Neuraxial labour analgesia is associated with a reduced risk of maternal depression at 2 years after childbirth

A multicentre, prospective, longitudinal study

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BACKGROUND Severe labour pain is an important risk factor of postpartum depression, and early depression is associated with an increased risk of long-term depression; whereas the use of epidural analgesia during labour decreases the risk of postpartum depression.

OBJECTIVE To investigate whether neuraxial labour analgesia was associated with a decreased risk of 2-year depression.

DESIGN This was a multicentre, prospective, longitudinal study.

SETTING The study was performed in Peking University First Hospital, Beijing Obstetrics and Gynecology Hospital and Haidian Maternal and Child Health Hospital in Beijing, China, between 1 August 2014 and 25 April 2017.

PATIENTS Five hundred ninety-nine nulliparous women with single-term cephalic pregnancy preparing for vaginal delivery were enrolled.

MAIN OUTCOME MEASURE Depressive symptoms were screened with the Edinburgh Postnatal Depression Scale at delivery-room admission, 6-week postpartum and 2 years after childbirth. A score of 10 or higher was used as the threshold of depression. The primary endpoint was the presence of depression at 2 years after childbirth. The association between the use of neuraxial labour analgesia and the development of 2-year depression was analysed with a multivariable logistic regression model.

RESULTS Five hundred and eight parturients completed 2-year follow-up. Of these, 368 (72.4%) received neuraxial analgesia during labour and 140 (27.6%) did not. The percentage with 2-year depression was lower in those with neuraxial labour analgesia than in those without (7.3% [27/368] vs. 13.6% [19/140]; \( P = 0.029 \)). After correction for confounding factors, the use of neuraxial analgesia during labour was associated with a significantly decreased risk of 2-year depression (odds ratio 0.455, 95% confidence interval 0.230 to 0.898; \( P = 0.023 \)).

CONCLUSION For nulliparous women with single-term cephalic pregnancy planning for vaginal delivery, the use of neuraxial analgesia during labour was associated with a reduced risk of maternal depression at 2 years after childbirth.

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Introduction

Postpartum depression is a common psychiatric disorder in parturients after childbirth.\(^1\)\(^,\)\(^2\) It is estimated that nearly 20% of new mothers will experience an episode of major or minor depression during the first 3-month postpartum.\(^3\) Clinical symptoms may include depressed mood, dysphoria, insomnia, anxiety, loss of interest and energy, despair and even recurrent suicide ideation.\(^2\)\(^,\)\(^4\) Postpartum depression is associated with substantial adverse effects not only for parturients themselves, but also for their family and children.\(^1\)\(^,\)\(^5\) Accumulating evidence suggests that maternal depression is related to an increased risk of cognitive and emotional disorders in...
children during infancy and later childhood.\textsuperscript{5–7} In most cases, postpartum depression occurs within 4 to 6 weeks after childbirth and self-restores after 3 to 6 months.\textsuperscript{4,8} But in some serious or chronic cases, depressive symptoms can last for years.\textsuperscript{9–11} And early depression is associated with an increased risk of developing long-term depression.\textsuperscript{9}

The cause of postpartum depression is multifactorial. For example, perinatal fluctuation of hormone levels is considered to be one of the underlying mechanisms.\textsuperscript{12} Previous history of mental disorder, prenatal depression and anxiety, experience of stressful life events during pregnancy or early puerperium, and low levels of social supports are regarded as important risk factors.\textsuperscript{13,14} In addition, the intense pain during labour is thought to be related to the development of postpartum depression.\textsuperscript{15–17} whereas the use of epidural labour analgesia is associated with a decreased risk of postpartum depression.\textsuperscript{16–18} We hypothesised that the use of neuraxial labour analgesia may also decrease the occurrence of long-term depression, but evidences regarding this topic are still lacking. The purpose of the current study was to investigate whether the use of neuraxial labour analgesia was associated with a reduced incidence of depression at 2 years after childbirth.

**Methods**

**Study design**

This was a multicentre, prospective, longitudinal study. The study protocol was approved by the local Clinical Research Ethics Committees in Peking University First Hospital, Beijing, China [No. 2014 (714) on 30 May 2013 and No. 2016 (1096) on 31 May 2016] and accepted by the participating centres. The study was conducted in Peking University First Hospital (a tertiary general hospital), Beijing Obstetrics and Gynecology Hospital (a tertiary specialised hospital) and Haidian Maternal and Child Health Hospital (a secondary specialised hospital) in Beijing, China. Written informed consents were obtained from all participants prior to data collection.

**Collection of baseline data**

A standard questionnaire was used for collecting baseline data of parturients at admission in the delivery room. These included sociodemographic variables, medical history before pregnancy (including dysmenorrhea, premenstrual syndrome and internal diseases), history of the current pregnancy (planned pregnancy, routine antenatal care, attendance at childbirth classes, pregnancy complications, smoking or drinking during pregnancy, gestational age, pain and stressful events during pregnancy), as well as data of spouse.

