

# Recovery after Nulliparous Birth

## A Detailed Analysis of Pain Analgesia and Recovery of Function

Ryu Komatsu, M.D., Brendan Carvalho, M.B.B.Ch., F.R.C.A., Pamela D. Flood, M.D., M.A.



This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

### 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 patients.

**Methods:** A total of 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 three of the 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 19 [11 to 26], for opioid cessation 0 [0 to 2], termination of all analgesic (including nonsteroidal antiinflammatories and acetaminophen) 11 [5 to 17], and pain resolution 14 [7 to 24]. Achievement of these endpoints after cesarean delivery required 27 [19 to 40], 9 [5 to 12], 16 [11 to 24], and 21 [14 to 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 predelivery function is similar after vaginal and cesarean delivery, and approximately half of the variance was explained by pain burden. (ANESTHESIOLOGY 2017; 127:684-94)

NEARLY four million births occur annually in the United States, approximately one third *via* cesarean delivery.<sup>1</sup> After hospital-based childbirth, healthy parturients are discharged from the hospital following a short hospital stay, and reassessment by the obstetric care provider is recommended at 6 weeks after delivery.<sup>2</sup> Postpartum pain, analgesic use, and functional recovery have been rarely assessed beyond 72 h postpartum.<sup>3,4</sup> Pain resolution after childbirth has only been described at specific time points after childbirth.<sup>5-7</sup> For example, evaluation at 2, 6, and 12 months after delivery revealed a 10.0%, 2.0%, and 0.3% prevalence, respectively, for persistent pain.<sup>6</sup> However, in that study only participants who reported pain at 2 months were additionally 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, as well as information regarding longitudinal pattern and characteristics of pain resolution after childbirth, consequentially are limited. Although it is commonly perceived that cesarean delivery results in considerable postpartum pain,<sup>5,8</sup> vaginal delivery is also associated with tissue damage to the birth canal and perineum, and associated pain may be underappreciated. In fact, recent

### What We Already Know about This Topic

- There is little information on the time course of pain resolution, analgesic cessation, and functional recovery after vaginal delivery and cesarean delivery in healthy, first-time mothers

### What This Article Tells Us That Is New

- After vaginal delivery, median time was 0 days for opioid cessation, 11 days for stopping all analgesics, and 14 days for pain resolution
- After cesarean delivery, median time was 9 days for opioid cessation, 16 days for stopping all analgesics, and 21 days for pain resolution
- There was substantial interpatient variability in these times

studies have reported a lack of association between mode of delivery and persistent postpartum pain<sup>9</sup> and a higher long-term incidence of pelvic pain among women who had vaginal delivery compared with cesarean delivery.<sup>10</sup>

Detailed information regarding analgesia requirements 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,

This article is featured in "This Month in Anesthesiology," page 1A.

Submitted for publication November 30, 2016. Accepted for publication June 16, 2017. From the Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, California.

Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. All Rights Reserved. Anesthesiology 2017; 127:684-94

often opioid-naïve women. Furthermore, leftover opioid could be diverted and abused by somebody for whom the prescription is not intended. An estimated 1 in 300 opioid-naïve women become persistent opioid users after cesarean delivery,<sup>11</sup> and cesarean delivery is associated with an increased risk of chronic opioid use compared with nonsurgical controls (odds ratio = 1.28; 95% CI, 1.12 to 1.46).<sup>12</sup> Due to the large population at risk, opioid exposure in the postpartum period is a significant public health consideration. In addition, although the time course for postpartum functional recovery has been studied in detail,<sup>13–16</sup> the potentially complex association among 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 among 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 (Stanford, California, protocol No. 30758, approved on July 11, 2014) and written informed consent from all of the 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 (Stanford, California), between August 2014 and June 2016 were approached and enrolled in this prospective cohort study. Women signed written informed consents and were enrolled before the final delivery mode (vaginal delivery or cesarean delivery) was known. Inclusion criteria were age 18 yr or older, gestational age greater or equal to 35 weeks, no significant maternal or fetal comorbidities, and able to understand English. Patients with multiple pregnancy; diabetes mellitus (preexisting or gestational), hypertension (chronic or gestational), or preeclampsia requiring pharmacologic treatment; or 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 were obtained after enrollment. Starting on postpartum day one, the subjects were contacted daily, either in person during their hospitalization or by telephone after discharge. A standardized questionnaire was used for daily follow-up assessment (appendix). 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 nonopioid 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 of the study endpoints. If participants had not met all of the study endpoints after 3 months postdelivery, they were contacted weekly thereafter until they met the study endpoints. Daily assessment *via* telephone took approximately 2 to 3 min per contact. We attempted to call patients once daily between 12:00 PM and 6:00 PM unless patients specified their preferred time for contact and left a discreet 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 functional recovery to predelivery 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 Obstetric Outcome Variables

Baseline demographic variables were collected by both patient interview and review of medical records before the delivery. Maternal, obstetric, 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 nonsteroidal antiinflammatory drugs and acetaminophen.

