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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 evidences suggest that maternal depression is related to an increased risk of cognitive and emotional disorders in

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children during infancy and later childhood.[5–7] In most cases, postpartum depression occurs within 4 to 6 weeks after childbirth and self-restores after 3 to 6 months.[4,8] But in some serious or chronic cases, depressive symptoms can last for years.[9–11] And early depression is associated with an increased risk of developing long-term depression.[9]

The cause of postpartum depression is multifactorial. For example, perinatal fluctuation of hormone levels is considered to be one of the underlying mechanisms.[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.[13,14] In addition, the intense pain during labour is thought to be related to the development of postpartum depression,[15–17] whereas the use of epidural labour analgesia is associated with a decreased risk of postpartum depression.[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.

Patient recruitment

The inclusion criteria were nulliparae with term singleton pregnancy in cephalic presentation who were admitted to the delivery room and planning for vaginal delivery. Exclusion criteria of parturients included the following: age less than 18 years or more than 34 years; a history of psychiatric disease (schizophrenia); contraindications to neuraxial analgesia, such as infectious diseases of the central nervous system (e.g. poliomyelitis, cerebrospinal meningitis, encephalitis), spinal or intraspinal diseases (e.g. trauma or surgery of spinal column, intraspinal canal mass), systematic infectious diseases (e.g. sepsis, bacteraemia), infection of skin or soft tissue at the puncturing site and coagulopathy; or delivery room admission outside daytime working hours (from 5 p.m. to next 8 a.m.).

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.[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).[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 higher score representing higher frequency of anxiety).[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 higher score representing better social support).[22] The Chinese versions of the above instruments have been validated.[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 $\mu g\,ml^{-1}$ 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 $\mu g\,ml^{-1}$ 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 was administered intrathecally. A PCEA pump was connected later, which was established with a mixture of 0.1% ropivacaine and 0.5 $\mu g\,ml^{-1}$ 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 implement 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 by answering 'I am satisfied with the overall perinatal care' 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.

A telephone interview was performed at 6 weeks (42 to 49 days) after childbirth. The presence of postpartum depression was assessed with EPDS. A total score of 10 or higher was defined as the threshold of postpartum depression.[23] Other data including the mode of baby feeding, the NRS pain score, the existence of persistent pain (defined as a NRS pain score $\geq$1 that persisted since childbirth) 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.

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), duration of breast-feeding and another childbirth were collected. Children's data including any congenital and/or acquired diseases that required therapy during the 2-year period were recorded. The presence of depression was assessed with EPDS. 2-Year depression was defined when the EPDS score was at least 10 at 2 years after childbirth. The level of social support was assessed with SSRS. The primary endpoint was the presence of depression at 2 years after the previous childbirth.

Statistical analysis

Sample size estimation

In previous studies, the reported incidence of depression at 2 years after childbirth varied from 14 to 21%.[11,26] 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.[16] We conservatively assumed that the incidence of 2-year depression would be decreased by 50% in women with neuraxial analgesia. 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 χ^2 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 ($\geq 37.5\,^{\circ}C$; $P = 0.003$), 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, lateral 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.

