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Evidence and Practice: Epidural Analgesia in Labour and Caesarean Section

Melanie Bannister-Tyrrell*, Jane B Ford, Jonathan M Morris, Christine L Roberts

Author affiliations

Kolling Institute of Medical Research, University of Sydney, Australia

***Corresponding author**

Melanie Bannister-Tyrrell, Clinical and Population Perinatal Health Research, University Department of Obstetrics and Gynaecology (Building 52), Royal North Shore Hospital, St Leonards, NSW 2065 Australia. Telephone +61 2 94629815. Email melanie.bannister-tyrrell@sydney.edu.au.

Abstract

Background: A Cochrane Systematic Review of randomised controlled trials of epidural analgesia compared to other or no analgesia in labour reported no overall increased risk of caesarean section. However, many trials were affected by substantial noncompliance and there are concerns about the external validity of some trials for contemporary maternity populations. We aimed to explore the association between epidural analgesia in labour and caesarean section in clinical practice and compare with findings from randomized controlled trials.

Methods: Population-based cohort of pregnant women (n=172,785) without major obstetric complications who delivered a singleton live infant in hospitals in New South Wales, Australia, 2007-2010. Data were obtained from linked, validated population-based data collections. Propensity score matching was used to analyse the association between epidural analgesia in labour and caesarean section.

Results: Epidural analgesia in labour was used by 54,668 (31.6%) women and 15,926 (9.2%) had a caesarean section. Epidural analgesia in labour was associated with increased risk of caesarean section (RR 2.63; 95% CI [2.53, 2.74]). The association with epidural analgesia in labour is higher for caesarean section for failure to progress (RR 3.09, 95% CI [2.94, 3.25]) than for caesarean section for fetal distress (RR 1.96, 95% CI [1.83, 2.09]).

Conclusions: In practice, epidural analgesia in labour is associated with caesarean section in a large maternity population. Population-based studies contribute important information about obstetric care, when research settings and participants may not represent the clinical settings or broader population in which obstetric interventions in labour are applied.

Epidural analgesia in labour is a highly effective method of labour pain relief but there is controversy over whether epidural analgesia in labour is associated with an increased risk of caesarean section delivery. A Cochrane Systematic Review of randomized controlled trials (RCTs) of epidural versus non-epidural or no analgesia in labour concludes that epidural analgesia in labour is not associated with a significant increased overall risk of caesarean section (RR 1.10, 95% CI [0.97, 1.25], 27 trials, 8,417 women).[1] In secondary analysis, an increased risk of caesarean section for fetal distress is reported (RR 1.43, 95% CI [1.03, 1.97], 11 trials, 4816 women). However, there are several issues that warrant consideration in the translation of findings from clinical trials to widespread clinical practice across a broad population base. Importantly, many of the RCTs in the Cochrane review had high rates of non-compliance, including 4 trials (1,974 [23%] women) with 50% or greater crossover from the non-epidural arm to the epidural arm.[2] An intention-to-treat analysis results in estimates of the effect of receiving epidural analgesia that are closer to the null when crossover is substantial. There are also concerns about external validity as the majority of included studies involved women at more than 36 weeks gestation with no obstetric or medical complications and there were strict protocols in place for labour management and care, and indication for caesarean section.[3, 4] Obstetric practice and women's preferences for epidural analgesia in labour may have changed considerably since the mid 1990s when most trials were conducted.[5]

Due to the settings and inclusion criteria of RCTs included in the review, and the risk of dilution of the true effect of epidural analgesia in labour because of high rates of non-compliance with allocated intervention, it is possible that the findings of the Cochrane review may not reflect widespread obstetric practice in epidural analgesia use in labour and associated outcomes. Large population-based studies may be useful to help determine the effect of epidural use on labour and birth outcomes, however have been limited by the actual recording of epidural analgesia, as many data collection systems do not

distinguish between epidural analgesia for *labour* or for *delivery* (as epidural is the most common analgesia for caesarean delivery).[6] Since 2006, separate data on epidural for labour and for delivery has been collected for all births in the state of New South Wales (NSW), Australia. NSW is the largest state in Australia and NSW births comprise approximately one third of all Australian births.

The aim of this study is to determine whether in practice, epidural for labour analgesia compared to no epidural for labour analgesia is associated with an increased risk of caesarean section.

Methods

Study population

The study population consisted of women who delivered a singleton live-born infant following labour at term (37-41 weeks) in NSW hospitals in 2007-2010 (Figure 1). We aimed to identify a relatively low risk study population to improve comparability with the participants included in the RCTs in the Cochrane meta-analysis.[1] To achieve this, the study was restricted to women delivering in hospitals in which epidural analgesia in labour is regularly available (maternity service level 4 or higher in the NSW health system).[7] Further, women who had caesarean sections without labour, previous caesarean sections, or a caesarean section for which the primary indication was either 'non-clinical' or 'other clinical' were excluded. Therefore, the only caesarean sections included in the study were performed after labour onset in women with no previous caesarean section for either failure to progress or fetal distress. Women with the following obstetric complications were also excluded: placenta praevia, placental abruption, large- or small-for-gestational-age infant (90^{th} percentile and 10^{th} percentile of birthweight for gestational age, respectively), and non-vertex birth presentations. Women for whom labour was induced using prostaglandin or oxytocin were only included if their primary indication for induction of labour was term pre-labour rupture of membranes or post-term gestation, as induction for

these conditions is not associated with increased risk of caesarean section.[8-10] Induction for fetal distress, maternal co-morbidities or suspected intrauterine growth restriction was excluded, as management of labour in these cases is likely to differ from the low-risk population.

