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# Recovery after Nulliparous Birth: A Detailed Analysis of Pain Analgesia and Recovery of Function

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## Abstract

**Background—**The majority of parturients in the United States first return for evaluation by their obstetric practitioner 6 weeks after delivery. As such, there is little granular data on the pain experience, analgesic requirements and functional recovery during the postpartum period. This prospective observational study was performed to evaluate these factors to provide expectations for patient.

**Methods—**213 nulliparous women were enrolled and assessed daily until they completed 3 outcomes: 1) pain resolution, 2) opioid cessation, and 3) self-assessed functional recovery from delivery. The primary endpoint, “pain and opioid free functional recovery” was the time required to reach all 3 endpoints. Pain burden was assessed as the area under the curve created by plotting the daily numerical pain rating scale against the days required to attain pain resolution. Times to attain study endpoints after cesarean delivery and vaginal delivery were compared using survival analysis.

**Results—**After vaginal delivery, days required for pain and opioid-free functional recovery (median [interquartile range (IQR)]) were 20 [11–26], for opioid cessation 0.5 [0.5–2], termination of all analgesic (including NSAIDs and acetaminophen) 11 [6–17], and pain resolution 15 [8–24]. Achievement of these endpoints after cesarean delivery required 27 [19–40], 8 [4–11], 17 [11–24], and 21 [14–27] days respectively.

**Conclusions—**There is clinically significant variability between healthy nulliparous parturients in the pain experience, opioid use and functional recovery after childbirth following vaginal and cesarean delivery. Recovery to pre-delivery function is similar after vaginal and cesarean delivery, and approximately half of the variance was explained by pain burden.

## INTRODUCTION

Nearly 4 million births occur annually in the United States, approximately one third via cesarean delivery.[1] After hospital-based childbirth, healthy parturients are discharged home

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after a short hospital stay and reassessment by the obstetrical care provider is recommended at 6 weeks after delivery.[2] Postpartum pain, analgesic use, and functional recovery have been rarely assessed beyond 72 hours postpartum.[3,4] Pain resolution after childbirth has only been described at specific time points after childbirth.[5–7] For example, evaluation at 2, 6, and 12 months after delivery revealed a 10%, 2%, and 0.3% prevalence respectively for persistent pain.[6] However, in that study only participants who reported pain at 2 months were further evaluated for pain at 6 and 12 months, and daily or weekly pain scores between these time-points were not examined. Granular data on the amount, duration and variability of postpartum pain, and information regarding longitudinal pattern and characteristics of pain resolution after childbirth consequentially is limited. While it is commonly perceived that cesarean delivery results in considerable postpartum pain,[5,8] vaginal delivery is also associated with tissue damage to the birth canal and perineum, and associated pain may be underappreciated. In fact, recent studies have reported a lack of association between mode of delivery and persistent postpartum pain,[9] and a higher long term incidence of pelvic pain among women who had vaginal delivery compared to cesarean delivery.[10]

Detailed information regarding analgesia requirement is also lacking during the postpartum period. Many parturients are released from a hospital with a prescription for an opioid analgesic and childbirth is therefore a common source of opioid exposure in a large population of young, often opioid naïve women. Further, leftover opioid could be diverted and abused by somebody for whom the prescription is not intended. An estimated 1 in 300 opioid-naive women become persistent opioid users after cesarean delivery,[11] and cesarean delivery is associated with an increased risk of chronic opioid use compared to non-surgical controls (odds ratio 1.28 [1.12–1.46]).[12] Due to the large population at risk, opioid exposure in the postpartum period is a significant public health consideration. Additionally, while the time course for postpartum functional recovery has been studied in detail,[13–16] the potentially complex association between recovery, pain burden and analgesic needs is not well defined.

The objectives of this study were to establish typical values and ranges for the expected time course for pain resolution, analgesic cessation, and functional recovery after vaginal delivery and cesarean delivery in healthy, first time mothers. The primary outcome variable was the time required to reach “pain and opioid free functional recovery”; a composite variable of no pain, opioid-free functional recovery after childbirth. We also evaluated the relationship between pain profiles, analgesic use and functional recovery during the postpartum period.

## MATERIALS AND METHODS

We conducted a prospective, daily, longitudinal, observational cohort study of three study endpoints (pain resolution, opioid cessation, and functional recovery). The completion of the study was predefined as completion of this composite variable (“pain and opioid free functional recovery” i.e. when all three of the above endpoints were attained). With approval from the Stanford University Institutional Review Board (Protocol #30758, approved on 7/11/2014) and written informed consent from all participants, we attempted daily observations of pain scores, analgesic use, and functional status after both vaginal delivery and cesarean delivery.

## Participants

Nulliparous women attempting vaginal delivery at Lucile Packard Children's Hospital, Stanford University between August 2014 and June 2016 were approached and enrolled in this prospective cohort study. Women signed written informed consents, and were enrolled prior to delivery before the final delivery mode (vaginal delivery or cesarean delivery) was known. Inclusion criteria were 18 years of age or older, gestational age greater or equal to 35 weeks, no significant maternal or fetal co-morbidities, and able to understand English. Patients with multiple pregnancy, diabetes mellitus (pre-existing or gestational), hypertension (chronic or gestational) or preeclampsia requiring pharmacological treatment, history of depression or anxiety were excluded from participation. Patients with chronic pain or ongoing opioid use were also excluded.