### Statistical Analysis

Statistical analyses were performed using the R statistical software package, version 3 (<https://www.r-project.org/>; accessed December 15, 2016), and SAS Enterprise Guide, version 6.1 (SAS Institute, USA). Visual inspection and the Shapiro–Wilk test were 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 exact test. Fisher exact test was substituted when the expected numbers in the chi-square matrix were less than five. 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 that they were successfully contacted before being deemed a dropout. 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 that 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 numeric 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 of the 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") was overlaid to depict population values for pain resolution after vaginal delivery and cesarean delivery. For those patients who completed all of the 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 among pain on postpartum day 1, pain burden, and time to functional recovery were investigated with Pearson correlation coefficients. Furthermore, a 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<sup>17</sup> using similar daily follow-up methodology that investigated pain resolution and opioid cessation after nonobstetric surgery, time to opioid cessation was successfully separated between different surgical types with statistical significance with a sample size of 134 patients (with 109 usable for analysis). We therefore enrolled patients until we attained 134 patients with successful completion of all study endpoints with the 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 a total of 3,343 daily telephone call attempts to 213 enrolled patients and successfully reached patients 1,610 times (48% success rate). On the days we failed to reach a patient, we assumed that the patient took the 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 ahold of patients for 2 weeks in a row, they were deemed lost to follow-up, and they were censored as of the last day that 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 1 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. A total of 134 women completed the study, reporting the primary endpoint of pain- and opioid-free functional recovery, whereas 79 did not complete the primary endpoint (*i.e.*, lost to follow-up before completing the composite primary endpoint; fig. 1). Demographic, obstetric, and neonatal characteristics of patients who did and did not complete the primary endpoint are reported in table 1. Asian patients were more

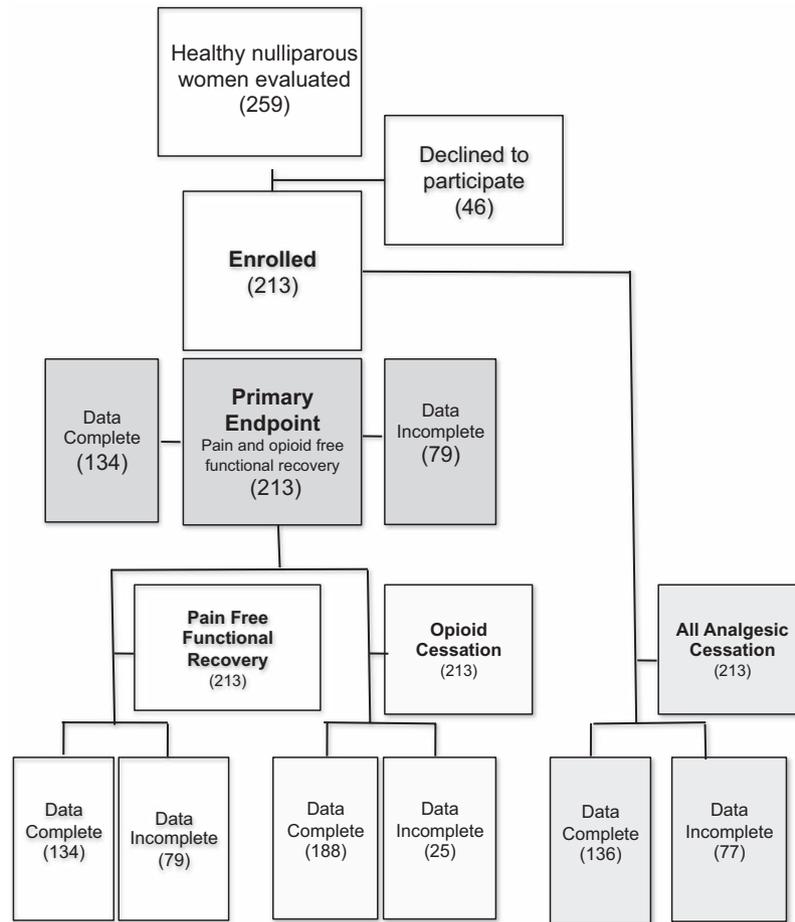
**Table 1.** Demographic, Obstetric, and Neonatal Characteristics of Patients Who Completed the Primary Endpoint and Patients Who Did Not Complete Primary Endpoint