Data sources

Data were obtained from two linked population-based data collections: the NSW Perinatal Collection (referred to as birth data), a statutory population-based registry of all live births and stillbirths of at least 20 weeks gestation or 400g birthweight occurring in NSW, and the Admitted Patients Data Collection (referred to as hospital data), a census of all discharges from NSW public and private hospitals and day procedure centres. For the birth data, the attending midwife or doctor records maternal and infant demographic, medical and obstetric information for pregnancy, labour and delivery. For the hospital data, diagnoses are coded using the most recent version of the International Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) and procedures are coded using the Australian Classification of Health Interventions (ACHI). The unit of analysis is a pregnancy rather than a unique woman, as some women may have had two or more pregnancies in the study period. Probabilistic record linkage of the birth and hospital data was conducted by the NSW Centre for Health Record Linkage. This study was approved by the NSW Population and Health Services Research Ethics Committee. As de-identified routinely collected population data were used, a waiver of the usual requirement for the consent of the individual to the use of their health information in a research project was granted.

Variables

The primary exposure was epidural for labour analgesia, as recorded in a tickbox on the birth data. The primary outcome was caesarean section during labour, as recorded in a tickbox on the birth

data. Subgroup analyses were conducted for caesarean section for failure to progress and caesarean section for fetal distress. Choice of data source for potential confounding variables was guided by local validation studies. Maternal age, maternal country of birth, parity, maternal smoking in pregnancy, gestational age by week, systemic opioid analgesia in labour and hospital level were derived from the birth data.[11, 12] Parity is defined as the number of previous pregnancies of at least 20 weeks gestation. Induction of labour with prostaglandin or oxytocin was included if reported in either the birth data or hospital data to increase ascertainment and reliability.[11] Marital status and patient financial status (private or public) were only available in hospital data. Reporting of maternal co-morbidities is more reliable using the hospital data than birth data, for which only maternal hypertension and diabetes are recorded.[13] The presence of any maternal conditions including chronic hypertension, gestational hypertension, pre-eclampsia, pre-existing diabetes, gestational diabetes, cardiac disease (except acute onset on birth admission record), renal disease, autoimmune disease and thyroid disease recorded on the birth admission in the hospital data was used to define a binary maternal co-morbidity variable. As management of maternal hypertension may include epidural, we also looked at this co-morbidity separately.

Statistical analysis

We determined the frequency (percentages) of epidural analgesia in labour and caesarean section by maternal and hospital characteristics. We used propensity score matching to analyse the association between epidural analgesia in labour and caesarean section delivery.[14] The aim of propensity score matching is to estimate the effect of a treatment by creating two groups that are matched on the characteristics that predict receiving treatment, so that the only important difference between the two groups is whether or not treatment was actually received. Thus, propensity score matching aims to replicate the baseline covariate balance that is achieved by randomization to the 'treatment' and

'control' arms in a RCT. Firstly, we calculated the probability of receiving an epidural for labour analgesia ('propensity score') using logistic regression with epidural analgesia as the outcome variable and age group, country of birth, parity, gestational age, birthweight, marital status, smoking in pregnancy, labour induction, systemic opioid analgesia in labour, maternal co-morbidities, hospital maternity service level and patient financial status included as independent variables. Only variables that may confound the association between epidural analgesia in labour and caesarean section, based on the descriptive analysis, were included.[15] The final choice of model specification used to calculate the propensity score was guided by covariate balance diagnostics after matching on propensity score.[16] The final propensity score model included interaction terms between induction of labour and parity, and between gestational age and birthweight. Missing data were minimal (<1%, see footnotes in Table 1) and addressed by restricting to complete-case analysis. Secondly, for each 'treated' observation (received epidural), a 'control' (did not receive epidural) was found with the smallest difference in propensity score. This was achieved using 1:1 nearest neighbour matching without replacement within a calliper equal to 0.2 times the standard deviation of the logit of the propensity score (0.04 in this study) to minimize bias.[17] Treated observations with a propensity score higher (or lower) than the highest (or lowest) control propensity score were excluded. Observations were ordered randomly before matching. Matching was implemented using the *psmatch2* command in Stata. Covariate balance between the matched treated and control observations was assessed by comparing means and proportions across treated and control groups and by calculating the absolute standardised difference of proportions (equation 1).[18] An absolute standard difference of 0.1 (10%) or greater was considered to show covariate imbalance. Chi-squared tests were used to assess differences between matched and unmatched treated observations.

To estimate the effect of receiving epidural analgesia in labour on caesarean section, the risk ratio and risk difference were calculated directly from the data and 95% confidence intervals were calculated using the method of Agresti and Min,[19] which accounts for matching (equations 2-5). McNemar's test for matched pairs was used to calculate p-values. We conducted a sensitivity analysis of the robustness of the effect estimates to confounding by unmeasured characteristics. Following the approach of Rosenbaum,[20] we estimated how strongly a binary confounder would need to be associated with epidural analgesia to fully explain the observed association between epidural analgesia in labour and caesarean section. Rosenbaum[20] defined 'gamma', which is the odds ratio of selection to the treatment group compared to the control group for a binary variable. For an unmeasured binary confounder, we estimated the level of statistical evidence for the association between epidural analgesia in labour and caesarean section at different levels of gamma. At a value for gamma with an associated p-value of greater than 0.05, the 95% confidence intervals for the effect estimates would include the null and thus the results would be sensitive to confounding at this level. We implemented this sensitivity analysis using the *mhbounds* command in Stata.[21]

Preparation of linked data and descriptive analyses were conducted in SAS v9.3. Propensity score analyses were conducted in StataIC 13.

