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Patterns of recovery from pain after cesarean delivery

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Abstract

We know very little about the change in pain in the first 2 months after surgery. To address this gap, we studied 530 women scheduled for elective cesarean delivery who completed daily pain diaries for two months after surgery via text messaging. Over 82% of subjects missed fewer than 10 diary entries and were included in the analysis. Completers were more likely to be Caucasian, non-smokers, and with fewer previous pregnancies than non-completers. Daily worst pain intensity ratings for the previous 24 hours were fit to a log(time) function and allowed to change to a different function up to 3 times according to a Bayesian criterion. All women had at least one change point, occurring 22 ± 9 days postoperatively, and 81% of women had only one change, most commonly to a linear function at 0 pain. Approximately 9% of women were predicted to have pain 2 months after surgery, similar to previous observations. Cluster analysis revealed 6 trajectories of recovery from pain. Predictors of cluster membership included severity of acute pain, perceived stress, surgical factors, and smoking status. These data demonstrate feasibility but considerable challenges to this approach to data acquisition. The form of the initial process of recovery from pain is common to all women, with divergence of patterns at 2–4 weeks after cesarean delivery. The change point model accurately predicts recovery from pain, its parameters can be used to assess predictors of speed of recovery, and it may be useful for future observational, forecasting, and interventional trials.

1. Introduction

Postoperative pain varies widely after the same surgical procedure. Although postoperative pain scores are well characterized during hospitalization for surgery, pain experience after hospital discharge is largely unknown with the exception of the one or two times that patients return for routine care. This lack of knowledge about the patterns of recovery from

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Conflict of Interest. JCE consults to Adynxx (San Francisco, CA, USA) regarding preclinical and clinical analgesic development of analgesics. Adynxx is developing non agents to speed recovery from surgery, but does not use the methods described in this manuscript and did not participate in this work or the manuscript.

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pain and its predictors after surgery limits our clinical ability to rationally prescribe an appropriate quantity of opioids, properly identify normal vs abnormal recovery patterns, and determine which patients need more frequent follow up visits or interventions.

In order to better address this gap in our knowledge, we recently described an approach using text messaging to assess daily pain scores for two months after lower extremity joint arthroplasty or cesarean delivery [9]. Compared to similar studies that utilized a smartphone mobile application [10] or daily telephone calls [13] to answer pain assessment questionnaires, this texting-based method had fewer missing data and patients lost to follow-up [9]. One goal of the current study was to determine the feasibility of this text messaging approach to over 500 women after cesarean delivery, the most common major surgery in the USA and affecting nearly twenty million women globally in 2008 [7].

Traditionally, the primary outcome measure for postoperative pain studies has dichotomized groups to those with pain or not with pain at arbitrary time points such as 3, 6, or 12 months postoperatively. This data poor approach does not address pain burden over time or the pattern of recovery in the first few months, the time where most recovery from pain occurs [14]. In our initial small study of daily pain assessments for 2 months after surgery, we determined that pain intensity scores initially followed a log(time) function followed by a transition to a different function which could be identified using Bayesian analysis [9]. A second goal of the current study was to determine the generalizability of this approach to a much larger sample size.

A non-biased approach to define clusters of patterns of change in pain after surgery has been applied to postoperative patients, but only on pain scores during the few days they are in hospital and receiving intensive and variable analgesic interventions [2] or a scant number of times thereafter [14]. A third goal of the study was to determine clusters of recovery patterns in the first two months after cesarean delivery.

Predictors of persistent pain after surgery have traditionally also relied on dichotomous outcomes at a single time remote from surgery. Most studies have identified a small group of psychobiological and surgical factors to predict these dichotomous outcomes. However, the proportion of variance described by these characteristics is modest [17]. A final goal of the study was to begin to explore whether predictors of modeled pattern of recovery in each individual could be identified from simple pre- and peri-operative data, leading the way to future studies which might provide a richer and stronger explanation for membership in subgroup patterns of recovery than a traditional dichotomous approach.

2. Methods

Following Institutional Review Board approval, adult patients (American Society of Anesthesiologists physical status 1, 2, or 3) were recruited from a single center (Maya Angelou Women's Center, Novant Medical Center, Winston-Salem, NC, USA). Patients were enrolled and written informed consent obtained preoperatively during their preoperative anesthesia visit or in the preoperative holding area. We excluded patients who

did not understand English or with history of chronic pain or chronic analgesic use. The trial was registered prior to enrollment of the first subject (NCT 01996592).

A portion of the current study group (first 157 subjects) was previously included in a study to explore growth curve modeling approaches to describe change in pain intensity scores after different surgical procedures [9]. An additional subgroup of 101 subjects wore accelerometers for 60 days after surgery for a planned secondary analysis to describe the pattern of recovery from inactivity after surgery and the autocorrelation between activity and pain.