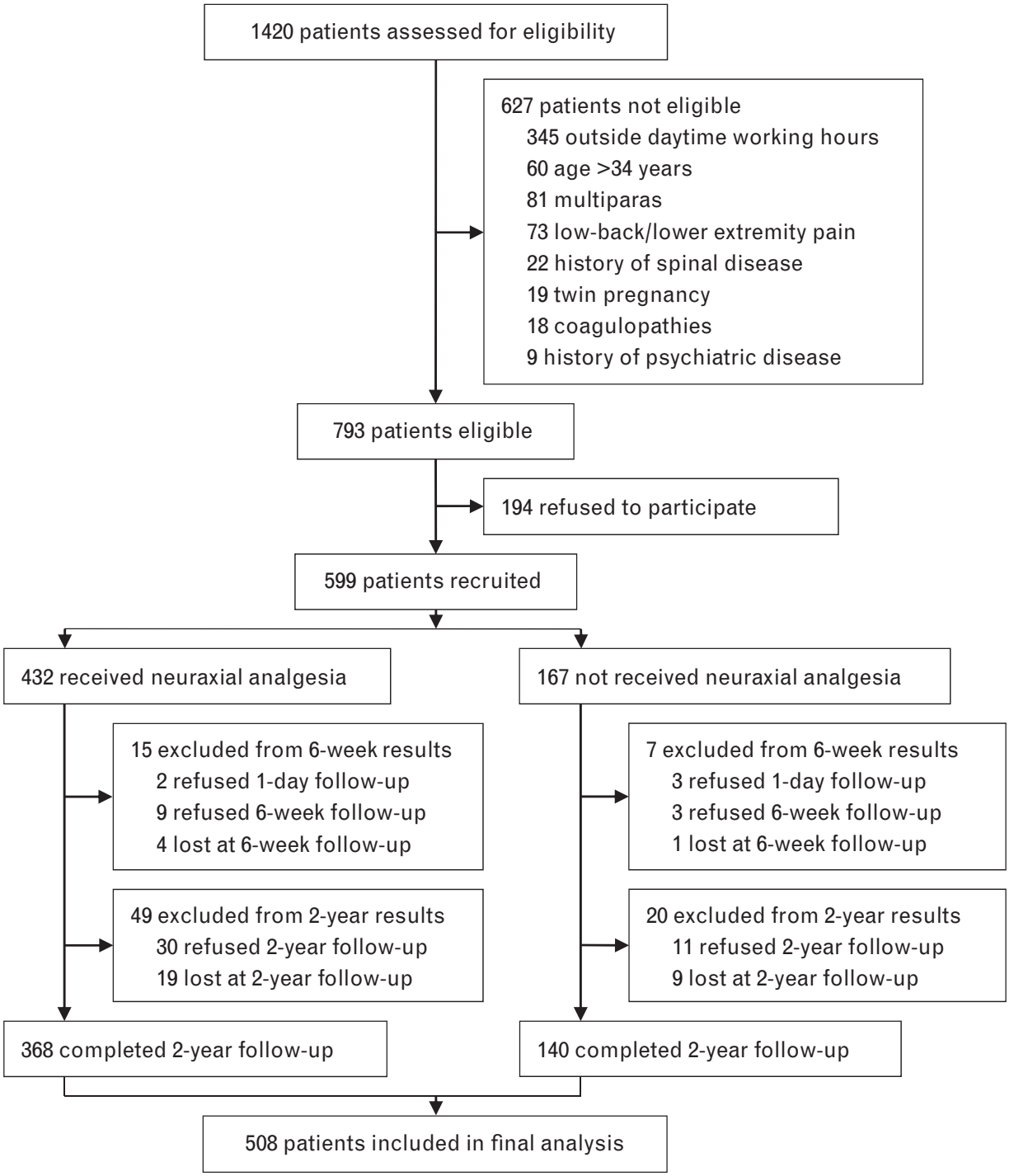
After adjusting for confounding factors, the use of neuraxial labour analgesia was significantly associated with a decreased risk of 2-year depression [odds ratio (OR) 0.455, 95% confidence interval (CI) 0.230 to 0.898, $P = 0.023$]. Among other factors, internal diseases before pregnancy (OR 2.792, 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

Fig. 1



Flow-chart of the study.