Equation 1: Absolute value of the standardised difference of proportions

$$d = \left| \frac{p_{treated} - p_{control}}{\sqrt{\frac{p_{treated}(1-p_{treated}) + p_{control}(1-p_{control})}{2}}} \right|$$

Equations 2-5 concern calculation of risk measures for matched pairs, where

a = pairs in which both the treated and control observations have the event of interest

b = pairs in which only the treated observation has event of interest

c = pairs in which only the control observation has the event of interest

d = pairs in which neither the treated or control observation have the event of interest

n = total number of pairs

Equation 2: Risk difference for matched pairs

$$RD = \frac{b-c}{n}$$

Equation 3: Variance of risk difference for matched pairs

$$\mathrm{var}(RD) = \frac{(b+c) - \left((c-b)^2 \big/ n \right)}{n^2}$$

Equation 4: Log-Risk Ratio for matched pairs

$$\log(RR) = \log\left[\frac{a+b}{a+c} \right]$$

Equation 5: Variance of log-Risk Ratio for matched pairs

$$\mathrm{var}(\log[RR]) = \frac{(c+b)}{(a+c)(a+b)}$$

Results

The study population comprised 172,785 women (Figure 1). Linkage of maternal birth and hospital records was achieved for 99% of birth records. In this low risk population, 15,926 (9.2%) women had a caesarean section, including 6.1% of women whose primary indication for caesarean section was failure to progress and 3.1% of women whose primary indication for caesarean section was fetal distress. Epidural analgesia in labour was used by 54,668 (31.6%) women, of whom 11,227 (20.5%) had a caesarean section. Labour was induced in 26.4% of women and 47.9% of women were nulliparous. Most women were aged 20-34 years (75.9%) and maternal age ranged from 12 to 53 years (median 30 years). Epidural analgesia in labour was more common among women aged 35 years and older, nulliparous women, women in induced labour, non-smokers, women at 41 weeks gestation, women with co-morbidities, private patients and in private hospitals (Table 1). Most (70.5%) intrapartum caesarean sections occurred in women who had epidural analgesia for labour. Caesarean section was also relatively more frequent among nulliparous women (89.2% of all caesareans), women with induced labour, women aged 35 years or older, women born outside Australia, non-smokers, women at 41 weeks gestation, women who had systemic opioid analgesia in labour, women with comorbidities, private patients and for deliveries in private hospitals.

A matched control was found for 43,745 of the 54,668 women who had an epidural in labour. Matched controls were found across the full range of propensity scores for the epidural group (propensity scores ranged from 0.022 – 0.883 for epidural group, 0.016 – 0.885 for control group). No match was found for 10,923 women who had an epidural in labour, all of whom had high propensity scores, because there were too few control observations with high propensity scores to find a unique match to all of these treated observations (Figure 2). In the matched pairs, the frequency of caesarean section was 18.6% in the treated group and 7.08% in the control group. In the unmatched treated

observations with high propensity scores, the frequency of caesarean section was 28.2%, 1.5 times the rate in the matched treated observations ($p<0.0001$).

After matching on propensity score, covariate imbalance between treated and control groups was substantially reduced. Parity was evenly distributed, with 62.6% of the treated group and 63.5% of the control group nulliparous, and 34.2% and 33.9% of the treated and control groups respectively had induced labour (Table 2). The largest absolute standardised difference after matching was 0.04 (4% difference) for birthweight and most standardised differences were 0.01 (1% difference) or less (Figure 3).

In the matched groups, the risk ratio for caesarean section was 2.63 (95% CI [2.53, 2.74], $p<0.0001$) for women receiving epidural analgesia in labour (Table 3). The absolute risk difference between women who received epidural analgesia compared to women who did not was 11.56% (95% CI [11.13%, 11.99%], $p<0.0001$), which is equivalent to 1 caesarean section for every 9 women who receive epidural analgesia for labour. In sensitivity analysis, the 95% confidence interval for the risk difference would include zero if an unmeasured confounding variable increased the odds of receiving epidural analgesia by at least 2.9 (at which $p=0.054$) (Table 3). For confounding below this bound, there would still be strong statistical evidence ($p<0.001$ for odds of 2.8 or below) of an effect of epidural analgesia in labour on caesarean section. The risk ratio for caesarean section for failure to progress is higher (RR 3.09, 95% CI [2.94, 3.25]) and contributes more to the risk difference (RD 8.81%, 95% CI [8.45, 9.18] than for caesarean section for fetal distress (RR 1.96, 95% CI [1.83, 2.09], RD 2.75%, 95% CI [2.48, 3.00]). Sensitivity to unmeasured confounding is greater for caesarean section for fetal distress ($p=0.052$ when odds of selection into treatment group increase to 1.9) and is less sensitive for caesarean section for failure to progress ($p=0.045$ when odds of selection to treatment group increase to 3.25).