Characteristic	Complete (N = 134)	Incomplete (N = 79)	P Value
Age, y	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 <sup>2</sup>	27.7 (25.9–30.5; 21.7–40.8)	27.5 (25.3–29.4; 18.6–42.6)	0.31*
Gestational age, d	278 (274–284; 255–292)	279 (272–285; 260–293)	0.90*
Gravity, n (%)			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, n (%)			0.02†
Previous smoker	19 (14.2)	3 (3.9)	
Never smoked	115 (85.8)	75 (96.2)	
Alcohol use, n (%)			0.13‡
Ever drank	117 (87.3)	62 (79.5)	
Never drank	17 (12.7)	16 (20.5)	
Ethnicity, n (%)			< 0.01†
White	74 (55.2)	23 (29.1)	
Asian	41 (30.6)	46 (58.2)	
Hispanic	14 (10.5)	9 (11.4)	
Other	5 (3.7)	1 (1.3)	
Educational status, n (%)			0.12‡
Graduate degree	84 (62.7)	37 (48.1)	
4-yr college degree	38 (28.4)	30 (39.0)	
Less than 4-yr college degree	12 (9.0)	10 (13.0)	
Labor type, n (%)			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, n (%)			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, n (%)			0.41†
Neuraxial	129 (96.3)	78 (98.7)	
Other§	5 (3.7)	1 (1.3)	
Degree of perineal laceration, n (%)			0.71‡
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, n (%)			
Apgar score at 1 min			0.65‡
< 7	14 (10.8)	7 (8.9)	
≥ 7	116 (89.2)	72 (91.1)	
Apgar score at 5 min			0.38†
< 7	0 (0.0)	1 (1.3)	
≥ 7	130 (100.0)	78 (98.7)	
Level of neonatal care, n (%)			0.61†
Well-baby nursery	111 (82.8)	70 (88.6)	
Intermediate care nursery	18 (13.4)	7 (8.9)	
Neonatal ICU	5 (3.7)	2 (2.5)	

Summary statistics was presented as number (percentage of patients) or median (interquartile range; 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. 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-Whitney U test. †Fisher exact test. ‡Chi-square test. §Other includes narcotics and no analgesia.

ICU = intensive care unit.



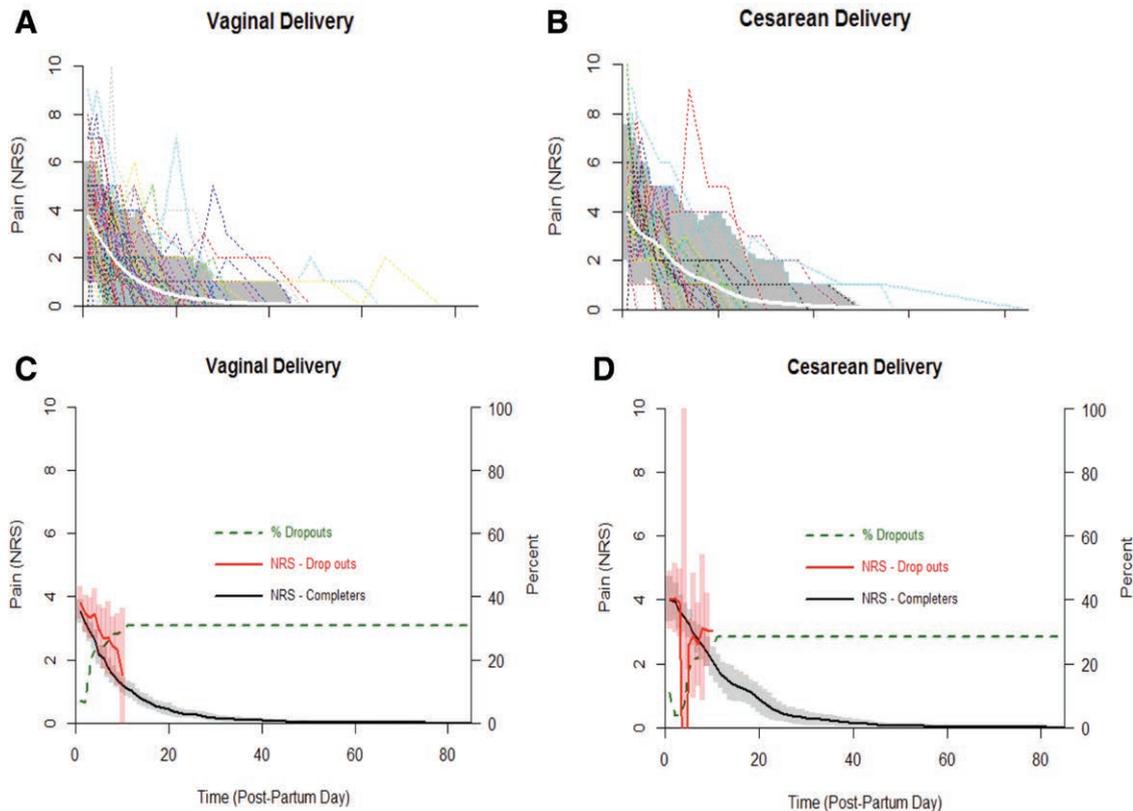
**Fig. 1.** Flow diagram for participant inclusion and data completion.