## Procedures

Baseline demographic and obstetric data was obtained after enrollment. Starting on postpartum day one, the subjects were contacted daily, either in person during their hospitalization, and by telephone after discharge. A standardized questionnaire was used for daily fellow-up assessment (Appendix 1). Specifically, the investigator read through questions D1 to D16 provided in the appended questionnaire, and asked the patient to choose answers from the indicated options. Women were asked about their pain (average daily pain using a 0 to 10 verbal numeric rating scale (NRS) where 0 is no pain and 10 is the worst possible pain), analgesic use and functional recovery. The subjects who underwent cesarean delivery were specifically instructed to report pain levels in the perineum, pelvis and surgical site, and those who underwent vaginal delivery were instructed to report pain levels in the perineum and pelvis. Daily analgesic medications used were reviewed by a study physician to confirm whether they contain an opioid or were non-opioid analgesics. To assess functional recovery, the subjects were asked, "Do you feel you have functionally recovered to the level you were during the last week of pregnancy before delivery?". Daily follow-ups were continued until the participants met all three study endpoints. If participants had not met all study endpoints after 3 months post-delivery, they were contacted weekly thereafter until they met the study endpoints. Daily assessment via phone took approximately 2 to 3 minutes per contact. We attempted to call patients once daily between 12PM and 6PM unless patients specified their preferred time for contact, and left a discrete message if they did not answer their telephone. The patients could call the investigator back any time of the day. When we could not get hold of patients for 2 weeks in a row, they were deemed lost to follow-up.

## Primary endpoint

Time to "pain and opioid free functional recovery", the primary outcome variable, was defined as the time from delivery until the first day a patient met all of the following three endpoints: (1) the first day a patient reported functionally recovery to pre-delivery level, (2) the first of 5 consecutive days of zero average pain ("pain free"), and (3) the first of 5 consecutive days of no opioid use ("opioid cessation").

### Demographic, neonatal and obstetrical outcome variables

Baseline demographic variables were collected by both patient interview and review of medical records prior to the delivery. Maternal, obstetrical and neonatal outcome variables were collected from electronic medical records after delivery.

### Secondary endpoints

Secondary endpoints evaluated were the three individual components of the primary composite endpoint described above, as well as "analgesic cessation" defined by time from delivery until the first day of no requirement for any analgesic drugs including non-steroidal anti-inflammatory drugs and acetaminophen.

### Statistical analysis

Statistical analyses were performed using the R statistical software package, version 3 (The R Foundation for Statistical Computing, Vienna, Austria), and SAS Enterprise Guide, version 6.1 (SAS, Cary, NC). Visual inspection and the Shapiro-Wilk test was used to assess for normal distribution of continuous variables. All of the continuous variables were compared with the Mann-Whitney U test, and categorical variables were compared with Chi-square test or Fisher's exact test. Fisher's exact test was substituted when the expected numbers in the Chi-square matrix was smaller than 5. Kaplan-Meier survival curves were constructed for the primary composite outcome, pain resolution, opioid cessation, and analgesic cessation, stratified by subjects who had cesarean delivery and those with vaginal delivery. The patients who were lost to follow-up and did not attain the endpoints were censored on the last day they were successfully contacted before deemed a drop-out. A log-rank statistic of equality with $P < 0.05$ was used to determine whether there were significant differences in those recovery profiles between the two delivery types. Cox proportional hazards regression was performed to evaluate association between the delivery type and the outcomes, with and without adjustment for baseline demographic and obstetric variables provided in Table 1, and excluding the degree of perineal laceration which was highly correlated with the delivery type (i.e. no patients with cesarean delivery had perineal laceration). Pain trajectories were constructed for individual subjects by connecting the daily average numerical rating scale for pain over time reported. Pain burden was calculated as area under the daily average pain level curve (AUC), and was computed for subjects who completed all endpoints using the trapezoid rule ($AUC = AUC + (X[i]-X[i-1])*((Y[i]+Y[i-1])/2)$, where X is the number of days since delivery and Y is the reported NRS score of daily average pain). A smoothing line (Friedman's supersmoother in R; "supersmu") is overlaid to depict population values for pain resolution after vaginal delivery and cesarean delivery. For those patients who completed all study endpoints, "pain and opioid free functional recovery" (primary outcome), pain burden, time to opioid cessation, time to analgesic cessation, and time to functional recovery were compared between vaginal delivery and cesarean delivery with the Mann-Whitney U test. A possible predictive relationship between pain on postpartum day 1, pain burden and time to functional recovery were investigated with Pearson's correlation coefficients. Further, sensitivity analysis was conducted by calculating correlation coefficients between time to functional recovery and

alternative pain burden AUCs calculated by pain levels at the time of daily assessment, and daily worst pain levels, to assess which correlated most closely with functional recovery.

### Sample Size Determination

In a previous study[17] using similar daily follow-up methodology that investigated pain resolution and opioid cessation after non-obstetric surgery, time to opioid cessation was successfully separated between different surgical types with statistical significance with a sample size of 134 (with 109 usable for analysis). We therefore enrolled patients until we attained 134 patients with successful completion of all study endpoints with assumption that this sample size would likely detect difference in the time to event outcomes between the vaginal and cesarean deliveries.

### Handling of missing data

We made total of 3343 daily phone call attempts to 213 enrolled patients, and successfully reached patients 1610 times (48% success rate). On the days we failed to reach a patient, we assumed the patient took same pain medications as the previous day that the patient was contacted, and assumed the same status in terms of pain resolution and functional recovery (last observation carried forward). If we could not get hold of patients for 2 weeks in a row, they were deemed lost to follow-up, and they were censored as of the last day they were successfully contacted. To quantify the effect of missing data (lost to follow-up) on time to event outcomes, we performed sensitivity analyses assigning earliest and longest possible times to the recovery endpoints for those who were lost to follow-up. The earliest possible time to each recovery endpoint in those lost to follow-up was assigned as one day after they were censored for the endpoint, and the longest possible time to each recovery endpoint for those lost to follow-up was assigned as the longest observed recovery time among patients who completed the outcome for each delivery type. The longest possible times to the recovery endpoints were 77 and 85 days for primary composite endpoint for vaginal and cesarean delivery patients, 77 and 85 days for pain resolution for vaginal and cesarean delivery, 14 and 39 days for opioid cessation for vaginal and cesarean delivery, and 77 and 55 days for analgesic cessation for vaginal and cesarean delivery. The median and interquartile range of the time to the endpoints calculated by assigning earliest and longest recovery time for those lost to follow-up were descriptively compared with the observed values. For calculation of pain burden (AUC), the trapezoidal rule was used according to the equation provided above. Missing NRS data were interpolated.