Comments

The aim of this study was to investigate the association between epidural analgesia in labour and caesarean section and then compare our findings with a recent Cochrane meta-analysis of RCTs of epidural analgesia in labour.[1] In our study epidural analgesia increased the relative risk of caesarean section by 2.63 and the absolute risk by 11.6%, in contrast to the findings of the Cochrane meta-analysis (RR 1.10, 95% CI [0.97, 1.25]). We found a strong association between epidural analgesia in labour and caesarean section for failure to progress (RR 3.09), which accounted for most of the observed association with caesarean section overall. We found a doubling of the risk of caesarean section for fetal distress (RR 1.96) associated with use of epidural analgesia in labour, which is within the 95% confidence interval (RR 1.43, [1.03, 1.97]) reported for this outcome in the Cochrane meta-analysis.[1]

An advantage of propensity score matching compared to logistic regression for analysing observational data is that risk ratios and risk differences can be calculated, which are more interpretable measures of risk than odds ratios and can be more readily compared to the results of RCTs.[16] In our study the risk difference is interpretable as the effect of epidural analgesia on caesarean section rates amongst women who received epidural analgesia (average effect of treatment on the treated - ATT), rather than the effect on caesarean section rates if every woman received epidural analgesia in labour (average treatment effect - ATE).[22] The ATT is the most relevant measure as epidural for labour analgesia is an elective procedure and no hospital in our study had epidural rates approaching 100%. However it should be noted that unlike for a RCT, the ATT and the ATE may not coincide and we would not extrapolate the ATT to the impact of epidural analgesia in labour on caesarean rates if it was used by all parturient women.

A RCT accounts for known and unknown confounders by randomly assigning treatment and analysing by intention to treat. However, the intention to treat analysis may not reflect the true effect of treatment if participants do not comply with their assigned treatment. Propensity scoring for observational studies attempts to control for confounding by conditioning on known potential confounders. We attempted to minimize confounding in this study partly through our study eligibility criteria, which excluded women with substantially increased likelihood of caesarean section. We then closely matched on demographic, obstetric and medical characteristics that are associated with both epidural analgesia in labour and caesarean section, thus creating a population where 'allocation' to epidural analgesia is exchangeable on measured factors. In any observational study, confounding due to unmeasured characteristics cannot be excluded. In this study, the estimates of the effect of epidural analgesia for labour pain on caesarean section risk are robust to confounding up to the point where a confounder increased the odds of receiving epidural analgesia by at least 2.9, which could be considered as a strong confounder. It is likely that some confounding persists because we did not have data on labour pain intensity, which may indicate dysfunctional labour leading to both request for epidural analgesia and increasing the risk of caesarean section.[23-25] However, Beilin, Mungall et al.[26] reported that labour pain intensity at time of request for epidural analgesia was not associated with caesarean delivery in women in induced labour. By excluding large-for-gestational-age infants, non-vertex birth presentations and multiple births, and then further closely matching on parity and induction of labour, it is likely that confounding by pain intensity is partially reduced due to correlation with these factors.

Additional limitations of our study include that we do not have data on the timing of administration of epidural analgesia in labour relative to the timing of a caesarean section for failure to progress (labour dystocia). However, a recent similar Danish cohort study excluded women who received epidural analgesia in labour after the diagnosis of dystocia and still found a strong association

between epidural analgesia in labour and caesarean section.[27] We did not have data on occiput posterior birth position, which could act as a confounder as an occiput posterior position is associated with longer, painful labours and a higher rate of operative delivery.[28] However, epidural analgesia has been associated with persistent occiput posterior at delivery regardless of fetal position at time of request for analgesia, which suggests occiput posterior position may be on the causal pathway between epidural analgesia and caesarean section.[29] We did not have data on maternal height or body size, however in other studies that did measure maternal BMI, the association between epidural analgesia in labour and caesarean section persists after adjustment.[27, 30] Finally, it is possible that there was some misclassification error in the coding of epidural analgesia specifically for labour rather than delivery.

Our study builds on several observational studies that have reported an association between epidural analgesia in labour and caesarean delivery.[27, 30-33] One study also used propensity score methods to analyse a cohort of 2052 women with data collected between 1994 and 1996.[30] Observations were grouped by quintile of propensity score rather than individually matched; nonetheless this study reported similar risk ratios for the association between epidural analgesia in labour and caesarean section (RR 2.4, 95% CI [1.5, 3.7] in nulliparous women, RR 1.8, 95% CI [0.6, 5.3] in multiparous women) as our study. Our study improves on previous observational studies through rigorous application of the propensity score matching method, including estimating sensitivity to confounding, and through use of recent data for a large population base.

An important difference between these observational studies and RCTs is that the underlying study population and clinical practice settings may differ substantially. As the most recent Cochrane review[1] found that epidural analgesia in labour increases the need for oxytocin augmentation of labour, the length of the second stage of labour, risk of instrumental delivery and the risk of caesarean section for fetal distress, it is surprising that no association was found with caesarean section overall. This

suggests that in the context of a RCT, labour progress and dystocia are likely to have been very well managed, including rigorous application of active management of labour protocols specifying the use of oxytocin augmentation for failure to progress, especially after initiation of epidural analgesia.[4] Thus, caesarean sections may have been avoided in the RCT setting, which is further supported by the low rate of caesarean sections in most of these trials, in comparison with higher rates in the countries in which the RCTs were conducted. Further, women who consent to be randomized to a method of pain relief in labour, and the university-affiliated institutions in which these RCTs are conducted, are not likely to represent the broad population base or clinical setting in which obstetric interventions in labour are applied.[34]

Epidural analgesia in labour is associated with increased risk of caesarean section in a large, contemporary maternity population. RCTs are generally considered 'gold standard' evidence; however in the context of obstetric care, evidence generated by RCTs has limitations due to substantial non-compliance (affecting internal validity) and the risk of limited external validity if the settings and participants of RCTs differ from the population base. Population-based studies contribute important information about how obstetric interventions are applied in practice. Further research should investigate the extent to which variation in clinical practice explains this association between epidural analgesia in labour and caesarean section, and whether different labour management strategies limit the risk of caesarean section for women who choose to use epidural analgesia as their preferred method of labour pain relief.