likely to be lost to follow-up compared with 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 for patients who completed all endpoints (i.e., not lost to follow-up), were 19 (11 to 26) and 27 (19 to 40) days (median [IQR]) in the vaginal delivery and cesarean delivery cohort, respectively (Table 2). Ninety-five percent of patients had attained the primary endpoint after 47 days in the vaginal delivery group and 57 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 2, A and B. Figure 2, C and D, shows pain trajectory after vaginal delivery and cesarean delivery in completers and noncompleters 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 1 day during the postpartum period. All of the 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 nonopioid analgesic use by delivery mode are shown in figure 3. The unadjusted Cox proportional hazard ratios (95% 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 to 0.85;  $P = 0.006$ ), 0.67 (0.45 to 0.99;  $P = 0.04$ ), 0.32 (0.21 to 0.47;  $P < 0.0001$ ), and 0.60 (0.41 to 0.89;  $P = 0.01$ ), respectively. After adjustment for baseline demographic and obstetric variables, hazard ratios (95% CIs) for pain- and opioid-free functional recovery, pain resolution, opioid cessation, and all analgesic cessation were 0.55 (0.36 to 0.84;  $P = 0.006$ ), 0.65 (0.42 to 0.99;  $P = 0.04$ ), 0.29 (0.19 to 0.45;  $P < 0.0001$ ), and 0.59 (0.38 to 0.91;  $P = 0.02$ ), respectively.

Sensitivity analyses 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 were lost to follow-up, were 10 (2 to 21) and 19 days (5 to 32 days; median [IQR]) in the vaginal delivery and cesarean delivery, respectively. Assigning longest observed time to the endpoint to the patients who were lost to follow-up

