Section** 7% vs. 9% p = > .05	Epidural: 0.25% bupivacaine 10 ml, with top-ups 5-10 ml prn. Non-epidural: pethidine 50-100 mg IM, prn Entonox available to both groups. Oxytocin protocol: Not provided. 62% of epidural group and 55% of non-epidural group received oxytocin. Crossover: Non-epidural to epidural:(28%) Dropout: Epidural:33% - some may have received pethidine – not clarified in study. Proportion in non-epidural group without analgesia not stated.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Loughnan B. et al. British Journal of Anaesthesia 2000;84(6) 715-9. **Randomised controlled comparison of epidural bupivacaine versus pethidine for analgesia in labour.**	United Kingdom N= 614 IM pethidine n= 310 Epidural bupivacaine n=304 Inclusion: • healthy, low risk, nulliparous • term • cephalic presentation Exclusion: • women with any risk factors determining method of analgesia during labour	**Epidural vs. IV meperidine** **Cesarean Section** 12.0% vs.13.0% p = .7	Oxytocin protocol: 4 mU/min, increased every 15 minutes up to maximum of 40 mU/min if cervix dilation <1 cm/h. 61% of epidural group and 57% of IV meperidine group received oxytocin. Cross over: Epidural group: 18.7% IV meperidine group: 57% Drop out: Epidural: (no epidural or pethidine): 1% Pethidine: 1%
Gambling, D R. et al. Anesthesiology. 1998:89(6):1336-44. **A randomized study of combined spinal-epidural analgesia versus intravenous meperidine during labor: impact on cesarean delivery rate**.	United States N = 644 nulliparous CSE nulliparous n = 330 IV meperidine nulliparous n = 314 Inclusion: • singleton fetus • mixed parity • 3-5 cm dilation and regular contractions • healthy women • spontaneous labour	**Combined spinal-epidural (CSE) vs. IV meperidine** **Cesarean Section (nulliparous alone)** 10.0% vs. 9.0%, p = > .05 **Cesarean Section (nulliparous alone, as treated)** 11.0% vs. 5%, p = < .023	CSE: 10 *u*g intrathecal sufentanil, then epidural bupivacaine and fentanyl at their next request for analgesia. IV meperidine: 50 mg on demand to a maximum of 200 mg in 4 h. Cross over: CSE: 13.3% IV meperidine: 26.1% Dropout:(no analgesia) CSE: 8.4% IV meperidine:6.9% An additional 6.9% in the CSE group and 4.9% in the meperidine group were noted to have had rapid deliveries but the analgesia used, if any, is not stated.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Clarke A. et al. AJOG, 1998:179 (6): 1527-1533. **The influence of epidural analgesia on caesarean delivery rates: A randomized, prospective clinical trial.**	United States N = 318 Epidural analgesia n = 156 Intravenous opioid n = 162 Inclusion: • nulliparous • ≥ 36 weeks • cephalic presentation • spontaneous labour (≥ 50% effacement, ROM and painful contractions ≥ 2 q 15 min) Exclusion: • medical conditions precluding epidural • multiple gestation • maternal or fetal conditions precluding trial of labour	**Epidural vs. Intravenous opioid** **Cesarean Section** 9.6% vs.13.6%, RR 0.71 (0.38-1.31) **Cesarean Section (as treated)** 7.7% vs. 8.8%, RR 1.15 (0.45-2.91)	Epidural: 9 ml 0.25% bupivacaine with 50 *u*g fentanyl in 3 doses over 10 min interval, followed by continuous infusion 0.125% bupivacaine with 50 *u*g fentanyl at 12 ml/hour. IV Opioid: meperidine 50-75 mg q 90 mins. prn Oxytocin protocol: 6 mU/min and increased by 6 mU every 15 minutes until there were 7 contractions every 15 minutes. 75% of epidural group and 72% IV opioid group received oxytocin. Cross over: Dropout: Epidural: 34% Epidural: 2.3% IV Opioid: 52% IV Opioid: not stated
Luxman D. International Journal of Obstetric Anesthesia.1998;7, 161-164. **The effect of early epidural block administration on the progression and outcome of labor**.	Israel N = 60 Early epidural < 4 cm n = 30 Late epidural ≥ 4 cm n = 30 Inclusion: • nulliparous • term • cephalic presentation • spontaneous labour	**Early epidural < 4 cm vs. Late epidural ≥ 4 cm** **Cesarean Section** 6.6% vs.10.0% p = > .05	Lumbar epidural 8.0 ml 0.25% bupivacaine with top-ups until full dilation. Mean cx dilation early group: 2.3 cm Mean cx dilation in late group: 4.5 cm Late group did not receive any analgesia prior to epidural. Oxytocin protocol: 2 mU every 30 min 53% of early group and 60% of late group received oxytocin. Insufficient power to evaluate outcomes.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Sharma,SK. Et al. Anesthesiology. 1997;87:487-494. **Cesarean delivery: a randomized trial of epidural versus patient-controlled meperidine analgesia during labor**	United States Nulliparous N = 386 Epidural nulliparous n =197 PCIA nulliparous n = 189 Inclusion: • healthy, term women • active labour (> 2cm dilation) • singleton, cephalic presentation • combined parity	**Epidural vs. Meperidine PCIA (patient controlled intravenous analgesia)** **Cesarean Section** 5% vs. 6% p = > .05 **Cesarean Section (as treated)** 5% vs. 7% p = > .05	Randomized at 3-5 cm cervical dilation Epidural: maintained with continuous epidural infusion of 0.125% bupivacaine with 2 micro gram/ml fentanyl. PCIA: maintained with 10-15 mg meperidine given every 10 min prn Oxytocin protocol: 6 mU/min, ans increased by 6 mU/min at 40-min intervals, to a max 42 mU/min. Cross-over: Dropout: Epidural: 2.2% Epidural:29.9% PCIA: 1.4% PCIA: 26.0%
Bofill JA. Et al. American Journal of Obstetrics and Gynecology 1997;177:1465–70. **Nulliparous active labor, epidural caesarean, and caesarean delivery for dystocia.**	United States N=100 Epidural n = 49 Narcotic n = 51 Inclusion: • healthy nulliparous • 36-42 weeks • cephalic presentation • spontaneous, active labour (≥4 cm to < 8 cm), 80% effacement and engagement of vertex Exclusion: • serious medical problems • twins	**Epidural vs. Narcotic** **Cesarean section for dystocia** 8% vs. 6% p = > .05	Epidural Group: Three to five ml boluses of 0.25% bupivacaine, with or without 50 to 100 l *u*g fentanyl, flowed by continuous infusion of 0.125% bupivacaine with 1.5 *u*g/ml fentanyl titrated to maintain level of analgesia. Narcotic group: women received 1 to 2 mg intravenous doses of butorphanol q 1 to 2 hours, prn. Oxytocin protocol: 6 mU/min, increased by 6 mU every 30 minutes up to maximum 42 mU/min if cervical dilation <1 cm/h. cont.