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Figure 1: Selection of study population of 172,785 women who gave birth in NSW, Australia, 2007-2010.

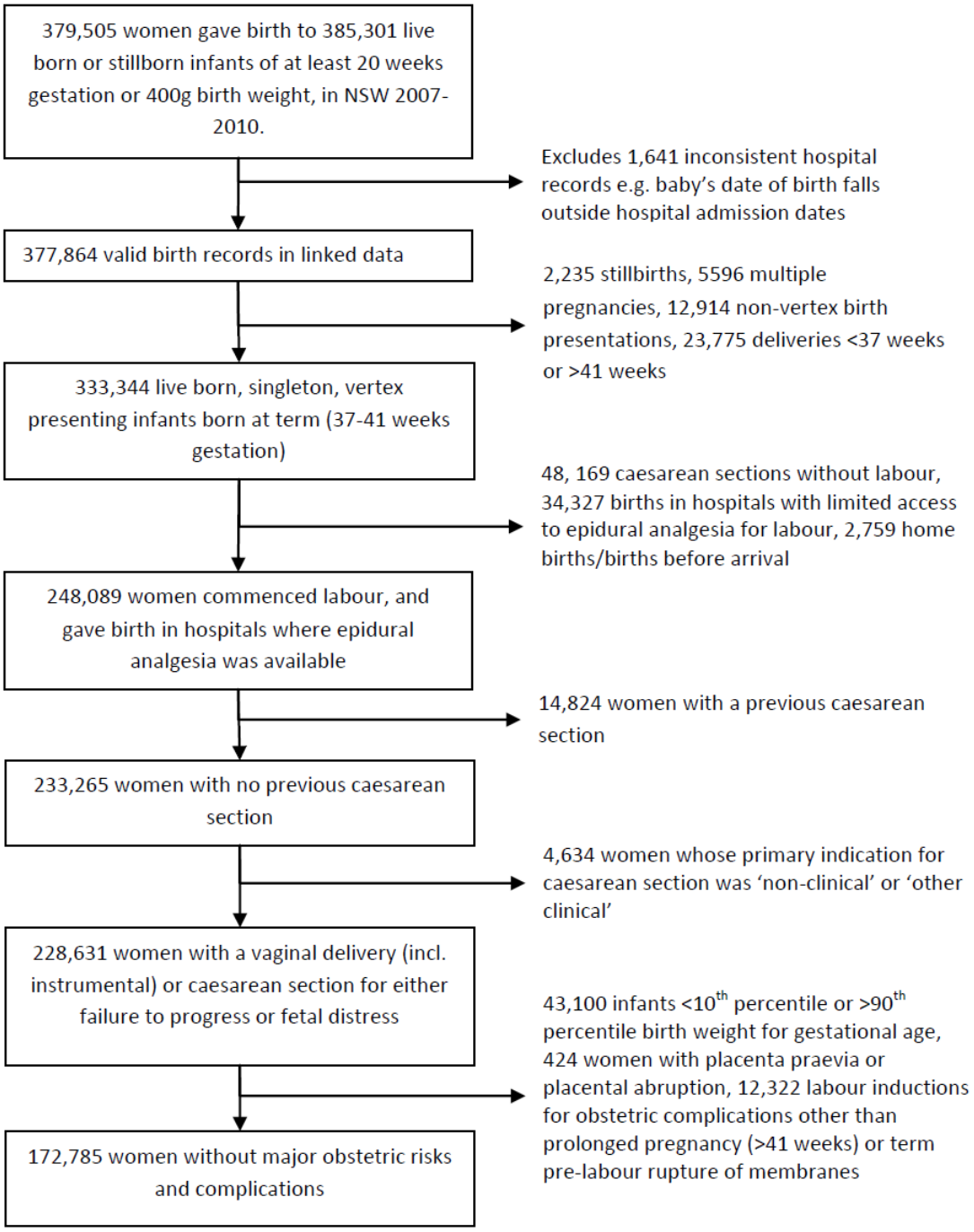