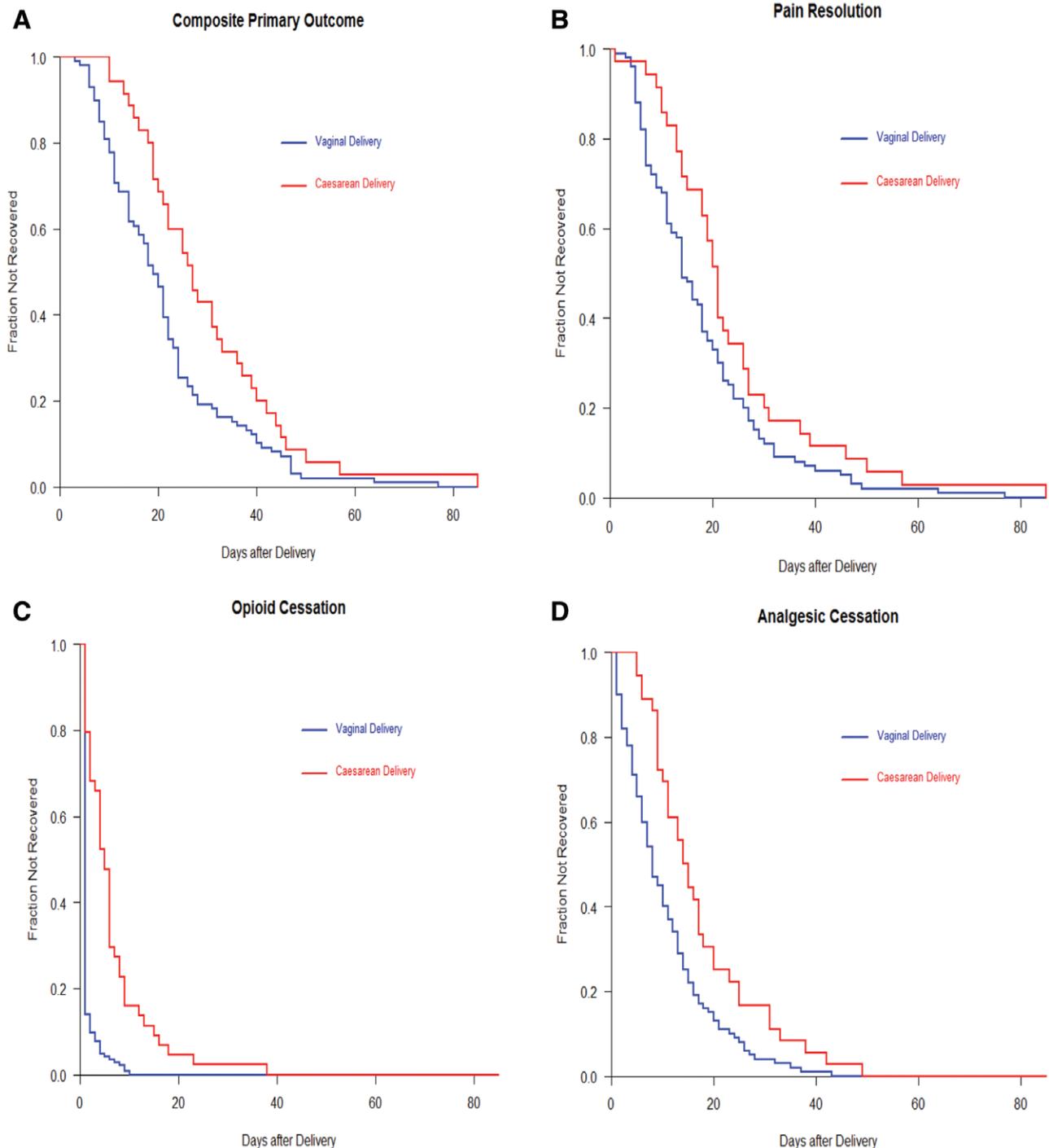


**Fig. 2.** Pain trajectory after vaginal and cesarean delivery. (A) Pain trajectory after vaginal delivery. *Colored dotted lines* represent pain reports from individual subjects, and *solid white line* is a moving average constructed with Friedman's supersmoother in R; "supersmu" (R statistical software package, version 3). *Shaded area* covers the range from the 5th to 95th percentile of the data. NRS = verbal numerical pain score from 0 to 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 *solid white line* is a moving average constructed with Friedman's supersmoother in R; "supersmu" (R statistical software package, version 3). *Shaded area* covers the range from the 5th to 95th percentile of the data. NRS = verbal numerical pain score from 0 to 10, with 0 = no pain and 10 = worse pain imaginable. (C) Pain trajectory in completers and noncompleters after vaginal delivery. *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% CIs. *Dashed green line* demonstrates the timing of dropout. The overlap of CI with the mean of the other curve demonstrates that the patients who dropped out of the study were not having a significantly different pain experience compared with those who were retained. (D) Pain trajectory in completers and noncompleters after cesarean delivery. *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% CIs. *Dashed green line* demonstrates the timing of dropout. The overlap of CI with the mean of the other curve demonstrates that the patients who dropped out of the study were not having a significantly different pain experience compared with those who were retained.

resulted in 28 (16 to 77) and 43 days (25 to 85 days; median [IQR]) in the vaginal delivery and cesarean delivery, respectively. 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 7.0 (IQR, 2.0 to 18.0), 0.5 (0.5 to 2.0), and 6.0 days (2.0 to 14.0 days), respectively. Median times to the same endpoints after cesarean delivery calculated by assigning earliest possible time to the endpoints to the patients who were lost to follow-up were 13 (IQR, 4 to 22), 5 (3 to 10), and 10 days (5 to 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 were lost to follow-up were 26.0 (IQR, 12.0 to 77.0), 0.5 (0.5 to 2.0), and 17.0 days (7.0 to 77.0 days), respectively. Median times to the same endpoints after cesarean delivery calculated by assigning longest possible time to the endpoints to the patients who were lost to follow-up were 30 (IQR, 19 to 85), 9 (5 to 25), and 26 days (14 to 55 days), respectively. The differences between the median time observed (for those who completed all endpoints) 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 of the endpoints (*i.e.*, were