Prenatal depressive symptoms were assessed by using the Edinburgh Postnatal Depression Scale (EPDS). This is a 10-item self-report questionnaire. Each item is graded from 0 to 3 representing the increasing severity of symptoms, resulting a total score from 0 to 30, with higher score indicating more severe depressive symptoms.\textsuperscript{19} The satisfaction of marriage was assessed with the ENRICH Marital Satisfaction Scale (EMS, a 10-item questionnaire; the total score ranges from 10 to 50, with a higher score representing a better marital satisfaction).\textsuperscript{20} The level of anxiety was assessed with the Zung Self-Rating Anxiety Scale (a 20-item questionnaire; the total score ranges from 25 to 100, with a higher score representing higher frequency of anxiety).\textsuperscript{21} The degree of social support was assessed with the Social Support Rating Scale (SSRS, a 10-item questionnaire; the total score ranges from 11 to 62, with a higher score representing better social support).\textsuperscript{22} The Chinese versions of the above instruments have been validated.\textsuperscript{22–25} All assessments were completed by parturients themselves without discussion with their family members.

**Conduct of neuraxial labour analgesia**

After admission to the delivery room, all participants were provided with information regarding the benefits and potential risks of neuraxial labour analgesia. The decision to receive neuraxial labour analgesia or not, was made by parturients themselves. For those who requested neuraxial analgesia, epidural analgesia (in Peking University First Hospital and Haidian Maternal and Child Health Hospital) or combined spinal–epidural analgesia (in Beijing Obstetrics and Gynecology Hospital) was performed. For those who did not request neuraxial analgesia, standard care was provided including intramuscular meperidine when necessary.

Neuraxial labour analgesia was initiated when the cervix was dilated to 1 cm or more. For epidural analgesia, a loading dose of 10 ml mixture (0.1% ropivacaine and 0.5 μg ml\textsuperscript{-1} sufentanil) was administered through the epidural catheter. An additional dose of 5 ml mixture was administered 10 min later if the numeric rating scale (NRS, an 11-point scale where 0 = no pain and 10 = the
worst pain) pain score remained at least 4. A patient-controlled epidural analgesia (PCEA) pump was connected 30 min later, which was established with a mixture of 0.1% ropivacaine and 0.5 μg ml⁻¹ sufentanil and programmed to deliver a 6-ml bolus with a 15-min lockout interval. For combined spinal–epidural analgesia, 2 to 3 ml of 0.1% ropivacaine and 0.5 μg ml⁻¹ sufentanil, programmed to deliver a 5-ml bolus with a 15-min lockout interval and a 5-ml h⁻¹ background infusion. Patient-controlled bolus administration was discontinued at full cervical dilation. The PCEA pump was stopped at the end of delivery.

In case of emergency Caesarean delivery, combined spinal–epidural anaesthesia was performed for those without neuraxial labour analgesia; otherwise, epidural anaesthesia was performed through the indwelling epidural catheter. PCEA was provided for 24 to 48 h after surgery.

Collection of perinatal data

Intrapartum data included the implant of labour induction, use of neuraxial analgesia, duration of labour, the highest body temperature, other medications during labour, mode of delivery, estimated blood loss and occurrence of maternal complications. For parturients who received neuraxial analgesia, the NRS pain scores were assessed before analgesia, at 10 and 30 min after analgesia, and at full cervical dilation. For those who did not receive neuraxial analgesia, the NRS pain scores were assessed at cervical dilation at least 1 cm (i.e. the same time point as those with neuraxial analgesia) and at full cervical dilation. Neonatal data included sex, birth weight, Apgar scores at 1 and 5 min after birth, occurrence of neonatal complications and admission to the neonatal ward.

The first postpartum follow-up was performed at 1 day (20 to 26 h) after childbirth. The mode of baby feeding (breast feeding, mixed feeding or formula feeding) and the NRS pain score were assessed and recorded. The overall perinatal care was assessed by parturients themselves, the primary caregiver within 6-week postpartum and other health related problems were recorded.

Follow-up at 2 years after childbirth

2-Year follow-ups were performed through face-to-face interviews from 23 to 24 months after childbirth. Maternal data including BMI, new-onset diseases after childbirth, any surgical procedures after childbirth, development of chronic pain (persistent or recurrent pain lasting for more than 3 months) and its impact on daily life (interfered with walking, mood, sleep or concentration, as judged by parturients themselves), the primary caregiver within 6-week postpartum and other health related problems were recorded.

Statistical analysis

Sample size estimation

In previous studies, the reported incidence of depression at 2 years after childbirth varied from 14 to 21%. We assumed that the incidence of 2-year depression would be 17% in women without neuraxial labour analgesia. Currently, there are no data regarding the incidence of long-term depression in women who received neuraxial analgesia during labour. However, use of epidural analgesia was associated with a 59.5% decrease (decreased from 34.6 to 14.0%) of postpartum depression at 6 weeks after childbirth. We conservatively assumed that the incidence of 2-year depression would be decreased by 50% in women with neuraxial analgesia during labour. With the power set at 80% and the two-sided significance level set at 0.05, 482 parturients were required. Sample size calculation was performed with the PASS 11.0 software (NCSS; LLC, Kaysville, Utah, USA).