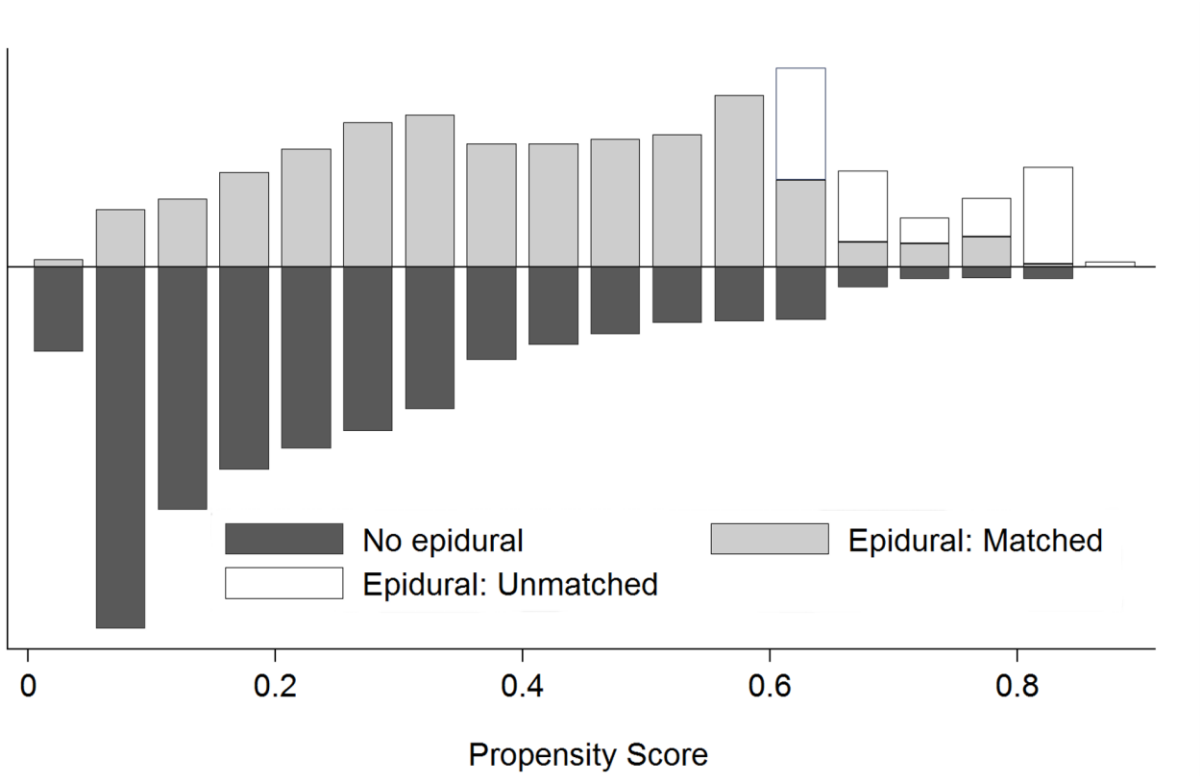
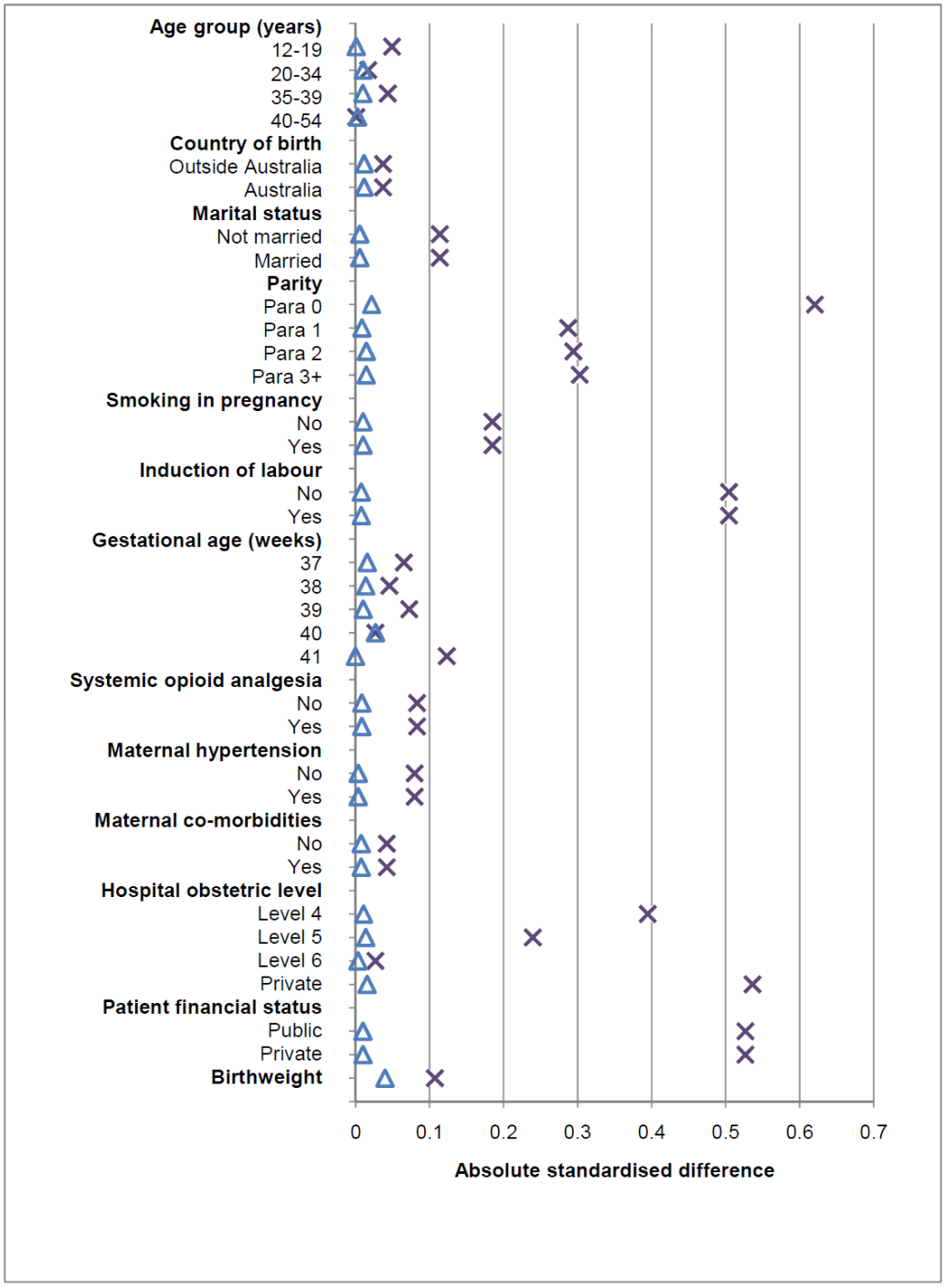


Figure 2: Histogram of propensity score by use of epidural analgesia in labour.