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.[28] The intense labour pain can lead to adverse outcomes including psychological trauma and postpartum depression.[29,30] On the other hand, neuraxial labour analgesia may reduce the occurrence of postpartum depression. For example, Hiltunen *et al.*[15] reported a lower depressive score in mothers who

Table 1 Demographic and baseline data

Variable	Total, $n = 508$	Neuraxial analgesia, $n = 368$	No neuraxial analgesia, $n = 140$	*P* value
Age at last childbirth (years)	30 (28 to 32)	30 (28 to 32)	30 (28 to 32)	0.881
BMI before childbirth ($kg\,m^{-2}$)	27.3 ± 2.8	27.4 ± 2.7	27.0 ± 3.1	0.182
Han nationality[a]	479 (94.3%)	347 (94.3%)	132 (94.3%)	0.997
With religious belief[b]	25 (4.9%)	18 (4.9%)	7 (5.0%)	0.960
Education >12 years	486 (95.7%)	350 (95.1%)	136 (97.1%)	0.314
Stable occupation	485 (95.5%)	354 (96.2%)	131 (93.6%)	0.204
Family income (¥ m^{-1})[c]				0.214
<5000	10 (2.0%)	5 (1.4%)	5 (3.6%)	
5000 to 10 000	97 (19.1%)	75 (20.4%)	22 (15.7%)	
10 000 to 20 000	264 (52.0%)	186 (50.5%)	78 (55.7%)	
>20 000	137 (27.0%)	102 (27.7%)	35 (25.0%)	
Medical history before pregnancy				
Dysmenorrhea	270 (53.1%)	202 (54.9%)	68 (48.6%)	0.202
Premenstrual syndrome[d]	49 (9.6%)	39 (10.6%)	10 (7.1%)	0.239
Internal diseases[e]	37 (7.3%)	26 (7.1%)	11 (7.9%)	0.759
Gynaecological diseases[f]	51 (10.0%)	36 (9.8%)	15 (10.7%)	0.755
Previous surgeries	76 (15.0%)	58 (15.8%)	18 (12.9%)	0.412
Abnormal pregnancies[g]	171 (33.7%)	116 (31.5%)	55 (39.3%)	0.098
History of current pregnancy				
Planned pregnancy	442 (87.0%)	321 (87.2%)	121 (86.4%)	0.811
Duration of pregnancy (day)	279 (273 to 281)	279 (273 to 281)	280 (273 to 282)	0.320
Smoking during pregnancy	2 (0.4%)	0 (0.0%)	2 (1.4%)	0.076
Drinking during pregnancy	2 (0.4%)	2 (0.5%)	0 (0.0%)	>0.999
Stressful events during pregnancy[h]	52 (10.2%)	39 (10.6%)	13 (9.3%)	0.663
Routine antenatal care	508 (100.0%)	368 (100.0%)	140 (100.0%)	–
Attendance at childbirth classes	409 (80.5%)	306 (83.2%)	103 (73.6%)	0.015
Chronic pain affecting daily life[i]	109 (21.5%)	87 (23.6%)	22 (15.7%)	0.052
Comorbidity during pregnancy	159 (31.3%)	116 (31.5%)	43 (30.7%)	0.861
Gestational diabetes mellitus	115 (22.6%)	86 (23.4%)	29 (20.7%)	0.523
Pregnancy-induced hypertension	28 (5.5%)	21 (5.7%)	7 (5.0%)	0.755
Hypothyroidism	40 (7.9%)	30 (8.2%)	10 (7.1%)	0.706
Prepartum haemoglobin ($g\,l^{-1}$)[j]	12.5 ± 1.2	12.5 ± 1.2	12.4 ± 1.1	0.862
Antenatal assessments				
EPDS (score)[k]	7 (5 to 8)	6 (5 to 8)	7 (5 to 8)	0.511
EMS (score)[l]	47 (45 to 49)	47 (45 to 48)	48 (46 to 49)	0.065
SAS (score)[m]	34 (31 to 38)	35 (31 to 38)	34 (31 to 38)	0.282
SSRS (score)[n]	40 (38 to 43)	40 (38 to 43)	40 (37 to 43)	0.700
Information of husband				
Education >12 years	488 (96.1%)	354 (96.2%)	134 (95.7%)	0.803
Stable occupation	504 (99.2%)	367 (99.7%)	137 (97.9%)	0.116
Han nationality[a]	484 (95.3%)	350 (95.1%)	134 (95.7%)	0.774
Smoking during pregnancy	155 (30.5%)	110 (29.9%)	45 (32.1%)	0.622
Drinking during pregnancy	198 (39.0%)	153 (41.6%)	45 (32.1%)	0.051
Mother's preference of baby sex				0.990
Male	40 (7.9%)	29 (7.9%)	11 (7.9%)	
Female	78 (15.4%)	57 (15.5%)	21 (15.0%)	
Both	390 (76.8%)	282 (76.6%)	108 (77.1%)	
Father's preference of baby sex				0.531
Male	43 (8.5%)	34 (9.2%)	9 (6.4%)	
Female	55 (10.8%)	41 (11.1%)	14 (10.0%)	
Both	410 (80.7%)	293 (79.6%)	117 (83.6%)	