**Fig. 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 (blue line) and cesarean delivery (red line;  $P = 0.004$ , log rank test). (B) Time to pain-free state after vaginal delivery (blue line) and cesarean delivery (red line;  $P = 0.045$ , log rank test). (C) Time to opioid cessation after vaginal delivery (blue line) and cesarean delivery (red line;  $P < 0.0001$ , log rank test). (D) Time to all analgesic cessation after vaginal delivery (blue line) and cesarean delivery (red line;  $P = 0.008$ , log rank test).

not lost to follow-up) are shown in table 2. Times to reach those endpoints were significantly longer after cesarean delivery than vaginal delivery (table 2). Pain burden (AUC) was strongly correlated with time to functional recovery (Pearson correlation coefficient of 0.75; 95% CI, 0.67 to 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 to 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 to 0.83;  $P < 0.0001$ ). The pain burden–time to

functional recovery association did not differ among the three different measures of pain. Pain on postpartum day 1 was modestly correlated with pain burden (Pearson correlation coefficient = 0.32; 95% CI, 0.16 to 0.47;  $P = 0.0001$ ), accounting for 10% of variance.

## Discussion

The current study provides granular data reflecting this pivotal period for recovery and transition to motherhood.<sup>18</sup> 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 use; however, both modes of delivery were associated with significant pain burden and long functional recovery with significant variability among parturients (figs. 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.<sup>19</sup> 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).

The study provides normative values for analgesic requirement during the postpartum 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 9 days and a range from 0 to 39 days (table 2). 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.<sup>17</sup> Ninety-five percent of the patients in our cohort had ceased using opioids by 23 days after cesarean delivery, and none became persistent opioid users. Recent population-based studies that have investigated opioid use after surgery have similarly found a relatively short duration of opioid requirements after cesarean delivery.<sup>11,12</sup> In the study by Sun *et al.*,<sup>12</sup> chronic opioid use was defined as having filled 10 or more prescriptions or having obtained a more than 120-day supply of opioids within 1 yr after cesarean delivery. The absolute risk of opioid-naïve women becoming chronic opioid users was 0.12%, which was a 28% higher risk than a matched nonsurgical control population. Bateman *et al.*<sup>11</sup> stratified opioid-naïve women into five categories according to the pattern of medication filling after cesarean delivery to identify persistent opioid users. 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 12.0 months after cesarean delivery. Our study is unique in providing daily opioid use data after cesarean delivery to outline use trajectories rather than just relative risk determinations.

**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, d	19	27	0.0003*
IQR	11–26	19–40	
2.5th to 97.5th percentile	4–64	10–85	
Range	3–77	10–85	
Time to opioid cessation, d	0	9	< 0.0001*
IQR	0–2	5–12	
2.5th to 97.5th percentile	0–12	0–39	
Range	0–14	0–39	
Time to analgesic cessation, d	11	16	0.0006*
IQR	5–17	11–24	
2.5th to 97.5th percentile	0–40	7–55	
Range	0–77	7–55	
Time to pain resolution, d	14	21	0.014*
IQR	7–24	14–27	
2.5th to 97.5th percentile	4–64	0–85	
Range	3–77	0–85	
Time to functional recovery, d	19	27	0.0002*
IQR	11–24	19–40	
2.5th to 97.5th percentile	4–59	10–85	
Range	3–77	10–85	
Pain AUC	25.5	44.0	0.0002*
IQR	10.5–43.0	29.5–58.0	
2.5th to 97.5th percentile	2.0–122.0	6.0–140.0	
Range	0.5–123.0	6.0–140.0	

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

\*Mann-Whitney U test.

Pain AUC = area under the curve of daily pain levels (0–10) times duration of pain in days.

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.<sup>11,12</sup>

After vaginal delivery, 31% of our patients required opioids for a short period in the hospital, with median time to opioid cessation of less than 1 day (fig. 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 for establishment of norms for opioid use after vaginal delivery. Minassian *et al.*<sup>20</sup> reported 76% of women with perineal laceration or episiotomy after vaginal delivery required opioids within the first 48 h, whereas Macarthur *et al.*<sup>21</sup> reported incidences of opioid use during 24 h after vaginal delivery of 7% in patients who received epidural morphine and 32% in those not receiving epidural morphine. Our study highlights that the majority of patients undergoing vaginal delivery do not require opioids after discharge from the hospital. Therefore, routine opioid prescription at discharge for women who had a 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 whether the parturient had returned to their prepartum level of physical function. A notable finding from our study is that, with the exception of three 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.<sup>22</sup> 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.<sup>23</sup> Our findings demonstrate that it took 47 days and 57 days for 95% of women undergoing vaginal delivery and cesarean delivery, respectively, to attain functional recovery. However, the recovery might have been even longer in the women who 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 that could affect postpartum recovery is