Data analysis

All enrolled women were divided into two groups, that is, those who received neuraxial labour analgesia and those who did not. Continuous variables with normal distribution were analysed using independent samples t test. Continuous variables with nonnormal distribution were analysed using Mann–Whitney U test. Categorical variables were analysed using χ² test or Fisher’s exact test. Univariate logistic regression analyses were performed to screen variables that might be associated with the occurrence of 2-year depression. Independent variables with P less than 0.15 were included in a multivariate logistic regression model to determine the risk adjusted association between the use of neuraxial labour analgesia and the development of 2-year depression with a backward
stepwise procedure (likelihood ratio). Missing data were not replaced. Two-tailed $P$ values less than 0.05 were considered to be of statistical significance. SPSS 25.0 software (IBM Corporation, Armonk, New York, USA) was used for statistical analyses.

**Results**

**Participants**

From 1 August 2014 to 29 May 2015, 793 parturients were identified eligible and 599 were recruited after obtaining written informed consents. Of these, 577 completed both 1-day and 6-week follow-up (17 refused follow-up and five were lost to follow-up) and were contacted at 2 years after childbirth. During the 2-year follow-up period, 41 refused follow-up and 28 were lost to follow-up. At last, 508 parturients completed the 2-year follow-up and were included in the final analysis (Fig. 1). Two-year follow-up was performed from 9 July 2016 to 25 April 2017. There were no significant differences regarding baseline variables between parturients who were enrolled and not enrolled in the study (Supplemental Digital Content 1, http://links.lww.com/EJA/A213), and between those who completed and did not completed the 2-year follow-up (Supplemental Digital Content 2, http://links.lww.com/EJA/A213).

**Baseline and perinatal data**

Of the 508 parturients who completed 2-year follow-up, 368 (72.4%) received neuraxial labour analgesia and 140 (27.6%) did not. When compared with parturients who did not receive neuraxial analgesia, those who received analgesia had higher attendance at childbirth classes ($P = 0.015$), lower rate of induced labour ($P = 0.002$), lower NRS pain score at 10-cm cervical dilation ($P < 0.001$), higher percentage of intrapartum fever (≥37.5°C; $P = 0.003$), longer duration of the first and second stages of labour (both $P < 0.001$), lower incidence of Caesarean delivery (and higher incidence of spontaneous and instrumental delivery; $P < 0.001$), higher proportion of 1-day breast-feeding ($P = 0.015$), lower NRS pain score at 1-day postpartum ($P = 0.014$; the percentage of NRS ≥ 4 was also lower, $P = 0.002$) and lower percentage of postpartum depression at 6 weeks ($P = 0.002$) (Tables 1 and 2).

**Results of 2-year follow-up**

Of all parturients included in final analysis, 9.1% (46/508) had 2-year depression, and 2.8% (14/508) had depression at both 6 weeks and 2 years. The EPDS score at 2 years was lower in women who received neuraxial labour analgesia than in those who did not (3 [1 to 4] vs. 3 [2 to 6], $P = 0.017$). The percentage with 2-year depression (7.3 [27/368] vs. 13.6% [19/140], $P = 0.029$) and the percentage with depression at both 6 weeks and 2 years (0.5 [2/368] vs. 8.6% [12/140], $P < 0.001$) were also lower in women who received neuraxial labour analgesia than in those who did not (Table 3).

**Association between neuraxial labour analgesia and 2-year depression**

Apart from neuraxial labour analgesia, univariate analyses identified 15 other variables with $P$ values less than 0.15, including internal diseases before pregnancy, attendance at childbirth classes, antenatal EPDS score, antenatal EMS score, induced labour, duration of first-stage labour, use of oxytocin during labour, laterl episiotomy during delivery, mode of delivery, EPDS score at 6 weeks, new-onset maternal diseases after childbirth, surgical procedure of mother after childbirth, chronic pain affecting daily life at 2 years, duration of breast-feeding and 2-year SSRS score (Supplemental Digital Content 3, http://links.lww.com/EJA/A213). Of these, duration of first-stage labour was excluded because of significant correlation with neuraxial analgesia. Other 15 variables were included in a multivariate regression model.

After adjusting for confounding factors, the use of neuraxial labour analgesia was significantly associated with a decreased risk of 2-year depression [odds ratio (OR) 0.455, 95% confidence interval (CI) 0.230 to 0.898, $P = 0.023$]. Among other factors, internal diseases before pregnancy (OR 2.792, 95% CI 1.050 to 7.425, $P = 0.040$) and chronic pain affecting daily life at 2-year postpartum (OR 5.545, 95% CI 2.369 to 12.980, $P < 0.001$) were associated with an increased risk, whereas long duration of breast-feeding (OR 0.933, 95% CI 0.888 to 0.980, $P = 0.006$) and a high 2-year SSRS score (OR 0.858, 95% CI 0.797 to 0.924, $P < 0.001$) were associated with a decreased risk of 2-year depression (Table 4).

**Discussion**

Our results showed that, in nulliparous women after childbirth, 9.1% suffered from depression at 2 years and 2.8% suffered from depression at both 6 weeks and 2 years. After correction for confounding factors, the use of neuraxial analgesia during labour was significantly associated with a decreased risk of 2-year depression. Women who received neuraxial labour analgesia also had a lower prevalence of depression at both 6 weeks and 2 years.