The propensity score defines the probability of receiving epidural analgesia conditional on the values of observed demographic and pregnancy-related variables included in the predictive logistic regression model. 'Treated' observations (received epidural analgesia in labour; shown as light grey bars) were matched without replacement to a 'control' observation (dark grey bars). There were insufficient control observations with high propensity scores to match all treated observations (white bars represent unmatched 'treated' observations).

Figure 3: Balance on observed demographic and pregnancy variables by use of epidural analgesia in labour.



The absolute standardised difference is used to compare the distribution of demographic and pregnancy-related characteristics in women receiving epidural compared to women not receiving epidural before (purple crosses) and after (blue triangles) matching on propensity score. For birthweight, the absolute standardised difference in means is shown; for all other characteristics the absolute difference in proportions is shown.

Tables

Table 1: Epidural analgesia and caesarean section by demographic and pregnancy characteristics in 172,785 women in NSW, Australia, 2007-2010

Maternal characteristic		N women (%)	Epidurals (%)	CS [a] (%)	CS FtP [b] (%)	CS FD [c] (%)
Total		*172785 (100.0)*	*54668 (31.6)*	*15926 (9.2)*	*10566 (6.1)*	*5370 (3.1)*
Epidural in labour	No	118117 (68.4)	-	4699 (29.5)	2710 (25.7)	1989 (37.0)
	Yes	54668 (31.6)	-	11227 (70.5)	7846 (74.3)	3381 (63.0)
Age group (years)	12-19	6414 (3.7)	1689 (3.1)	534 (3.4)	365 (3.5)	169 (3.2)
	20-34	131065 (75.9)	41192 (75.4)	11883 (74.6)	7888 (74.7)	3995 (74.4)
	35-39	30095 (17.4)	10145 (18.6)	2992 (18.4)	1918 (18.2)	1074 (18.7)
	40-54	5205 (3.0)	1640 (3.0)	587 (3.7)	385 (3.7)	202 (3.8)
Born in Australia	No	58193 (33.7)	17755 (32.5)	5871 (36.9)	3904 (37.0)	1967 (36.6)
	Yes	114592 (66.3)	36913 (67.5)	10055 (63.1)	6652 (63.0)	3403 (63.4)
Married or de facto	No	26900 (15.7)	6997 (12.9)	2453 (15.6)	1608 (15.4)	845 (15.9)
	Yes	144246 (84.3)	47070 (87.1)	13300 (84.4)	8836 (84.6)	4464 (84.1)
Parity	Para 0	82644 (47.9)	37209 (68.1)	14182 (89.2)	9611 (91.1)	4571 (85.3)
	Para 1	53107 (30.8)	12024 (22.0)	1081 (6.8)	591 (5.6)	490 (9.1)
	Para 2	23486 (13.6)	3920 (7.2)	390 (2.5)	206 (2.0)	184 (3.4)
	≥Para 3	13305 (7.7)	1483 (2.7)	255 (1.6)	138 (1.3)	117 (2.2)
Smoking in pregnancy	No	154243 (89.4)	50868 (93.1)	14650 (92.1)	9761 (92.5)	4889 (91.2)
	Yes	18334 (10.6)	3774 (6.9)	1261 (7.9)	789 (7.5)	472 (8.8)
Induction of labour	No	127165 (73.6)	31816 (58.2)	7915 (49.7)	5040 (47.8)	2875 (53.5)
	Yes	45607 (26.4)	22848 (41.8)	8010 (50.3)	5515 (52.3)	2495 (46.5)
Gestational age (wks)	37	8826 (5.1)	2266 (4.2)	482 (3.0)	308 (2.9)	174 (3.2)
	38	24699 (14.3)	7221 (13.2)	1423 (8.9)	931 (8.8)	492 (9.2)

	39	47269 (27.4)	13757 (25.2)	3130 (19.7)	2037 (19.3)	1093 (20.3)
	40	58736 (34.0)	19058 (34.9)	5393 (33.9)	3540 (33.5)	1853 (34.5)
	41	33255 (19.3)	12366 (22.6)	5498 (34.5)	3740 (35.4)	1758 (32.7)
Opioid analgesia	No	139082 (80.5)	45223 (82.7)	11970 (75.2)	7655 (72.5)	4315 (80.4)
	Yes	33703 (19.5)	9445 (17.3)	3956 (24.8)	2901 (27.5)	1055 (19.7)
Hypertension	No	167148 (96.7)	52335 (95.7)	14894 (93.5)	9850 (93.3)	5044 (93.9)
	Yes	5637 (3.3)	2333 (4.3)	1032 (6.5)	706 (6.7)	326 (6.1)
Co-morbidities	No	160011 (92.6)	50206 (91.8)	14168 (89.0)	9355 (88.6)	4813 (89.6)
	Yes	12774 (7.4)	4462 (8.2)	1758 (11.0)	1201 (11.4)	557 (10.4)
Hospital obstetric level	Level 4	40335 (23.3)	6919 (12.7)	2951 (18.5)	1962 (18.6)	989 (18.4)
	Level 5	34913 (20.2)	7595 (13.9)	3148 (19.8)	2128 (20.2)	1020 (19.0)
	Level 6	54099 (31.3)	17582 (32.2)	5584 (35.1)	3795 (36.0)	1789 (33.3)
	Private	43438 (25.1)	22572 (41.3)	4243 (26.6)	2671 (25.3)	1572 (29.3)
Patient financial status	Public	112766 (65.7)	26468 (48.7)	9793 (62.0)	6622 (63.3)	3171 (59.6)
	Private	58846 (34.3)	27839 (51.3)	6000 (38.0)	3848 (36.8)	2152 (40.4)
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Birthweight		3464 (333)	3489 (328)	3548 (333)	3583 (328)	3479 (332)

[a] CS: Caesarean section; [b] CS FtP: Caesarean section for failure to progress; [c] CS FD: Caesarean section for fetal distress. Missing data is as follows: <50 for age group, induction of labour and birthweight; marital status, 1639; parity, 243; smoking in pregnancy, 208; patient financial status, 1173. Percentages may not add to 100% due to rounding.