## RESULTS

The study flow diagram is shown in Figure 1. One hundred and thirty-four women completed the study, reporting the primary endpoint of “pain and opioid free functional recovery” while 79 did not complete the primary endpoint (i.e. lost to follow-up prior to completing the composite primary endpoint; Figure 1). Demographic, obstetric, and neonatal characteristics of patients who did and did not complete primary endpoint are reported in Table 1. Asian patients were more likely to be lost to follow-up compared to other ethnicities ($P<0.01$). Patients who completed the primary endpoint weighed more ($P=0.03$), and were

more likely to have a history of smoking (P=0.02) than those who did not complete the primary endpoint (Table 1).

Times to the primary endpoint, “pain and opioid free functional recovery”, calculated by censoring patients who lost to follow-up, were 20 (11–26) and 27 (19–40) days [median (IQR)] in the vaginal delivery and cesarean delivery cohort respectively. Ninety-five percent of patients had attained the primary endpoint after 47 days in the vaginal delivery group and 50 days in the cesarean delivery cohort. Longitudinal pain trajectories derived from the pain reports of individual patients who had vaginal delivery and cesarean delivery are shown in Figure 2a and 2b. Figure 2c and 2d shows pain trajectory after vaginal delivery and cesarean delivery in completers and non-completers of the study. Thirty-one percent of vaginal delivery patients, and 91% of cesarean delivery patients required treatment with an opioid analgesic for at least one day during the postpartum period. All patients delivered by cesarean delivery received an opioid prescription at discharge.

Kaplan-Meier survival curves for time to “pain and opioid free functional recovery”, pain resolution, opioid cessation and non-opioid analgesic use by delivery mode, are shown in Figure 3a, b, c, d. Patients who had a cesarean delivery took longer to attain the primary outcome of “pain and opioid free functional recovery” (log-rank P= 0.004, Figure 3a), pain-free state (log-rank P= 0.045, Figure 3b), opioid cessation (log-rank P< 0.0001, Figure 3c), and all analgesic cessation (log-rank P< 0.008, Figure 3d) during postpartum period than those who had vaginal delivery. The unadjusted Cox Proportional Hazard ratios (95% confidence interval (CI)) comparing cesarean delivery (vs vaginal delivery) for “pain and opioid free functional recovery”, pain resolution, opioid cessation, and all analgesic cessation were 0.58 (0.39–0.85, P=0.006), 0.67 (0.45–0.99, P=0.04), 0.32 (0.21–0.47, P<0.0001), and 0.60 (0.41–0.89, P=0.01), respectively. After adjustment for baseline demographic and obstetrical variables, hazard ratios (95% CI) for “pain and opioid free functional recovery”, pain resolution, opioid cessation, and all analgesic cessation were 0.55 (0.36–0.84, P=0.006), 0.65 (0.42–0.99, P=0.04), 0.29 (0.19–0.45, P<0.0001), and 0.59 (0.38–0.91, P=0.02), respectively. Median times to pain resolution, opioid cessation, and analgesic cessation after vaginal delivery calculated by censoring patients who lost to follow-up were 15 (IQR: 8–24), 0.5 (0.5–2), and 11 (6–17) days respectively. Median times to the same endpoints after cesarean delivery calculated by censoring patients who lost to follow-up were 21 (IQR: 14–27), 8 (4–11), and 17 (11–24) days respectively. Ninety five percent of vaginal delivery patients attained the individual endpoints for pain resolution, opioid cessation, and analgesic cessation after 47, 10, and 36 days, and 95 % of cesarean delivery patients attained the same endpoints after 50, 24, and 43 days, respectively.

Sensitivity analysis for time to the primary endpoint, “pain and opioid free functional recovery”, calculated by assigning earliest possible time to the endpoint to the patients who lost to follow-up, were 10 (2–21) and 19 (5–32) days [median (IQR)] in the vaginal delivery and cesarean delivery, respectively. Assigning longest observed time to the endpoint to the patients who lost to follow-up resulted in 28 (16–77) and 43 (25–85) days [median (IQR)] in the vaginal delivery and cesarean delivery. Median times to pain resolution, opioid cessation, and analgesic cessation after vaginal delivery calculated by assigning earliest possible time to the endpoints to the patients who lost to follow-up were 7 (IQR: 2–18), 0.5 (0.5–2), and 6

(2–14) days respectively. Median times to the same endpoints after cesarean delivery calculated by assigning earliest possible time to the endpoints to the patients who lost to follow-up were 13 (IQR: 4–22), 5 (3–10), and 10 (5–19) days respectively. Median times to pain resolution, opioid cessation, and analgesic cessation after vaginal delivery calculated by assigning longest possible time to the endpoints to the patients who lost to follow-up were 26 (IQR: 12–77), 0.5 (0.5–2), and 17 (7–77) days respectively. Median times to the same endpoints after cesarean delivery calculated by assigning longest possible time to the endpoints to the patients who lost to follow-up were 30 (IQR: 19–85), 9 (5–25), and 26 (14–55) days respectively. The differences between the median time observed (calculated by censoring patients who lost to follow-up) and those calculated by assigning possible earliest or longest time for those lost to follow-up for the endpoints were as large as 16 days as observed for time to primary endpoint in cesarean delivery.

Pain, analgesic use and functional recovery parameters for patients who completed all endpoints (i.e. were not lost to follow-up) are shown in Table 2. Time to “pain and opioid free functional recovery” was significantly different after vaginal delivery and cesarean delivery (Table 2). Pain burden (AUC) was strongly correlated with time to functional recovery (Pearson’s correlation coefficient of 0.75 (95% CI: 0.67–0.82, P<0.0001)), accounting for 56% of variance. The sensitivity analysis correlation coefficient between AUC derived from pain levels at the time of daily assessment and time to functional recovery was 0.67 (95% CI: 0.57–0.76, P<0.0001), and that between AUC derived from daily worst pain levels and time to functional recovery was 0.77 (95% CI: 0.69–0.83, P<0.0001). The pain burden-time to functional recovery association did not differ amongst the three different measures of pain. Pain on postpartum day 1 was modestly correlated with pain burden (Pearson’s correlation coefficient 0.32 (95% CI: 0.16–0.47, P=0.0001), accounting for 10% of variance.