As defined, postpartum depression usually occurs within 4 to 6 weeks after childbirth and self-restores after 3 to 6 months.4,8 However, recent studies revealed that perinatal depressive symptoms can last longer. For example, in a longitudinal study of 1735 women followed up from pregnancy to 2-year postpartum, 7% had chronic depressive symptoms and 7% had late onset depressive symptoms.26 In another study of 579 women followed up until 2-year postpartum, 21% had persistent depressive symptoms and 3% had persistent highly intense depressive symptoms.11 Similar results were reported by longitudinal studies for a longer period (until 5 to 7-year postpartum), which found that 5 to 16% of women experienced persistent high depressive symptoms and 4.9% had high depressive symptoms in the late period.10,27 Results of
the current study are within the range of the previous reports.

For most women, childbirth is one of the most painful events during their life. The intense labour pain can lead to adverse outcomes including psychological trauma and postpartum depression. On the other hand, neuraxial labour analgesia may reduce the occurrence of postpartum depression. For example, Hiltunen et al. reported a lower depressive score in mothers who...
received epidural or paracervical blockade during vaginal delivery immediately after childbirth, but not that at 4 months. In a prospective cohort study of 214 parturients preparing to give vaginal delivery, Ding et al.\textsuperscript{16} found that the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks. A later case–control study revealed that no epidural analgesia, but the use of epidural labour analgesia was associated with a decreased risk of postpartum depression at 6 weeks.

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Table 2 Perinatal data

| Variable                                | Total, n = 508 | Neuraxial analgesia, n = 368 | No neuraxial analgesia, n = 140 | P value |
|-----------------------------------------|---------------|------------------------------|---------------------------------|---------|
| Maternal data during labour             |               |                              |                                 |         |
| Induced labour<sup>b</sup>              | 165 (32.5%)   | 105 (28.5%)                  | 60 (42.9%)                      | 0.002   |
| Premature rupture of membrane           | 96 (19.8%)    | 75 (20.4%)                   | 21 (15.0%)                      | 0.166   |
| NRS pain score<sup>b</sup>              |               |                              |                                 |         |
| Before analgesia                        | 8 (7 to 9)    | 8 (7 to 9)                   | 8 (7 to 9)                      | 0.242   |
| 10 min after analgesia<sup>c</sup>      | –             | 4 (2 to 5)                   | –                               | –       |
| 30 min after analgesia<sup>c</sup>      | –             | 2 (1 to 3)                   | –                               | –       |
| At 10-cm cervical dilation<sup>d</sup>  | 6 (5 to 9)    | 6 (5 to 7)                   | 9 (9 to 10)                     | <0.001  |
| Highest temperature during labour       | ≥37.5 °C      | 65 (12.8%)                   | 57 (15.5%)                      | 0.003   |
|                                         | <38.0 °C       | 10 (2.0%)                    | 9 (2.4%)                        | 0.368   |
| Duration of labour                      |               |                              |                                 |         |
| First stage (min)<sup>e</sup>          | 540 (350 to 780) | 600 (420 to 840)          | 318 (221 to 540)                | <0.001  |
| Second stage (min)<sup>e</sup>         | 46 (28 to 79) | 51 (32 to 83)                | 34 (20 to 56)                   | <0.001  |
| Prolonged second stage<sup>f</sup>      | 1 (0.2%)      | 1 (0.3%)                     | 0 (0.0%)                        | >0.999  |
| Third stage (min)<sup>f</sup>           | 7 (5 to 10)   | 7 (5 to 10)                  | 8 (4 to 10)                     | 0.887   |
| Use of oxytocin during labour           | 344 (67.7%)   | 243 (66.0%)                  | 101 (72.1%)                     | 0.188   |
| Artificial rupture of foetal membrane   | 195 (38.4%)   | 148 (39.7%)                  | 49 (35.0%)                      | 0.353   |
| Lateral episiotomy                      | 162 (31.9%)   | 130 (35.3%)                  | 32 (22.9%)                      | 0.216   |
| Mode of delivery                        |               |                              |                                 |         |
| Spontaneous delivery                    | 336 (66.1%)   | 255 (69.3%)                  | 81 (57.9%)                      |         |
| Forceps delivery                        | 49 (9.6%)     | 42 (11.4%)                   | 7 (5.0%)                        |         |
| Caesarean delivery                      | 123 (24.2%)   | 71 (19.3%)                   | 52 (37.1%)                      |         |
| Estimated blood loss (ml)               | 200 (150 to 300) | 200 (150 to 348)          | 260 (200 to 300)                | 0.810   |
| Neonatal data                           |               |                              |                                 |         |
| Neonatal sex                            |               |                              |                                 |         |
| Male                                    | 274 (53.9%)   | 205 (55.7%)                  | 69 (49.3%)                      | 0.195   |
| Consistent with father’s preference     | 463 (91.1%)   | 336 (91.3%)                  | 127 (90.7%)                     | 0.854   |
| Consistent with mother’s preference     | 452 (89.0%)   | 328 (89.1%)                  | 124 (88.6%)                     | 0.857   |
| Birth weight (g)                        | 3416 ± 405    | 3429 ± 399                   | 3383 ± 420                      | 0.256   |
| Apgar score after birth (score)         |               |                              |                                 |         |
| 1-min                                   | 10 (10 to 10) | 10 (10 to 10)                | 10 (10 to 10)                   | 0.976   |
| 5-min                                   | 10 (10 to 10) | 10 (10 to 10)                | 10 (10 to 10)                   | 0.547   |
| Admission to neonatal ward<sup>g</sup>  | 48 (9.4%)     | 36 (9.8%)                    | 12 (8.6%)                       | 0.677   |
| 1-Day postpartum                        |               |                              |                                 |         |
| Breast-feeding                          | 412 (81.1%)   | 308 (83.7%)                  | 104 (74.3%)                     | 0.015   |
| NRS pain score<sup>h</sup>              | 3 (2 to 5)    | 3 (2 to 5)                   | 4 (3 to 5)                      | 0.014   |
| NRS score ≥4                            | 200 (39.4%)   | 130 (35.3%)                  | 70 (50.0%)                      | 0.002   |
| NRS score ≥7                            | 16 (3.1%)     | 14 (3.8%)                    | 2 (1.4%)                        | 0.278   |
| Satisfied with perinatal care<sup>h</sup> | 473 (93.1%)  | 347 (94.3%)                  | 126 (90.0%)                     | 0.088   |
| 6-Week postpartum                       |               |                              |                                 |         |
| Breast-feeding                          | 251 (69.1%)   | 257 (69.8%)                  | 94 (67.1%)                      | 0.557   |
| Persistent pain<sup>i</sup>             | 117 (23.0%)   | 90 (24.5%)                   | 27 (19.3%)                      | 0.216   |
| NRS score ≥4                            | 63 (12.4%)    | 49 (13.3%)                   | 14 (10.0%)                      | 0.311   |
| NRS score ≥7                            | 4 (0.8%)      | 2 (0.5%)                     | 2 (1.4%)                        | 0.657   |
| Persistent pain affecting daily life<sup>i</sup> | 57 (11.2%)  | 39 (10.6%)                   | 18 (12.9%)                      | 0.471   |
| Postpartum care by mother-in-law        | 95 (18.7%)    | 64 (17.4%)                   | 31 (22.1%)                      | 0.220   |
| EPDS (score)<sup>j</sup>                | 4 (4 to 9)    | 6 (4 to 9)                   | 6 (4 to 10)                     | 0.077   |
| Postpartum depression<sup>j</sup>       | 90 (17.7%)    | 53 (14.4%)                   | 37 (26.4%)                      | 0.002   |