different between nulliparous and multiparous women.<sup>24</sup> Previous birth experience and the impact of older children at home may add noise to the already highly variable outcomes evaluated above. Furthermore, very few nulliparous women who underwent elective cesarean delivery without labor met the study inclusion criteria due to comorbidities, 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 a high drop-out rate. We made a total of 3,343 daily telephone call attempts to 213 enrolled patients and successfully reached patients 1,610 times (48% overall success rate). During the immediate postpartum period (7 days or less after the delivery), we successfully contacted patients 918 times out of 1,178 attempts (78% success rate). We were only able to contact patients 692 times out of 2,165 attempts after 7 postpartum days (32% success rate). Because 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 10.0 by postpartum day 7 in the typical parturient, and contribution of data after postpartum day 7 on the pain burden AUC calculation is small. Therefore, despite overall 52% missingness of data, we consider the magnitude of bias acceptably small with regard 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.

### Conclusions

We found significant variability in pain, opioid use, and functional recovery after both vaginal delivery and cesarean delivery. Recovery to predelivery 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. If opioid requirement exceeds expectation set by this study, the patients should be individually evaluated by their providers.

### Acknowledgments

The authors thank Aramina Aksamit, R.N., research assistant, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, California.

### Research Support

Supported by the Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medi-

cine, Stanford, California, and by grant No. T32GM089626 from the National Institute of General Medical Sciences, Bethesda, Maryland (to Dr. Komatsu).

## Competing Interests

The authors declare no competing interests.

## Correspondence

Address correspondence to Dr. Komatsu: Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, 300 Pasteur Drive, Room H3580, Stanford, California 94305. ryukomatsu80@gmail.com. This article may be accessed for personal use at no charge through the Journal Web site, [www.anesthesiology.org](http://www.anesthesiology.org).