## DISCUSSION

The current study provides granular data to reflect this pivotal period for recovery and transition to motherhood.[18] The key finding was significant variability in pain, opioid use and functional recovery after both vaginal delivery and cesarean delivery. As expected, patients undergoing cesarean delivery had more pain and opioid utilization, however both modes of delivery were associated with significant pain burden and long functional recovery with significant variability among parturients (Figure 2, and 3).

Pain AUC is a significant aspect of pain burden perceived by the patients that has been used recently in the characterization of the pain experience during medical and surgical hospitalization.[19] Total postpartum pain burden was 1.7 times greater after cesarean delivery than vaginal delivery due to both greater pain intensity and longer pain duration after cesarean delivery (Table 2).

We have provided normative values for analgesic requirement during the post-partum period for healthy first time parturients. Ninety-one percent of patients recovering from cesarean delivery required opioids for pain management during the postpartum period, with a median time to opioid cessation of 8 days and a range from 0 to 39 days (Figure 3). The time

required for pain management with opioids was significantly shorter than that observed in non-pregnant patients who underwent major surgical procedures including thoracotomy, hip replacement, and mastectomy.[17] Ninety-five percent of the patients in our cohort had ceased using opioids by 24 days after cesarean delivery, and none became persistent opioid users. Recent population based studies that have investigated opioid utilization after surgery, have similarly found relatively short duration of opioid requirements after cesarean delivery.[11,12] In the study by Sun and colleagues,[12] chronic opioid use was defined as having filled 10 or more prescriptions or having obtained more than 120 days' supply of opioids within 1-year after cesarean delivery. The absolute risk of opioid naïve women becoming a chronic opioid user was 0.12%, which was 28% higher risk than a matched non-surgical control population. Bateman et al. stratified opioid naïve women into 5 categories according to the pattern of medication filling after cesarean delivery to identify persistent opioid users.[11] They demonstrated that 0.36% of women fell into the category of persistent opioid users, who on average dispensed opioids in 6.1 out of 12 months following cesarean delivery. Our study is unique in providing daily opioid utilization data after cesarean delivery to outline use trajectories rather than just relative risk determinations. We were not surprised that we did not identify persistent opioid use given the sample size of our individualized, daily follow-up study relative to the large population-based studies outlined above.[11,12]

After vaginal delivery, 31% of our patients required opioids for a short period in hospital, with median time to opioid cessation of less than one day (Figure 3). Less than 10% of our cohort who had a vaginal delivery required opioids beyond the hospitalization. There is scant previously published data available to allow establishment of norms for opioid utilization after vaginal delivery. Minassian et al.[20] reported 76% of women with perineal laceration or episiotomy after vaginal delivery required opioids within first 48 hours, while Macarthur et al.[21] reported incidences of opioid use during 24 hours after vaginal delivery of 7% in patients who received epidural morphine, and 32% in those not receiving epidural morphine. Our study highlights that the vast majority of patients undergoing vaginal delivery do not require opioids after discharge home. Therefore, routine opioid prescription at discharge for women having had vaginal delivery is not recommended. Patients who have high degree lacerations, previous pain syndromes or other special circumstances that increase the risk of postpartum pain should be closely followed and treated individually as appropriate.

We chose to evaluate functional recovery with a single, simple patient-centered question inquiring if the parturient had returned to their pre-partum level of physical function. A notable finding from our study is that with the exception of 3 women, functional recovery was always reported after pain resolution and analgesic cessation.

The postpartum period refers to the time after childbirth required for the reproductive organs to return to their non-pregnant state, a process that takes approximately 6 weeks.[22] Accordingly, several states in the United States have Temporary Disability Insurance policies which enable women to take short medical leaves in connection with childbirth, typically up to 6 weeks after vaginal delivery and 8 weeks after cesarean delivery.[23] Our finding demonstrate that it took 47 days and 50 days for 95% for women undergoing vaginal delivery and cesarean delivery respectively to attain functional recovery. However, the recovery might be even longer in the women that dropped out and did not contribute to the

data. Therefore, the observed time to recovery in the current study might underestimate true recovery time.

The primary outcome measure, pain resolution and opioid free functional recovery after childbirth has not been evaluated with the metric used in the current study (i.e. time to event determined by daily assessment) Accordingly, our primary goal was to establish the norms for the recovery endpoints in healthy women who underwent uneventful delivery. There are several limitations inherent to our study not yet discussed. We restricted enrollment to healthy nulliparous parturients for several reasons. The incidence of obstetrical complications which could affect postpartum recovery is different between nulliparous and multiparous women.[24] Previous birth experience and the impact of older children at home may add noise to the already highly variable outcomes evaluated above. Further, very few nulliparous women who underwent elective cesarean delivery without labor met the study inclusion criteria due to co-morbidities, and they were not included in the study. It is important to remember that the results of this study are relevant to healthy nulliparous parturients who labored and may not extend to patients with preexisting health challenges or multiparous women. In addition, significant bias might have been introduced due to high drop out rate. We made total of 3343 daily phone call attempts to 213 enrolled patients, and successfully got hold of patients 1610 times (48% overall success rate). During immediate postpartum period (≤ 7 days after the delivery), we successfully contacted patients 918 times out of 1178 attempts (78% success rate). We were only able to contact patients 692 times out of 2165 attempts after 7 postpartum days (32% success rate). As the missing portion of data is small, the information collected within 7 postpartum days is most accurate. The average pain score was reduced to 2.1 out of 10 by the 7th postpartum day in the typical parturient, and contribution of data after 7 postpartum day on the pain burden AUC calculation is small. Therefore, despite overall 52% missingness of data, we consider the magnitude of bias acceptably small in regards to pain burden AUC. The mean time lag between the day patients attained the primary composite endpoint (or were censored), and when patients were successfully contacted before that day was 3.7 days. Therefore, the calculated time to the primary endpoint may have overestimated the true value by up to 3.7 days.