Data are presented as mean ± SD, number (%) or median (interquartile range). ¥, Chinese Yuan; EPDS, Edinburgh Postnatal Depression Scale; EMS, ENRICH Marital Satisfaction Scale; SAS, Zung Self-Rating Anxiety Scale; SSRS, Social Support Rating Scale. [a] Other nationalities include Manchu, Mongol, Huis, Koreans and Yi. [b] Include Buddhism, Islam and Christianism. [c] Total income of husband and wife. [d] Refers to symptoms of irritability, fatigue, depression and headache that repeatedly occurred during the luteal phase of the menstrual cycle and affected daily life. Diagnosis was confirmed by the gynaecologists. [e] Include asthma, arrhythmia, thyroid disease, nephritis, nephritic syndrome and positive hepatitis B surface antigen. [f] Include uterine fibroid, ovarian cyst, endometriosis, polycystic ovary syndrome and primary amenorrhea. [g] Include arrest of foetal development, spontaneous abortion and induced abortion. [h] Include bereavement, accidental injury, layoff and unemployment. [i] Refers to the chronic pain in the low back, pelvis, leg, head or other parts that affected daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. [j] Missing data in one participant. [k] Edinburgh Postnatal Depression Scale, score range 0 to 30, with higher score indicating more severe depression. [l] ENRICH Marital Satisfaction Scale, score range 10 to 50, with higher score indicating higher satisfaction of marriage. [m] Zung Self-Rating Anxiety Scale, score range 25 to 100, with higher score indicating higher frequency of anxiety. [n] Social Support Rating Scale, score range 11 to 62, with higher score indicating better social support.

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.*[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 during labour was associated with an increased risk

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[a]	165 (32.5%)	105 (28.5%)	60 (42.9%)	0.002
Premature rupture of membrane	96 (18.9%)	75 (20.4%)	21 (15.0%)	0.166
NRS pain score[b]				
Before analgesia	8 (7 to 9)	8 (7 to 9)	8 (7 to 9)	0.242
10 min after analgesia[c]	–	4 (2 to 5)	–	–
30 min after analgesia[c]	–	2 (1 to 3)	–	–
At 10-cm cervical dilation[d]	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%)	8 (5.7%)	0.003
≥38.0 °C	10 (2.0%)	9 (2.4%)	1 (0.7%)	0.368
Duration of labour				
First stage (min)[e]	540 (350 to 780)	600 (420 to 840)	318 (221 to 540)	<0.001
Second stage (min)[e]	46 (28 to 79)	51 (32 to 83)	34 (20 to 56)	<0.001
Prolonged second stage[f]	1 (0.2%)	1 (0.3%)	0 (0.0%)	>0.999
Third stage (min)[e]	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%)	146 (39.7%)	49 (35.0%)	0.333
Lateral episiotomy	162 (31.9%)	130 (35.3%)	32 (22.9%)	0.216
Mode of delivery				<0.001
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%)	0.834
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[g]	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[b]	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[h]	473 (93.1%)	347 (94.3%)	126 (90.0%)	0.088
6-Week postpartum				
Breast-feeding	351 (69.1%)	257 (69.8%)	94 (67.1%)	0.557
Persistent pain[i]	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[j]	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)[k]	6 (4 to 9)	6 (4 to 9)	6 (4 to 10)	0.077
Postpartum depression[l]	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. [f] Defined as the second-stage labour duration more than 120 min. [g] 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 atresia. [h] 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. [i] Defined as NRS pain score at least 1 that persisted since childbirth, including pain in pelvis, low back, incision and perineum. [j] Defined as persistent pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. [k] Edinburgh Postnatal Depression Scale, score range 0 to 30, with higher score indicating more severe depression. [l] Defined as EPDS score at least 10 at 6 weeks postpartum.