## References

- Hamilton BE, Martin JA, Osterman MJK, Curtin SC, Mathews TJ: Births: Final data for 2014. *Natl Vital Stat Rep* 2015; 64: 1–64.
- Committee Opinion No. 666: Optimizing postpartum care. *Obstet Gynecol* 2016; 127: e187–92
- Sunshine A, Olson NZ, Zighelboim I, De Castro A: Ketoprofen, acetaminophen plus oxycodone, and acetaminophen in the relief of postoperative pain. *Clin Pharmacol Ther* 1993; 54:546–55
- Carvalho B, Zheng M, Harter S, Sultan P: A prospective cohort study evaluating the ability of anticipated pain, perceived analgesic needs, and psychological traits to predict pain and analgesic usage following cesarean delivery. *Anesthesiol Res Pract* 2016; 2016:7948412
- Declercq E, Cunningham DK, Johnson C, Sakala C: Mothers' reports of postpartum pain associated with vaginal and cesarean deliveries: Results of a national survey. *Birth* 2008; 35:16–24
- Eisenach JC, Pan P, Smiley RM, Lavand'homme P, Landau R, Houle TT: Resolution of pain after childbirth. *ANESTHESIOLOGY* 2013; 118:143–51
- Nikolajsen L, Sørensen HC, Jensen TS, Kehlet H: Chronic pain following caesarean section. *Acta Anaesthesiol Scand* 2004; 48:111–6
- Kainu JP, Sarvela J, Tiippana E, Halmesmäki E, Korttila KT: Persistent pain after caesarean section and vaginal birth: A cohort study. *Int J Obstet Anesth* 2010; 19:4–9
- Eisenach JC, Pan PH, Smiley R, Lavand'homme P, Landau R, Houle TT: Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. *Pain* 2008; 140:87–94
- Bjelland EK, Owe KM, Pingel R, Kristiansson P, Vangen S, Eberhard-Gran M: Pelvic pain after childbirth: a longitudinal population study. *Pain* 2016; 157:710–6
- Bateman BT, Franklin JM, Bykov K, Avorn J, Shrank WH, Brennan TA, Landon JE, Rathmell JP, Huybrechts KF, Fischer MA, Choudhry NK: Persistent opioid use following cesarean delivery: Patterns and predictors among opioid-naïve women. *Am J Obstet Gynecol* 2016; 215:353.e1–353.e18
- Sun EC, Darnall BD, Baker LC, Mackey S: Incidence of and risk factors for chronic opioid use among opioid-naïve patients in the postoperative period. *JAMA Intern Med* 2016; 176:1286–93
- Webster J, Nicholas C, Velacott C, Cridland N, Fawcett L: Validation of the WHOQOL-BREF among women following childbirth. *Aust N Z J Obstet Gynaecol* 2010; 50:132–7
- Stewart AL, Greenfield S, Hays RD, Wells K, Rogers WH, Berry SD, McGlynn EA, Ware JE Jr: Functional status and well-being of patients with chronic conditions: Results from the Medical Outcomes Study. *JAMA* 1989; 262:907–13
- Liu YQ, Maloni JA, Petrini MA: Effect of postpartum practices of doing the month on Chinese women's physical and psychological health. *Biol Res Nurs* 2014; 16:55–63
- Jansen AJ, Duvekot JJ, Hop WC, Essink-Bot ML, Beckers EA, Karsdorp VH, Scherjon SA, Steegers EA, van Rhenen DJ: New insights into fatigue and health-related quality of life after delivery. *Acta Obstet Gynecol Scand* 2007; 86:579–84
- Carroll I, Barelka P, Wang CK, Wang BM, Gillespie MJ, McCue R, Younger JW, Trafton J, Humphreys K, Goodman SB, Dirbas F, Whyte RI, Donington JS, Cannon WB, Mackey SC: A pilot cohort study of the determinants of longitudinal opioid use after surgery. *Anesth Analg* 2012; 115:694–702
- Aber C, Weiss M, Fawcett J: Contemporary women's adaptation to motherhood: The first 3 to 6 weeks postpartum. *Nurs Sci Q* 2013; 26:344–51
- Kannampallil T, Galanter WL, Falck S, Gaunt MJ, Gibbons RD, McNutt R, Odwazny R, Schiff G, Vaida AJ, Wilkie DJ, Lambert BL: Characterizing the pain score trajectories of hospitalized adult medical and surgical patients: A retrospective cohort study. *Pain* 2016; 157:2739–46
- Minassian VA, Jazayeri A, Prien SD, Timmons RL, Stumbo K: Randomized trial of lidocaine ointment *versus* placebo for the treatment of postpartum perineal pain. *Obstet Gynecol* 2002; 100:1239–43
- Macarthur A, Imarengiaye C, Tureanu L, Downey K: A randomized, double-blind, placebo-controlled trial of epidural morphine analgesia after vaginal delivery. *Anesth Analg* 2010; 110:159–64
- Gjerdingen DK, Center BA: First-time parents' prenatal to postpartum changes in health, and the relation of postpartum health to work and partner characteristics. *J Am Board Fam Pract* 2003; 16:304–11
- Houser L, Vartanian TP: Policy Matters: Public Policy, Paid Leave for New Parents, and Economic Security for U.S. Workers., Center for Women and Work. New Brunswick, NJ, Rutgers University, 2012
- Khaskheli M, Baloch S, Baloch AS: Obstetrical trauma to the genital tract following vaginal delivery. *J Coll Physicians Surg Pak* 2012; 22:95–7

### Appendix: Daily Pain and Opioid Use Questionnaire

D1	Please rate your pain from 0 to 10 where 0 is no pain and 10 is the worst pain you can imagine on the AVERAGE in the last 24 h.	0-10
D2	Please rate your pain from 0 to 10 where 0 is no pain and 10 is the worst pain you can imagine right NOW.	0-10
D3	Please rate your pain from 0 to 10 where 0 is no pain and 10 is the worst pain you can imagine at its WORST in the last 24 h.	0-10
D4	In the last 24 h, what medications did you take for your pain?	
	0 = none    1 = hydrocodone/acetaminophen    2 = hydrocodone    3 = oxycodone/acetaminophen    4 = oxycodone    5 = acetaminophen    6 = nonsteroidal    7 = other	0-10
D5	In the last 24 h, how much relief has pain medication provided?	0-10
D6	In the last 24 h, have you needed to take your pain medication to help you sleep?	Yes = 1 No = 0
D7	In the last 24 h, 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?	Mood = 3 Other = 4
D9	In the last 24 h, 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 h, 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 per hour = 2 Every few minutes = 3 Constantly = 4	0-10
D11	Rate the severity of any pain medication side effects you have experienced over the last 24 h: On a 0 to 10 scale where 0 is no interference and 10 is complete interference, please rate, during the past 24 h, how pain has interfered with your:	0-10
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 predelivery level of activity?	Yes = 1 No = 0
D16	How much of your baby's daily nutrition is from breast feeding? None = 0 Less than half = 1 About half = 2 All = 4	All = 4