In conclusion, we found significant variability in pain, opioid use and functional recovery after both vaginal delivery and cesarean delivery. Recovery to pre-delivery function appears largely driven by pain resolution, and opioid use is more apparent after cesarean delivery than vaginal delivery. Based on our observations, routine opioid prescription for patients after vaginal delivery is not recommended, and prescription of opioids at discharge from the hospital for women undergoing cesarean delivery should be limited, and if opioid requirement exceeds expectation set by this study, the patients should be individually evaluated by their providers.

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## Appendix 1. Daily pain and opioid use questionnaire

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| **D1** | **Please rate your pain from zero to ten where zero is no pain and ten is the worst pain you can imagine on the AVERAGE in the last 24 hours.** | | | | | | 0–10 | | |
| **D2** | **Please rate your pain from zero to ten where zero is no pain and ten is the worst pain you can imagine right NOW.** | | | | | | 0–10 | | |
| **D3** | **Please rate your pain from zero to ten where zero is no pain and ten is the worst pain you can imagine at its WORST in the last 24 hours.** | | | | | | 0–10 | | |
| **D4** | **In the last 24 hours, what medications did you take for your pain?** | 0 = none | 1 = hydrocodone/acetaminophen | 2 = hydrocodone | 3 =oxycodone/acetaminophen | 4 = oxycodone | 5= acetaminophen | 6 = Non-Steroidal | 7 = Other |
| **D5** | **In the last 24 hours, how much relief has pain medication provided?** | | | | | | 0–10 | | |
| **D6** | **In the last 24 hours, have you needed to take your pain medication to help you sleep?** | | | | | | Yes = 1 | No = 0 | |
| **D7** | **In the last 24 hours, have you needed to take your pain medication for any reason other than just pain, for example to reduce anxiety, or to improve mood?** | | | | | | Yes = 1 | No = 0 | |
| **D8** | **If yes for what?** | Sleep=1 | | Anxiety=2 | | | Mood=3 | Other=4 | |
| **D9** | **In the last 24 hours, has it been necessary for you to take any more pain medication than recommended?** | | | | | | Yes = 1 | No = 0 | |
| **D10** | **In general, over the last 24 hours which of these options best describes how often you have thought about your pain or pain medication:** | Less than once per hour = 1 | | Several times an hour = 2 | | | Every few minutes = 3 | Constantly = 4 | |
| **D11** | **Rate the severity of any pain medication side effects you have experienced over the last 24 hours?** | | | | | | 0–10 | | |
| | **On a zero to ten scale where zero is "no interference" and ten is "complete interference" Please rate, during the past 24 hours, how pain has interfered with your:** | | | | | | | | |
| **D12a** | **General Activity** | | | | | | 0–10 | | |
| **D12b** | **Mood** | | | | | | 0–10 | | |
| **D12c** | **Sleep** | | | | | | 0–10 | | |
| **D13** | **Do you consider yourself to have completely recovered from your delivery?** | | | | | | Yes = 1 | No = 0 | |
| **D14** | **If you worked before your delivery have you returned to work (whether paid or not--any vocational activity)?** | | | | | | Yes = 1 | No = 0 | |
| **D15** | **If not employed outside the home before your delivery, have you returned to your pre-delivery level of activity?** | | | | | | Yes = 1 | No = 0 | |
| **D16** | **How much is of your baby's daily nutrition is from breast feeding?** | None = 0 | | Less than half = 1 | | | About half = 2 | All = 4 | |