2.1 In hospital study measures

Demographic information, obstetrical history including number of prior cesarean deliveries and indication, and past medical and surgical history were collected. Patients also completed three preoperative surveys: Patient Reported Outcomes Measurement Information System (PROMIS) Emotional Distress-Depression instrument [18], the 14-item Perceived Stress Scale [3], and a 3-item preoperative questionnaire to predict severity of acute postoperative pain in this population that was previously validated at our institution [16]. The latter included patient assessment of anxiety, anticipated pain, and anticipated analgesic need.

Anesthetic care for cesarean delivery was not controlled in this study and followed routine practice at our institution. Subarachnoid anesthesia typically consisted of an intrathecal injection of hyperbaric bupivacaine 10–12 mg, fentanyl 15–20 mcg, and preservative free morphine 150–200 mcg. Patients who received epidural anesthesia typically received 2% lidocaine or 3% chloroprocaine with 3–4 mg preservative free morphine. Patients who required general anesthesia and did not receive neuraxial morphine were excluded from the study. Additional opioid medications were given intraoperatively as necessary for analgesia. Patients were monitored per standard protocol in the post anesthesia care unit until resolution of their neuraxial blockade. Patients were treated for pain, nausea/vomiting, and/or itching with routine orders.

On the first postoperative day, patients responded to three questions regarding their pain using a 10 cm line visual analog pain scale anchored at no pain on the left worst pain imaginable on the right and we measured the distance in mm from the left anchor. The three questions were: What is your pain intensity right now? What was the worst pain in the past 24 hours? What was your average pain in the past 24 hours? The patients were then instructed that they would be answering 6 daily questions for the next 60 days by electronic diary via daily email link, paper and pencil diary, or SMS texting to their cell phone. The patient's preferred method of daily contact as well as contact information were confirmed at this time.

2.2 Study measures after hospital discharge

Patients responded to the following 6 questions daily for 60 days after surgery: What is your pain intensity right now? What is your pain unpleasantness right now? What was your worst pain in the past 24 hours? What was your worst pain unpleasantness in the past 24 hours? What was your average pain in the past 24 hours? What was your average pain unpleasantness in the past 24 hours? Patients were instructed to answer each question on a

numerical scale between 0 (no pain or unpleasantness) and 10 (worst pain or unpleasantness imaginable). Please note that the in hospital pain scores were performed with a visual analog scale and are measured from 0 to 100 whereas the post hospital discharge scores were obtained on a 0 to 10 numeric scale and were measured in single digit increments. Patients were instructed to rate pain in, surrounding, or deep to their incision, including pelvic pain, and to not rate other types of pain such as headache or backache. Study personnel provided daily reminders via SMS text messaging to submit assessments and contacted patients by additional text messages or telephone calls if they failed to provide their assessments for several days. Patients who completed at least 85% of the daily pain assessments over 60 days received a \$25 gift card as compensation for their participation. Patients were able to withdraw from the study at any time.

All data were entered by study personnel into a secured Research Electronic Data Capture (REDCap) database [8] and were verified and corrected as necessary, prior to analysis.

2.3. Statistical Methods

Statistical analyses were conducted using R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria), RStudio version 1.0.153 (RStudio, Inc.) and the Statistical Package for the Social Sciences (SPSS for Windows, version 24, Chicago, IL, USA). Descriptive statistics were calculated for all variables such that mean (standard deviation) were used for normally distributed variables; median [range] for nonparametric data; and frequency (percentage) for count data. For all analyses, two-tailed hypothesis testing was used with $p < 0.05$ interpreted for statistical significance.

Due to the sensitivity of the modeling to missing data, of the 530 participants who contributed at least one daily diary entry during the observation period, those who missed more than 10 daily diary entries ($n=92$) or more than three consecutive daily diary entries before day 30 ($n=3$) were excluded. The 435 remaining participants were considered to have followed protocol and are included in the primary analysis.

Daily worst pain intensity score was collected as the primary outcome from day of discharge through day 60. The primary analytic plan was comprised of four phases. First, to examine the resolution of pain and based upon previous work in exploring the multi-phased pattern of recovery in this population [9], a Bayesian change-point analysis was performed in R with MCMCpack (Martin AD, Quinn KM, Park JH. MCMCpack, version 1.4–0, 2017). Second, cluster analysis was also performed in R via finite mixture regression modeling (Gruen, B, Leisch, F, Sarkar, D, Mortier, F, Picard, N. flexmix package, version 2.3–14, 2017) to identify similar participant patterns of recovery. Finite mixture models cluster individual participants based on the parameters of their individual trajectories (i.e., participants with similar intercepts and slopes are grouped together in a cluster). Third, to explore predictors of cluster membership, multinomial logistic regression was conducted in SPSS. Finally, to quantify the diagnostic ability of the multinomial model to predict cluster membership, receiver operator characteristic curves were generated in SPSS.