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Bofill JA. Et al. American Journal of Obstetrics and Gynecology 1997;177:1465–70. cont.	• women who received cervical ripening agents		Crossover: Epidural: 0 Narcotic:23.5% Dropout: 4.0% Narcotic group:0 Oxytocin augmentation: 69% in the epidural group and 82.3% in the narcotic group. Insufficient power to evaluate outcomes.
Ramin SM. Obstet Gynecol. 1995;86:783-789. **Randomized trial of epidural versus intravenous analgesia during labor**.	United States N=1330 combined parity n = 673 nulliparous Epidural n= 338 IV analgesia n= 335 Inclusion: • healthy, term pregnancies • mixed parity • spontaneous labour • 3- 5 cm dilated Exclusion: • pregnancy complications	**Epidural vs. IV analgesia** **Cesarean section (nulliparous "as treated")** Risk ratio: 2.55 (95% CI 1.5-4.3)	For combined parity: Epidural group: protocol violations 35% IV analgesia group: protocol violations 55% Oxytocin protocol: 6 mU/min, increased by 6 mU every 40 minutes up to maximum 42 mU/min. 32% of epidural group and 23% of IV analgesia group received oxytocin. Intention to treat reports only as operative deliveries for combined parity. Cross-over: Dropout: Epidural: 0 Epidural:35% Meperidine: 15.4% Meperidine 18.9%

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Chestnut, D. Anesthesiology 1994. 80:1193-200. **Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are receiving intravenous oxytocin**?	United States N = 150 Early n = 74 Late n = 75 Inclusion: • healthy nulliparous • singleton fetus • vertex presentation • ≥ 36 weeks • Induction or augmentation with oxytocin • 3-5 cm dilated Exclusion: • preeclampsia • insulin dependent diabetes • estimate fetal weight ≥ 4500 g	**Early (3-<5 cm) vs. late (≥ 5 cm) epidural analgesia** **Cesarean Section** 18% vs. 19% RR 0.94 (0.48-1.84)	Early group: 3 ml 1.5% lidocaine with epinephrine, and after 10 minutes 5 ml 0.25% bupivacaine, then boluses prn. At 5 cm dilation, continuous infusion of 0.125% bupivacaine at 12 ml/hour. Late group: nalbuphine 10 mg IV if < 5 cm; then epidural protocol as per early group once ≥ 5 cm. Oxytocin protocol: Oxytocin augmentation (1 mU every 30 min) until an adequate labor pattern.
Chestnut, D. et al. Anesthesiology 1994; 80; 1201-8. **Does early administration of epidural analgesia affect obstetric outcome in nulliparous women who are in *spontaneous* labour?**	United States N = 334 Early n = 172 Late n = 162 Inclusion: • healthy nulliparous • singleton fetus • vertex presentation • ≥ 36 weeks • spontaneous labour • 3-5 cm dilated Exclusion: • Preeclampsia • insulin dependent diabetes • estimate fetal weight ≥ 4500 g	**Early (3-<5 cm) vs. late (≥ 5 cm) epidural analgesia** **Cesarean Section** 10% vs. 8% RR 1.22 (0.62-2.4)	Early group: 3 ml 1.5% lidocaine with epinephrine, and after 10 minutes 5 ml 0.25% bupivacaine, then boluses prn. At 5 cm dilation, continuous infusion of 0.125% bupivacaine at 12 ml/hour. Late group: nalbuphine 10 mg IV if < 5 cm; then epidural protocol as per early group once ≥ 5 cm. Oxytocin protocol: Dose not reported. 31% of early group and 38% of late group required oxytocin. Results not analyzed for 5 subjects in the late group who received early epidural