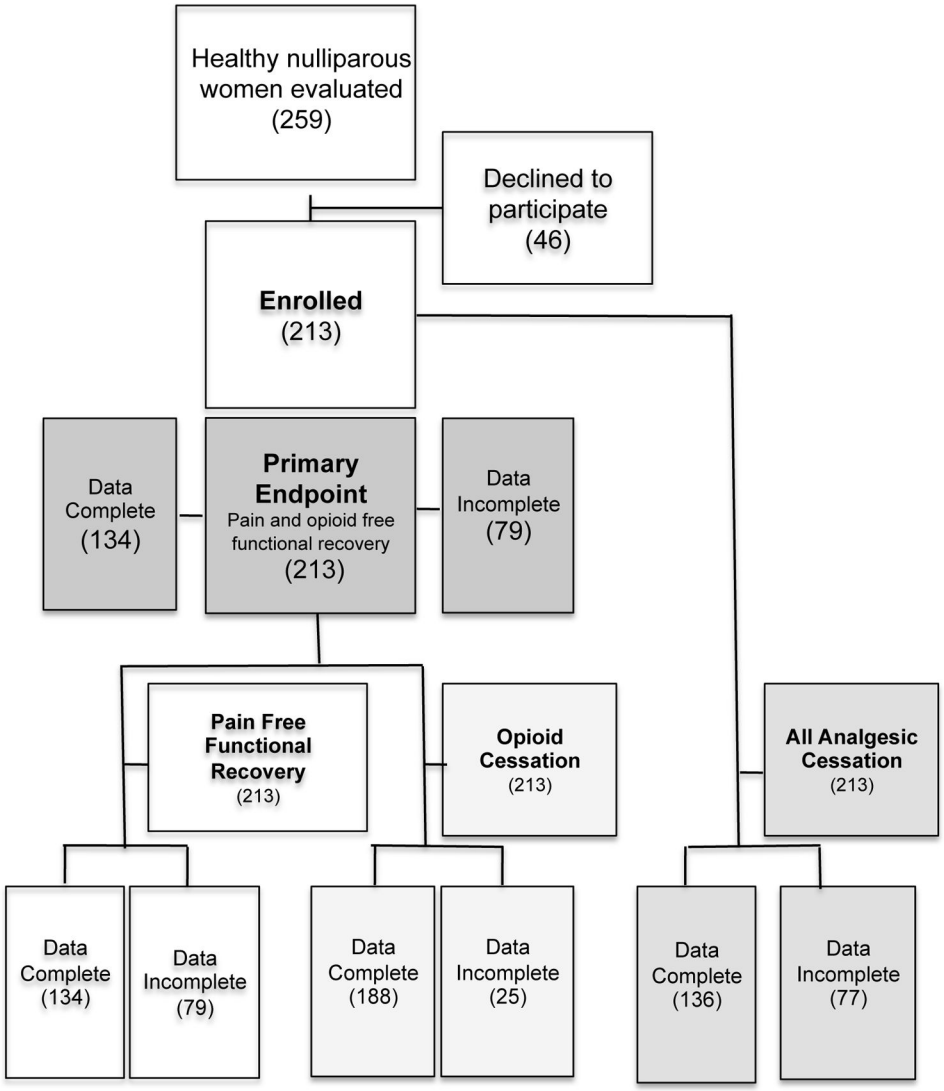


**Figure 1.**
Flow diagram for participant's inclusion and data completion.

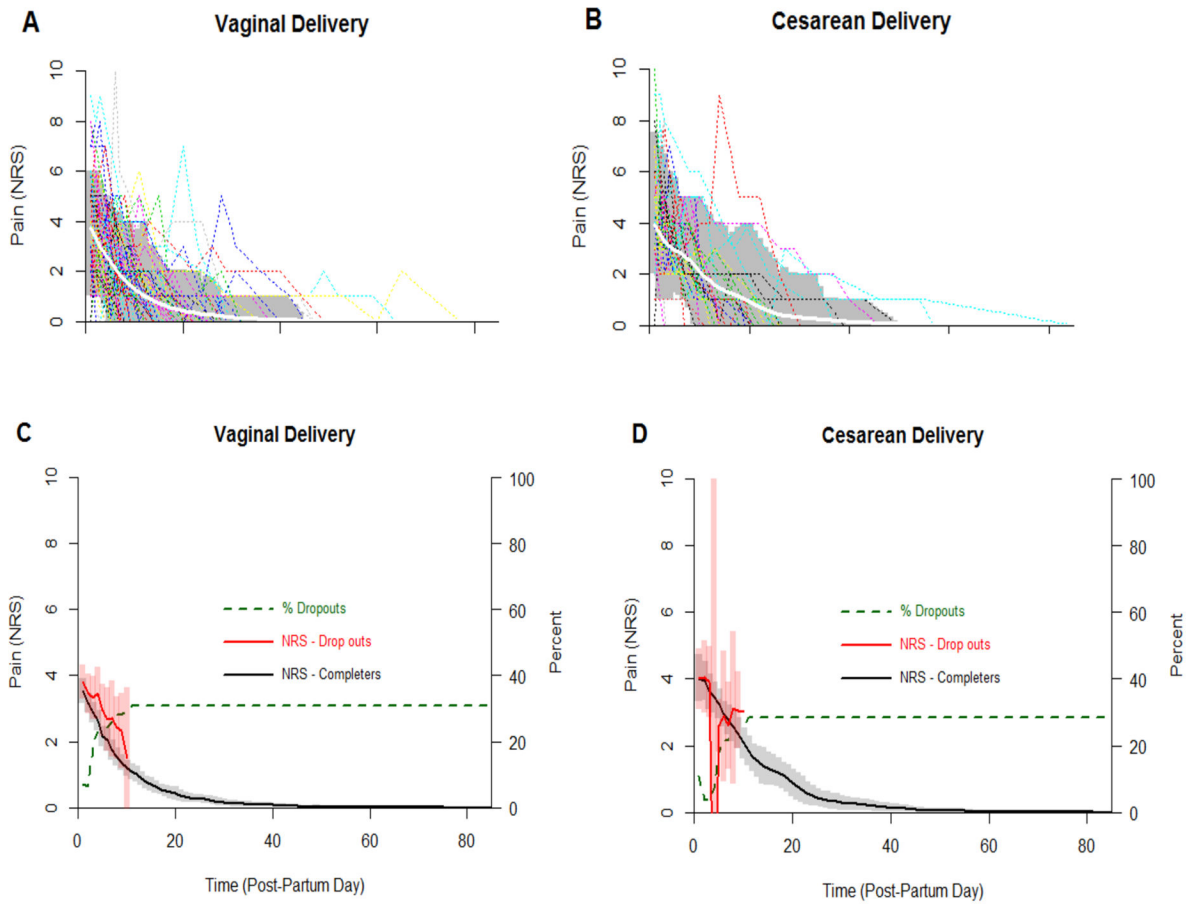


**Figure 2. Pain trajectory after vaginal and cesarean delivery**

**A.** **Pain trajectory after vaginal delivery.** Colored dotted lines represent pain reports from individual subjects, and the solid white line is a moving average constructed with Friedman's supersmoother in R; "supersmu" (R statistical software package, version 3). The shaded area covers the range from the 5$^{th}$ to 95th percentile of the data. NRS=verbal numerical pain score from 0–10, with 0=no pain and 10=worse pain imaginable.

**B.** **Pain trajectory after cesarean delivery.** Colored dotted lines represent pain reports from individual subjects, and the solid white line is a moving average constructed with Friedman's supersmoother in R; "supersmu" (R statistical software package, version 3). The shaded area covers the range from the 5$^{th}$ to 95th percentile of the data. NRS=verbal numerical pain score from 0–10, with 0=no pain and 10=worse pain imaginable.