of depression development at 4 to 8-week postpartum.[17] 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 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 ($kg\,m^{-2}$)[a]	21.7 ± 2.6	21.8 ± 2.5	21.7 ± 2.6	0.702
New-onset diseases after childbirth[b]	37 (7.3%)	28 (7.6%)	9 (6.4%)	0.647
Surgical procedure after childbirth[c]	30 (5.9%)	25 (6.8%)	5 (3.6%)	0.169
Chronic pain after childbirth[d]	81 (15.9%)	64 (17.4%)	17 (12.1%)	0.149
Chronic pain affecting daily life[e]	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[f]	52 (10.2%)	38 (10.3%)	14 (10.0%)	0.933
SSRS (score)[g]	37 ± 5	37 ± 5	37 ± 5	0.690
EPDS (score)[h]	3 (1 to 5)	3 (1 to 4)	3 (2 to 6)	0.017
2-Year depression[i]	46 (9.1%)	27 (7.3%)	19 (13.6%)	0.029
Chronic depression[j]	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. [a] Missing data in five participants. [b] 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. [c] 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. [d] Defined as persistent or recurrent pain that lasted for more than 3 months after childbirth. [e] Defined as chronic pain that interfered daily life activities including walking, mood, sleep or concentration, as judged by parturients themselves. [f] Includes any congenital (atrial septal defect, anal atresia and urachal fistula) and acquired diseases (bronchiolitis, febrile convulsion, Kawasaki disease, infant rash, eczema, urticaria, allergic dermatitis, pneumonia, anaemia, inguinal hernia and enteritis) that requires therapy during the 2-year period. [g] Social Support Rating Scale, score range 11 to 62, with higher score indicating better social support. [h] Edinburgh Postnatal Depression Scale, score range 0 to 30, with higher score indicating more severe depression. [i] Defined as EPDS score at least 10 at 2 years after childbirth. [j] 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.[16,17] It was found that early depression is an important risk factor for the development of long-term depression.[9] Second, the use of epidural labour analgesia might have lowered the risk of long-term negative memory.[31,32] As reported, such memory can evoke intense negative emotions and reactions in some women.[32,33]

Table 4 Factors associated with the development of 2-year depression

Factors	Univariate analysis[a] OR (95% CI)	*P* value	Multivariate analysis[b] OR (95% CI)	*P* value
Neuraxial analgesia during labour	0.504 (0.271 to 0.940)	0.031	0.455 (0.230 to 0.898)	0.023
Internal diseases before pregnancy[c]	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[d]	2.254 (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			–	–
Spontaneous delivery	Reference		–	–
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[e]	3.143 (1.343 to 7.355)	0.008	–	–
Surgical procedure after childbirth[f]	2.132 (0.775 to 5.865)	0.143	–	–
Chronic pain affecting daily life[g]	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). [a] The presence of 2-year depression was modelled as a function of a single factor. [b] 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: $\chi^2 = 5.411$, df = 8, $P = 0.713$. [c] Include asthma, arrhythmia, thyroid disease, nephritis, nephritic syndrome and positive hepatitis B surface antigen. [d] 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. [e] Refer to diseases that occurred during the 2-year period and required 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. [f] 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 metatarsal fracture. [g] Defined as persistent or recurrent pain lasting for more than 3 months 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%], $P = 0.002$). 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 childbirth[42,43] 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 early[47]; 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 breast-feeding 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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