Table 2: Covariate imbalance in use of epidural analgesia in labour before and after matching on propensity score

Maternal characteristic		Before matching		After matching	
		Epidural (%)	No Epidural (%)	Epidural (%)	No epidural (%)
Total		*54668 (31.6)*	*118117 (68.4)*	*43745 (50.0)*	*43745 (50.0)*
Age group (years)	12-19	1689 (3.0)	4725 (4.0)	1643 (3.8)	1652 (3.8)
	20-34	41192 (75.4)	89873 (76.1)	33290 (76.1)	33094 (75.7)
	35-39	10145 (18.6)	19950 (16.9)	7556 (17.3)	7722 (17.7)
	40-54	1640 (3.0)	3565 (3.0)	1256 (2.9)	1277 (2.9)
Born in Australia	No	17755 (32.5)	40438 (34.2)	14494 (33.1)	14253 (32.6)
	Yes	36913 (67.5)	77679 (65.8)	29251 (66.9)	29492 (67.4)
Married or defacto	No	6997 (12.9)	19903 (17.0)	6264 (14.3)	6173 (14.1)
	Yes	47070 (87.1)	97176 (83.0)	37481 (85.7)	37572 (85.9)
Parity	Para 0	37209 (68.1)	45435 (38.5)	27361 (62.6)	27822 (63.6)
	Para 1	12024 (22.0)	41083 (34.8)	11040 (25.2)	10873 (24.9)
	Para 2	3920 (7.2)	19566 (16.6)	3878 (8.9)	3697 (8.5)
	≥Para 3	1483 (2.7)	11822 (10.0)	1466 (3.4)	1353 (3.1)
Smoking in pregnancy	No	50868 (93.1)	103375 (87.7)	40244 (92.0)	40366 (92.3)
	Yes	3774 (6.9)	14560 (12.4)	3501 (8.0)	3379 (7.7)
Induction of labour	No	31816 (58.2)	95349 (80.7)	28773 (65.8)	28938 (66.2)
	Yes	22848 (41.8)	22759 (19.3)	14972 (34.2)	14807 (33.9)
Gestational age (weeks)	37	2266 (4.2)	6560 (5.6)	2104 (4.8)	1957 (4.5)
	38	7221 (13.2)	17478 (14.8)	6285 (14.4)	6072 (13.9)
	39	13757 (25.2)	33512 (28.4)	11627 (26.6)	11423 (26.1)
	40	19058 (34.9)	39678 (33.6)	14343 (32.8)	14905 (34.1)
	41	12366 (22.6)	20889 (17.7)	9386 (21.5)	9388 (21.5)

Opioid analgesia	No	45223 (82.7)	93859 (79.5)	34821 (79.6)	34667 (79.3)
	Yes	9445 (17.3)	24258 (20.5)	8924 (20.4)	9078 (20.8)
Hypertension	No	52335 (95.7)	114813 (97.2)	42056 (96.1)	42088 (96.2)
	Yes	2333 (4.3)	3304 (2.8)	1689 (3.9)	1657 (3.8)
Co-morbidities	No	50206 (91.8)	109805 (93.0)	40280 (92.1)	40372 (92.3)
	Yes	4462 (8.2)	8312 (7.0)	3465 (7.9)	3373 (7.7)
Hospital obstetric level	Level 4	6919 (12.7)	33416 (28.3)	6786 (15.5)	6613 (15.1)
	Level 5	7595 (13.9)	27318 (23.1)	7438 (17.0)	7209 (16.5)
	Level 6	17582 (32.2)	36517 (30.9)	14930 (34.1)	15006 (34.3)
	Private	22572 (41.3)	20866 (17.7)	14591 (33.4)	14917 (34.1)
Patient financial status	Public	26468 (48.7)	86298 (73.6)	24593 (56.2)	24371 (55.7)
	Private	27839 (51.3)	31007 (26.4)	19152 (43.8)	19374 (44.3)
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Birthweight		3489 (328)	3453 (334)	3463 (331)	3475 (331)

Table 3: Association between epidural analgesia and caesarean section after matching on propensity score

Outcome	RR [a]	[95% CI]	RD [b] (%)	[95% CI]	p	Gamma [c]
CS	2.63	[2.53, 2.74]	11.56	[11.13, 11.99]	<0.0001	>2.8
CS failure to progress	3.09	[2.94, 3.25]	8.81	[8.45, 9.18]	<0.0001	>3.2
CS fetal distress	1.96	[1.83, 2.09]	2.75	[2.48, 3.00]	<0.0001	>1.8

[a] RR: Risk ratio; [b] RD (%): Risk difference percent; [c] Sensitivity to unmeasured confounding; if an unmeasured binary confounder increases the odds of receiving epidural analgesia in excess of gamma, the 95% confidence intervals for the association between epidural analgesia in labour and caesarean section will include the null effect. [c] CS: Caesarean section.