Data are presented as mean ± SD, number (%), or median [interquartile range]. NRS, numeric rating scale; EPDS, Edinburgh Postnatal Depression Scale. a Labour induced with vaginal prostaglandin and intravenous oxytocin in women without uterine contraction or other signs of labour commencement at or over 41 weeks of pregnancy. b Numeric rating scale, an 11-point scale from 0 to 10, where 0 = no pain and 10 = the worst pain. c Data were only evaluated in parturients who received neuraxial labour analgesia. d Excluded those (n=100) who underwent emergency Caesarean delivery before the cervix dilated to 10 cm. e Excluded those who underwent Caesarean delivery. Defined as the second-stage labour duration more than 120 min. f Neonates were admitted to neonatal ward because of foetal distress/asphyxia, aspiration pneumonia, premature birth/low-birth weight, glucopenia, jaundice/hyperbilirubinemia, infection, convulsion and anal stress. g Question asked was ‘I am satisfied with the overall perinatal care’, which was assessed with a five-point scale, that is strongly agree, agree, neutral, disagree, and strongly disagree. Those who reported the first two scales were classified as satisfied. h Defined as NRS pain score at least 1 that persisted since childbirth, including pain in pelvis, low back, incision and perineum. i Defined as persistent pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. j Edinburgh Postnatal Depression Scale, score range 0 to 30, with higher score indicating more severe depression. k Defined as EPDS score at least 10 at 6 weeks postpartum.

of depression development at 4 to 8-week postpartum. In accordance with the above studies, results in the current study also showed a lower incidence of postpartum depression at (6 weeks) in parturients with neuraxial analgesia than in those without. More importantly, we found that the use of neuraxial labour analgesia was significantly associated with a decreased risk of 2-year depression; and those who received neuraxial analgesia also had a lower percentage of depression at both 6 weeks and 2 years. To our knowledge, this is the first study to report that the use of neuraxial labour analgesia may have effects on mothers’ long-term mental health after.
Table 4 Factors associated with the development of 2-year depression

| Factors                                           | OR (95% CI) | P value | OR (95% CI) | P value |
|---------------------------------------------------|-------------|---------|-------------|---------|
| Neuraxial analgesia during labour                 | 0.504 (0.271 to 0.940) | 0.031 | 0.455 (0.230 to 0.989) | 0.023 |
| Internal diseases before pregnancy                | 2.585 (1.066 to 6.266) | 0.036 | 2.792 (1.050 to 7.425) | 0.040 |
| Attendance at childbirth classes during pregnancy | 0.581 (0.293 to 1.150) | 0.119 | –           | –     |
| Antenatal EPDS score                              | 1.207 (1.072 to 1.360) | 0.002 | –           | –     |
| Antenatal EMS score                               | 0.914 (0.829 to 1.008) | 0.073 | –           | –     |
| Induced labour                                   | 2.256 (1.223 to 4.151) | 0.009 | –           | –     |
| Lateral episiotomy                                | 1.894 (0.892 to 4.019) | 0.096 | –           | –     |
| Use of oxytocin during labour                     | 2.076 (0.977 to 4.410) | 0.058 | –           | –     |
| Mode of delivery                                  | Reference  | –       | –           | –     |
| Spontaneous delivery                             | –           | –       | –           | –     |
| Forceps delivery                                  | 0.468 (0.108 to 2.030) | 0.310 | –           | –     |
| Caesarean delivery                                | 1.645 (0.857 to 3.158) | 0.135 | –           | –     |
| EPDS score at 6 weeks                             | 1.074 (0.993 to 1.162) | 0.074 | –           | –     |
| New-onset diseases after childbirth               | 3.143 (1.343 to 7.355) | 0.008 | –           | –     |
| Surgical procedure after childbirth               | 2.192 (0.775 to 5.865) | 0.143 | –           | –     |
| Chronic pain affecting daily life                 | 6.441 (2.965 to 13.993) | <0.001 | 5.545 (2.369 to 12.980) | <0.001 |
| Duration of breast-feeding (month)                | 0.927 (0.886 to 0.971) | 0.001 | 0.933 (0.888 to 0.980) | 0.006 |
| SSRS score at 2 years                            | 0.860 (0.803 to 0.921) | <0.001 | 0.858 (0.797 to 0.924) | <0.001 |