Randomized controlled trials	Inclusion	Intervention/Findings	Comments
Thorp, et al. AJOG. 1993;169:851–8. **The effect of intrapartum epidural analgesia on nulliparous labor: a randomized, controlled, prospective trial.**	United States N = 93 Narcotic analgesia n = 45 Epidural analgesia n = 48 Inclusion: • healthy nulliparous • singleton fetus • spontaneous labour	**Narcotic vs. Epidural** **Cesarean section** 25% vs. 2.2% p = < .05	Narcotic: 75 mg meperidine and 25 mg promethazine hydrochloride IV q 90 min. prn Epidural: continuous infusion 0.125% bupivacaine, into 2nd stage Oxytocin protocol: 1 mU/min, increased by 1 mU/min every 30-45 minutes. Crossover rates: Epidural: 0 Narcotic: 2.1% Dropout: Epidural: 2.2% Narcotic: 0 7 CS occurred in second stage. Mean second stage 115 min.

Prospective Cohort Study	Inclusion	Intervention/Findings	Comments
Uyen-Sa, t. Maternal Child Health: 2009;Septemver 18. **Epidural analgesia and risks of caesarean and operative vaginal deliveries in nulliparous and multiparous women.**	San Diego, 1994-1996 N=2052 Inclusion: • combined parity • women at low risk for medical complications Exclusion: • multiple births • private or military insurance • first prenatal visit > 32 weeks • any medical condition that would require emergency or preclude epidural placement • induction with oxytocin and/or prostaglandin and/or ARM • preterm < 37 weeks • birth weight ≥ 4500 grams • no previous cesarean delivery	**Epidural vs. no regional analgesia** **Cesarean section (nulliparous)** 17.6% vs. 4.6% Unadjusted RR 3.8 (2.4-6.0) *Adjusted RR 2.4 (1.5-3.7) * Adjusted for model of care, cervical dilation at admission < 4 cm, major antepartum complications, any complications at presentation, birth weight, gestational age at birth, infant's sex, maternal age, height, weight, education, marital status, maternal race, language spoken, station, maternal country of origin, and maternal narcotics use.	Epidural management in 1994-1996 may have been different than that offered today. Oxytocin protocol: Not provided.
Retrospective Cohort Study	**Inclusion**	**Intervention/Findings**	**Comments**
Lieberman E. 1996.Obstetrics and Gynecology:88(6). **Association of epidural analgesia with caesarean delivery in nulliparas.**	USA, 1991 - 1993 N=1733 Inclusion: • low-risk • term • singleton vertex presentation • spontaneous labour • no medical contraindications to	**Epidural vs. non-regional analgesia** **Cesarean section (nulliparous)** 17.0% vs. 4.0% *Adjusted RR 3.7 (2.4-5.7) * Adjusted for maternal age, race, insurance (private, public, other), prepregnant weight, height, infant	Epidural – 0.25% bupivacaine (12-16 ml) via the L 2-3 or L 3-4 at < 8 cm dilation, followed by continuous infusion of 0.125% bupivacaine plus 2 *u*G/mL fentanyl. Oxytocin protocol: Not stated. 27% of epidural group and 34% of non-regional analgesia group received oxytocin.

Retrospective Cohort Study	Inclusion	Intervention/Findings	Comments
Lieberman E. 1996.Obstetrics and Gynecology:88(6). cont.	• epidural analgesia • at least one hour of first stage of labour after admission	birth weight, gestational age, infant sex, dilation at admission, initial rate of cervical dilation, station of the fetal head at admission, active management of labour protocol, ruptured membranes on admission, maternal chronic hypertension, and pregnancy-induced hypertension.	