**C.** **Pain trajectory in completers and non-completers after vaginal delivery.** The solid lines represent the pain score mean values for subjects retained in the study (black) and those who dropped out (red) before completing the composite primary outcome of "pain and opioid free functional recovery" after vaginal delivery. Shaded areas are 95% confidence intervals. The dashed green line

demonstrates the timing of dropout. The overlap of confidence interval with the mean of the other curve demonstrate that the patients who dropped out of the study were not having a significantly different pain experience compared to those who were retained.

**D.** **Pain trajectory in completers and non-completers after cesarean delivery.** The solid lines represent the pain score mean values for subjects retained in the study (black) and those who dropped out (red) before completing the composite primary outcome of “pain and opioid free functional recovery” after cesarean delivery. Shaded areas are 95% confidence intervals. The dashed green line demonstrates the timing of dropout. The overlap of confidence interval with the mean of the other curve demonstrate that the patients who dropped out of the study were not having a significantly different pain experience compared to those who were retained.

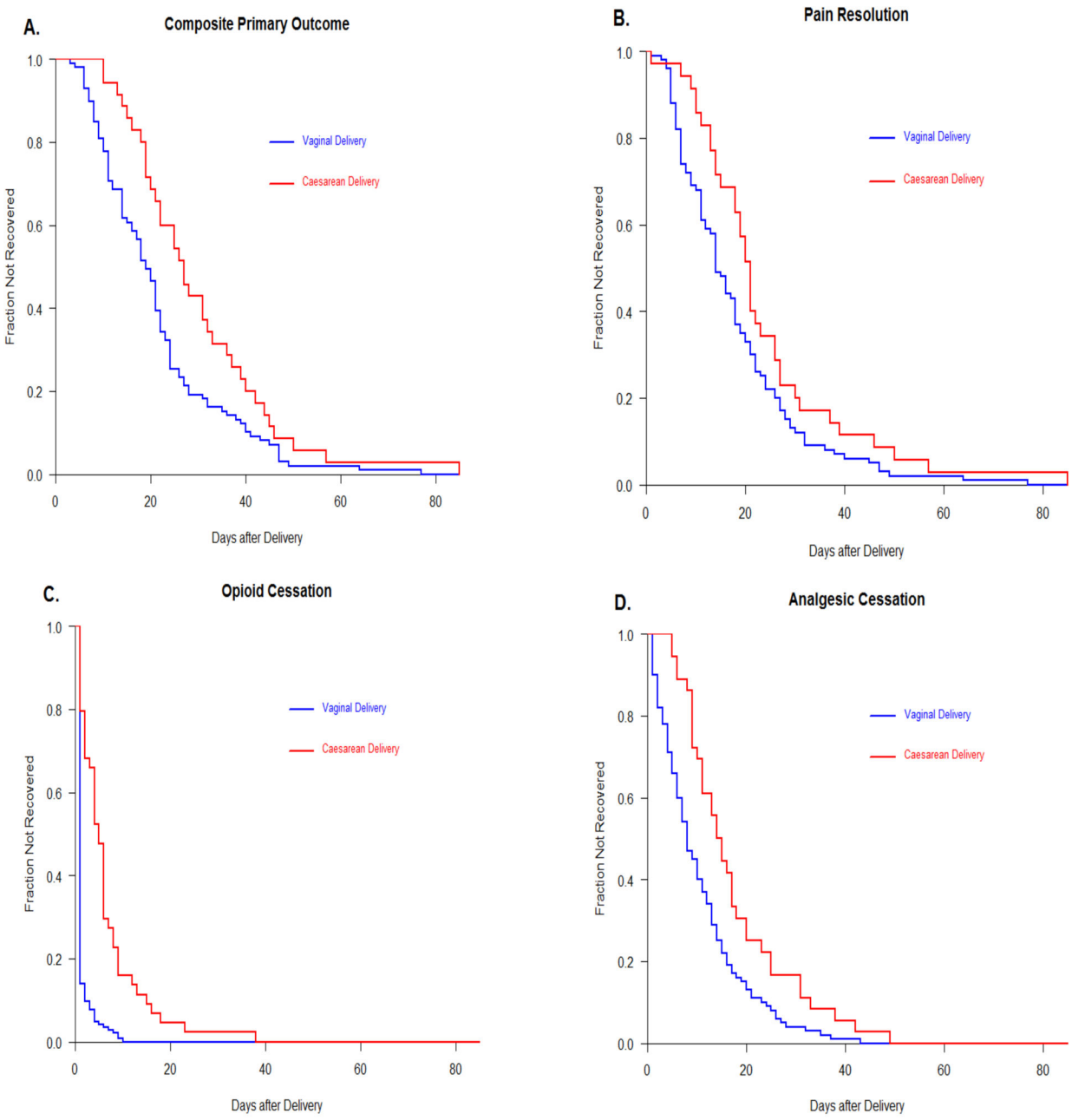


**Figure 3. Kaplan-Meier estimates of daily probability of obtaining study outcomes**

**A.** Time to "pain and opioid free functional recovery" (primary outcome) after vaginal delivery (solid line) and cesarean delivery (dotted line). (P=0.004, log rank test).

**B.** Time to pain-free state after vaginal delivery (solid line) and cesarean delivery (dotted line). (P=0.045, log rank test).

**C.** Time to opioid cessation after vaginal delivery (solid line) and cesarean delivery (dotted line). (P<0.0001, log rank test).

**D.** Time to all analgesic cessation after vaginal delivery (solid line) and cesarean delivery (dotted line). (P=0.008, log rank test).