CI, confidence interval; EMS, ENRICH Marital Satisfaction Scale (score range 10 to 50, with higher score indicating higher satisfaction of marriage); EPDS, Edinburgh Postnatal Depression Scale (score range 0 to 30, with higher score indicating more severe depression); OR, odds ratio; SSRS, Social Support Rating Scale (score range 11 to 62, with higher score indicating better social support). 4 The presence of 2-year depression was modelled as a function of a single factor. 5 The presence of 2-year depression was modelled as a function of all factors with P values less than 0.15 in the univariate analyses. Multivariate logistic regression analysis was performed by using a backward stepwise procedure (likelihood ratio). Hosmer–Lemeshow test of goodness of fit of the model: χ² = 5.411, df = 8, P = 0.713. 6 Include asthma, arthritis, thyroid disease, nephritis, nephritic syndrome and positive hepatitis B surface antigen. 7 Labour induced with vaginal prostaglandin and intravenous oxytocin in women without uterine contractions or other signs of labour commencement at or over 41 weeks of pregnancy. 8 Refer to conditions that occurred during the 2-year period and required therapy, including mammitis/mammary abscess, pelvic floor dysfunction, poly cystic ovary syndrome, hypothyroidism, hyperthyroidism, Hashimoto’s thyroiditis, thyroid cancer, cerebral infarction, IgA nephropathy, lumbar disc herniation, scoliosis and phalangeal fracture. 9 Defined as any congenital (atrial septal defect, anal atresia and urethral fistula) and acquired diseases (bronchiolitis, febrile convulsion, Kawasaki disease, infant rash, eczema, urticaria, allergic dermatitis, pneumonia, anaemia, inguinal hernia and ententis) that requires therapy during the 2-year period. 10 Defined as persistent or recurrent pain lasting for more than 3 months after childbirth. 11 Defined as persistent or recurrent pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. 12 Defined as new-onset diseases that occurred during the 2-year period after childbirth and requires therapy, including mammitis/mammary abscess, pelvic floor dysfunction, polycystic ovary syndrome, hypothyroidism, hyperthyroidism, Hashimoto’s thyroiditis, chronic pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. 13 Defined as any surgical procedure performed during the 2-year period after childbirth, including Caesarean delivery, induced abortion, vaginal polypectomy, hysteromyomectomy, adnexectomy, incision and drainage of mammary abscess, cholecystectomy, thyroidectomy, and incision and internal fixation of metatarsal fracture. 14 Defined as EPDS score at least 10 at 2 years after childbirth. 15 Defined as EPDS score at least 10 at both 6 weeks and 2 years after childbirth.

Childbirth. Reasons leading to less 2-year depression in parturients with neuraxial labour analgesia are not totally clear but may include the following. First, the use of neuraxial labour analgesia might have decreased the risk of early postpartum depression. It was found that early depression is an important risk factor for the development of long-term depression. Second, the use of epidural labour analgesia might have lowered the risk of long-term negative memory. As reported, such memory can evoke intense negative emotions and reactions in some women.

Table 3 2-Year follow-up data

| Variable                      | Total, n = 508 | Neuraxial analgesia, n = 368 | No neuraxial analgesia, n = 140 | P value |
|-------------------------------|----------------|-------------------------------|---------------------------------|---------|
| BMI at 2 years (kg m⁻²)       | 21.7 ± 2.6     | 21.8 ± 2.5                    | 21.7 ± 2.6                      | 0.702   |
| New-onset diseases after childbirth | 37 (7.3%)     | 28 (7.6%)                    | 9 (6.4%)                        | 0.647   |
| Surgical procedure after childbirth | 30 (5.9%)    | 25 (6.8%)                    | 5 (3.6%)                        | 0.169   |
| Chronic pain after childbirth | 81 (15.9%)     | 64 (17.4%)                   | 17 (12.1%)                      | 0.149   |
| Chronic pain affecting daily life | 36 (7.1%)     | 24 (6.5%)                    | 12 (8.6%)                       | 0.421   |
| Duration of breast-feeding (month) | 13 (9 to 18)  | 13 (8 to 18)                 | 13 (10 to 19)                   | 0.276   |
| Another childbirth            | 19 (3.7%)      | 14 (3.8%)                    | 5 (3.6%)                        | 0.902   |
| Children with a history of disease | 52 (10.2%)    | 38 (10.3%)                   | 14 (10.0%)                      | 0.933   |
| SSRS (score)                  | 37 ± 5         | 37 ± 5                       | 37 ± 5                          | 0.690   |
| EPDS (score)                  | 3 (1 to 5)     | 3 (1 to 4)                   | 3 (2 to 6)                      | 0.017   |
| 2-Year depression              | 46 (9.1%)      | 27 (7.3%)                    | 19 (13.6%)                      | 0.029   |
| Chronic depression            | 14 (2.8%)      | 2 (0.5%)                     | 12 (8.6%)                       | <0.001  |

Data are presented as mean ± SD, number (%) or median (interquartile range). SSRS, Social Support Rating Scale; EPDS, Edinburgh Postnatal Depression Scale. 4 Missing data in five participants. 5 Refer to new-onset diseases that occurred during the 2-year period after childbirth and requires therapy, including mammitis/mammary abscess, pelvic floor dysfunction, polycystic ovary syndrome, hypothyroidism, hyperthyroidism, Hashimoto’s thyroiditis, thyroid cancer, cerebral infarction, IgA nephropathy, lumbar disc herniation, scoliosis and phalangeal fracture. 6 Refers to any surgical procedure performed during the 2-year period after childbirth, including second Caesarean delivery, induced abortion, vaginal polypectomy, hysteromyomectomy, adnexectomy, incision and drainage of mammary abscess, cholecystectomy, thyroidectomy, and incision and internal fixation of metatarsal fracture. 7 Defined as persistent or recurrent pain that lasted for more than 3 months after childbirth. 8 Defined as chronic pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. 9 Includes any congenital (atrial septal defect, anal atresia and urethral fistula) and acquired diseases (bronchiolitis, febrile convulsion, Kawasaki disease, infant rash, eczema, urticaria, allergic dermatitis, pneumonia, anaemia, inguinal hernia and ententis) that requires therapy during the 2-year period. 10 Social Support Rating Scale, score range 11 to 62, with higher score indicating better social support. 11 Defined as EPDS score at least 10 at 2 years after childbirth. 12 Defined as EPDS score at least 10 at both 6 weeks and 2 years after childbirth.
In the current study, it is interesting to note that women with induced labour received less neuraxial analgesia than in those without (105/165 [63.6%] vs. 263/343 [76.7%]). This might be due to the worry of parturients on the potential unfavourable effects of neuraxial analgesia, including prolonged labour, increased requirement of oxytocin and increased risks of instrumental delivery.34-36 Further analysis of our results showed that, when compared with women without labour induction and neuraxial analgesia, those with one or two of these factors (i.e. labour induction and no neuraxial analgesia) were both at an increased risk of 2-year depression (with one factor: unadjusted OR 2.867, 95% CI 1.419 to 5.793, P = 0.003; with two factors: unadjusted OR 3.394, 95% CI 1.377 to 8.361, P = 0.008). Therefore, it might be proper to encourage women with induced labour to consider neuraxial analgesia. Further studies are necessary to explore this issue.

The presence of chronic disease is associated with an increased risk of depressive disorders.37,38 Chronic diseases may also affect women’s mental health during the perinatal period. For example, in observational studies, it was found that women with more than one chronic health problem or medical complications were at an increased risk of developing postpartum depression.39,40 It should be noted that, in these studies, depression was assessed during the early postpartum period (up to 6 months). In the current study, we found that internal diseases before pregnancy was also associated with an increased risk of depression at 2 years after childbirth. Chronic pain, defined as any persistent or recurrent pain lasting for more than 3 months,41 is common in women after childbirth42,43 and is an important risk factor of postpartum depression.44,45 In women of the current study, chronic pain affecting daily life was also an independent risk factor of 2-year depression.

As the best nutrition for infants, exclusive breastfeeding is recommended during the first 6 months after birth.46 Furthermore, breastfeeding is also important for mothers’ mental health. There is a reciprocal relationship between breastfeeding cessation and postpartum depression, that is, women with depression at 8-week postpartum tend to stop breastfeeding early47; and early breastfeeding cessation is an important risk factor for increased depression at 6 months after delivery.48 On the other hand, continued breast-feeding is associated with a decreased risk of postpartum depression.16–18 Results of the current study showed that a long duration of breastfeeding was significantly associated with a decreased risk of 2-year depression. Social support, including the emotional, practical and financial assistance or companionship from others, is very important for new mothers.49 High level of social support provides preventive effects against depression development, whereas inadequate social support is associated with higher odds of depression.49–51 Consistent with these results, the current study also showed that a higher SSRS score at 2 years was a protective factor for the development of 2-year depression.

There are several limitations of the current study. First, only nulliparae with single cephalic term pregnancy planning for vaginal delivery were included in the current study. This limited the generalisability of our results. Second, maternal depression was not diagnosed by psychiatrists. However, as a screening instrument, the EPDS is the most extensively studied one with moderate psychometric soundness for nonpsychiatric health team members.52 Third, as an observational study, the causal relationship between the use of neuraxial analgesia during labour and the reduced depression at 2 years after childbirth cannot be established. However, our results provide an important indication that the use of neuraxial labour analgesia may have long-term effects on mothers’ mental health after childbirth.