## Table 1

Demographic, obstetric, and neonatal characteristics of patients who completed the primary endpoint and patients who did not complete primary endpoint

| Characteristic | Complete (N =134) | Incomplete (N =79) | P-value |
|---|---|---|---|
| Age -yrs | 32 [29–34; 25–44] | 31 [28–34; 20–42] | 0.30§ |
| Height -cm | 163 [160–170; 149–178] | 160 [157–167; 147–180] | 0.05§ |
| Weight -kg | 77 [68–83; 51–120] | 72 [67–77; 43–118] | 0.03§ |
| BMI -kg/m$^2$ | 27.7 [25.9–30.5; 21.7–40.8] | 27.5 [25.3–29.4; 18.6–42.6] | 0.31§ |
| Gestational age -days | 278 [274–284; 255–292] | 279 [272–285; 260–293] | 0.90§ |
| Gravity (%) | | | 0.19¶ |
| 1 | 115 (85.8) | 64 (81.0) | |
| 2 | 12 (9.0) | 13 (16.5) | |
| ≧3 | 7 (5.2) | 2 (2.5) | |
| Smoking status (%) | | | 0.02¶ |
| Previous smoker | 19 (14.2) | 3 (3.9) | |
| Never smoked | 115 (85.8) | 75 (96.2) | |
| Alchohol use (%) | | | 0.13# |
| Ever drank | 117 (87.3) | 62 (79.5) | |
| Never drank | 17 (12.7) | 16 (20.5) | |
| Ethnicity (%) | | | < 0.01¶ |
| Caucasian | 74 (55.2) | 23 (29.1) | |
| Asian | 41 (30.6) | 46 (58.2) | |
| Hispanic | 14 (10.5) | 9 (11.4) | |
| Others | 5 (3.7) | 1 (1.3) | |
| Educational status (%) | | | 0.12# |
| Graduate degree | 84 (62.7) | 37 (48.1) | |
| Four year college degree | 38 (28.4) | 30 (39.0) | |
| Less than four year college degree | 12 (9.0) | 10 (13.0) | |
| Labor type (%) | | | 0.22# |
| Induction | 60 (44.8) | 27 (34.2) | |
| Augmentation | 65 (48.5) | 43 (54.4) | |
| Spontaneous | 9 (6.7) | 9 (11.4) | |
| Delivery type (%) | | | 0.89# |
| Normal spontaneous vaginal delivery | 91 (67.9) | 52 (65.8) | |
| Assisted vaginal delivery | 8 (6.0) | 6 (7.6) | |
| Cesarean delivery | 35 (26.1) | 21 (26.6) | |
| Labor analgesia (%) | | | 0.41¶ |
| Neuraxial | 129 (96.3) | 78 (98.7) | |
| Others[a] | 5 (3.7) | 1 (1.3) | |
| Degree of perineal laceration (%) | | | 0.71# |

| Characteristic | Complete (N =134) | Incomplete (N =79) | P-value |
|---|---|---|---|
| None | 37 (27.6) | 23 (29.1) | |
| 1 | 18 (13.4) | 7 (8.9) | |
| 2 | 72 (53.7) | 43 (54.4) | |
| ≧3 | 7 (5.2) | 6 (7.6) | |
| Neonatal outcomes | | | |
| Apgar score at 1 minute (%) | | | 0.65# |
| <7 | 14 (10.8) | 7 (8.9) | |
| ≧7 | 116 (89.2) | 72 (91.1) | |
| Apgar score at 5 minute (%) | | | 0.38¶ |
| <7 | 0 (0.0) | 1 (1.3) | |
| ≧7 | 130 (100.0) | 78 (98.7) | |
| Level of neonatal care (%) | | | 0.61¶ |
| Well-baby nursery | 111 (82.8) | 70 (88.6) | |
| Intermediate care nursery | 18 (13.4) | 7 (8.9) | |
| Neonatal ICUΨ | 5 (3.7) | 2 (2.5) | |

Summary statistics was presented as number (% of patients), or median [IQR; range]. Data may not add up to total number of patients due to missing values. Data may not add up to 100 % due to rounding. Others[a] : includes narcotics and no anlagesia. ICUΨ: intensive care unit. Completed patients are those who attained the primary and secondary endpoints. Censored patients did not attain all endpoints, and contributed partial but not complete data.

§Mann-whiteny U test.

¶Fisher's exact test.

#Chi-square test.

## Table 2

Postpartum pain burden, opioid and analgesic use, and recovery profile

| Characteristic | Vaginal delivery (N =99) | Cesarean delivery (N =35) | P-value |
|---|---|---|---|
| Time to pain and opioid free functional recovery -days | 19 | 27 | 0.0003§ |
| IQR | 11 to 26 | 19 to 40 | |
| 2.5th to 97.5th percentile | 4 to 64 | 10 to 85 | |
| range | 3 to 77 | 10 to 85 | |
| Time to opioid cessation -days | 0 | 9 | <0.0001§ |
| IQR | 0 to 2 | 5 to 12 | |
| 2.5th to 97.5th percentile | 0 to 12 | 0 to 39 | |
| range | 0 to14 | 0 to 39 | |
| Time to analgesic cessation -days | 11 | 16 | 0.0006§ |
| IQR | 5 to 17 | 11 to 24 | |
| 2.5th to 97.5th percentile | 0 to 40 | 7 to 55 | |
| range | 0 to 77 | 7 to 55 | |
| Time to pain resolution -days | 14 | 21 | 0.014§ |
| IQR | 7 to 24 | 14 to 27 | |
| 2.5th to 97.5th percentile | 4 to 64 | 0 to 85 | |
| range | 3 to 77 | 0 to 85 | |
| Time to functional recovery -days | 19 | 27 | 0.0002§ |
| IQR | 11 to 24 | 19 to 40 | |
| 2.5th to 97.5th percentile | 4 to 59 | 10 to 85 | |
| range | 3 to 77 | 10 to 85 | |
| Pain AUC* | 25.5 | 44.0 | 0.0002§ |
| IQR | 10.5 to 43.0 | 29.5 to 58.0 | |
| 2.5th to 97.5th percentile | 2.0 to 122.0 | 6.0 to 140.0 | |
| range | 0.5 to 123.0 | 6.0 to 140.0 | |

Summary statistics was presented as median [IQR, 2.5th to 97.5th percentile, range].

Pain AUC*: area under the curve of daily pain levels (0 to 10) × duration of pain in days.

§Mann-Whitney U test.