In conclusion, for nulliparous women with single cephalic term pregnancies planning vaginal delivery, use of neuraxial analgesia during labour was significantly associated with a decreased risk of depression at 2 years after childbirth. Long-term effects of neuraxial labour analgesia on maternal mental health deserve further study.

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References

1. Bruggmann D, Wagner C, Klingelhofer D, et al. Maternal depression research: socioeconomic analysis and density-equalizing mapping of the global research architecture. Arch Womens Ment Health 2017; 20:25–37.
2. Wisner KL, Parry BL, Piontek CM. Clinical practice. Postpartum depression. N Engl J Med 2002; 347:194–199.
3. Werner E, Miller M, Osborne LM, et al. Preventing postpartum depression: review and recommendations. Arch Womens Ment Health 2015; 18:41–60.
4. Kim S, Soeken TA, Cromer SJ, et al. Oxytocin and postpartum depression: delivering on what’s known and what’s not. Brain Res 2014; 1580:219–232.
5. Stein A, Pearson RM, Goodman SH, et al. Effects of perinatal mental disorders on the fetus and child. Lancet 2014; 384:1800–1819.

Eur J Anaesthesiol 2019; 36:745–754
Sanger C, Ills JE, Andrew CS, et al. Associations between postnatal maternal depression and psychological outcomes in adolescent offspring: a systematic review. *Arch Womens Ment Health* 2015; 18:147–162.

Smith-Nielsen J, Thorner A, Krogh MT, et al. Effects of maternal postpartum depression in a well resourced sample: early concurrent and long-term effects on infant cognitive, language, and motor development. *Scand J Psychol* 2016; 57:571–583.

Woinarowicz KL, Musse-Koko EL, Sit DK. Postpartum depression: a disorder in search of a definition. *Arch Womens Ment Health* 2010; 13:37–40.

Giallo R, Cooklin A, Nicholson JM. Risk factors associated with trajectories of perinatal depressive symptoms from pregnancy to 4 years postpartum. *Soc Psychiatry Psychiatr Epidemiol* 2017; 52:815–828.

Giallo R, Cooklin A, Nicholson JM. Risk factors associated with trajectories of mothers’ depressive symptoms across the early parenting period: an Australian population-based longitudinal study. *Arch Womens Ment Health* 2014; 17:115–125.

Sutter-Dalay AL, Cosnefroy O, Glattiny-Dalay E, et al. Evolution of perinatal depressive symptoms from pregnancy to two years postpartum in a low-risk sample: the MATQUID cohort. *J Affect Disord* 2012; 139:23–29.

Workman JL, Barha CK, Gales LA. Endocrine substrates of cognitive and affective changes during pregnancy and postpartum. *Behav Neurosci* 2012; 126:54–72.

Robertson E, Grace S, Wallington T, et al. Antenatal risk factors for postpartum depression: a synthesis of recent literature. *Hosp Psychiatry* 2004; 26:289–295.

Milgrom J, Gemmill AW, Blixta JL, et al. Antenatal risk factors for postnatal depression: a large prospective study. *J Affect Disord* 2008; 108:147–157.

Hiltunen PRT, Ebeling H, Mollanen I, et al. Does pain relief during delivery decrease the risk of postnatal depression? *Acta Obstet Gynecol Scand* 2004; 83:267–261.

Ding T, Wang X, Qiu Y, et al. Episodic labor analgesia is associated with a decreased risk of postpartum depression: a prospective cohort study. *Anesth Analg* 2014; 119:383–392.

Suhithan T, Pham TP, Chen H, et al. Investigating anaesthetic and psychological factors associated with risk of postpartum depression development: a case–control study. *Neuropsychiatr Dis Treat* 2016; 12:1333–1339.

Lim G, Farrell LM, Facco FL, et al. Labor analgesia as a predictor for reduced postpartum depression scores: a retrospective observational study. *Anesth Analg* 2018; 126:1598–1605.

Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987; 150:782–786.

Olson BFD. ENRICHD Mental Satisfaction Scale: A brief research and clinical tool. *J Psychol* 1993; 7:176–185.

Zung WW. A rating instrument for anxiety disorders. *Psychosomatics* 1971; 12:371–379.

Xiao SY. The theoretical basis and applications of Social Support Rating Scale (SSRS). *J Clin Psychiatry* 1994; 4:98–100.

Lee DT, Yp SK, Chiu HF, et al. Detecting postnatal depression in Chinese women. Validation of the Chinese version of the Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1998; 172:439–437.

Li LJ. Olson Marriage Quality Questionnaire (ENRICH). In: Wang XD, eds. *Rating scales for mental health. Chin Ment Health J* 1999; 13(Suppl): S153–S159.

Wu WY. Self-Rating Anxiety Scale. In: Zhang ZJ, editor. *Behavioral Medicine Inventory Manual*. Beijing: The Chinese Medicine Electronic Audio and Video Publishing House; 2005, pp. 213–214.

Mora PA, Bennett IM, Eio IT, et al. Distinct trajectories of perinatal depressive symptomatology: evidence from growth mixture modeling. *Am J Epidemiol* 2009; 169:24–32.

van der Waerden J, Galera C, Saurel-Cubizolles MJ, et al. Predictors of persistent maternal depression trajectories in early childhood: results from the EDEN mother–child cohort study in France. *Psychol Med* 2015; 45:1999–2012.