To study the uncertainty in the primary analysis due to missing data, an imputation strategy was used to predict the values of the missing data in the context of the temporal trends and

recent fluctuations in pain that predated the missing value. A single imputation strategy was used that imputed embedded missing data of all 530 participants except three that were missing more than three consecutive daily diary entries before day 30. The imputation was done in R using an autofit ARIMA model with a Kalman filter (i.e. forecasting embedded missing data). As a sensitivity analysis, the change-point models were then re-estimated on the imputed series that contained no missing values and compared to the primary model set that contained missing data to examine the impact of the missing data on the estimation of the change-points and class membership.

2.4. Sample size determination

To calculate the statistical power for this study, we created a mathematical simulation modifying the work of Zhang & Wang [22] and relied on previous simulations conducted by Nylund [15]. Briefly, we simulated scenarios for which we instilled known relationships between the random effects of polynomial change models (i.e., correlations between intercepts and slopes) as well as a range of predictors of those parameters that were themselves correlated (the assumptions were all generated from pilot data). Results indicated that enrolling $N = 530$ (with 10% attrition) would provide $> 80\%$ chance that the model selection criteria will select a correct number of latent classes based on previous simulation studies [15].

3. Results

Enrollment occurred between April 2013 and November 2015. During this 30 month period, a total of 27,955 daily diaries entries were recorded with as many as 45 active participants at one time providing data. The large majority of subjects (87%) provided diary data by text message, with 12% logging in to REDCap for direct entry and 0.4% (2 subjects) completing paper diaries.

3.1. Missing data and excluded patients

A total of 575 subjects consented the study and 530 provided data (Figure 1). Accuracy of growth modeling degrades with increasing missing data, so we excluded subjects with more than 10 missing data points in the 60 day postoperative period. In addition, since a previous analysis of a portion of these subjects indicated that a Bayesian change-point analysis was likely to be the most appropriate, and since that study suggested that the initial change in form occurred most commonly within 30 days of surgery [9], we further excluded 3 subjects with 3 consecutive days of missed data in the first 30 days after surgery. These exclusions are referred to as the embedded missing dataset ($n=95$). The remaining subjects are referred to as being in the complete dataset ($n=435$). The 95 subjects removed from the primary analysis were then included in the secondary sensitivity analysis.

Subjects in the complete dataset missed 1.8 ± 2.1 daily entries in the two month period. The majority of subjects missed 0 or 1 days, with over 90% missing 4 or fewer days (Figure 2). Subjects in the embedded missing dataset missed 36 ± 18 daily entries (Figure 2). Compared to the complete dataset, participants in the embedded missing dataset were more likely to be African-American, smokers, and with higher gravida and parity (Table 1). Subjects in the

embedded missing dataset also had a higher predicted acute pain score than those in the complete dataset (62 ± 18 versus 56 ± 18 ; $p=0.0035$, respectively, but did not differ in the perceived stress scale (13 ± 6.4 versus 12 ± 5.8) or the PROMIS emotional distress-depression instrument (12 ± 4.7 vs 11 ± 3.9).

3.2. Modeling pain intensity scores in the complete dataset

As anticipated, there was a wide variability in this measure each day, with individual values covering the entire 0–10 scale on each day of the entire study period (Figure 3A). For depiction purposes, the mean score for each day of the 435 participants was smoothed and is shown as a thick black line (Figure 3A).

For each individual, worst pain intensity score for the past 24 hr over the study period were modeled using a Bayesian change-point analysis. The change-point model assumes that the nature of change of pain (e.g., either the level or slope of change) itself changes during the observation recovery period. Based on previous exploration of data from a subset of these patients and those recovering from orthopedic surgery [9], we chose a unique $\log(\text{time})$ model which optimized the number and location of change-points by participant. Each participant was allowed up to three change-points. All subjects in the primary analysis had at least one change-point, with a small proportion having a second and third change point (19% and 5%, respectively). Figure 3B shows the timing of these three change points as a cumulative proportion of subjects at each day after surgery. The first change point occurring 22 ± 9 days [range 3–50 days] after surgery. Modeling predicted that only 9% of subjects would have pain 60 days after surgery.

The sensitivity analysis considering missing data resulted in similar estimates as the primary models. A total of 1536 (5.5%) values were imputed and then re-analyzed using the same modeling strategy as the primary analysis. In this sensitivity analysis the average intercept (i.e., pain at time 0) increased by 0.2% and the slope (decrease in pain over time increased by 0.1%). The average time to first change-point remained unchanged. At 60 days after surgery the number of patients estimated to have non-zero pain increased from 9% to 12%.

3.3. Cluster analysis

We termed the period of time before and after change-points as states. The state, along with $\log(\text{time})$ and the interaction of $\log(\text{time}) \times \text{state}$ were entered into the finite mixture regression model to estimate the number of unique clusters of recovery within the study population. The intercept for each state was allowed to vary by participant. The optimal number of clusters were determined based on an increasing iterative process of 1 to 9 components with five repetitions of each. The best fitting model identified six clusters as determined by Bayesian Information Criterion (BIC) and from inspection of the rootogram of posterior probabilities which showed that the components were well separated.

Figure 4 shows the mean of the individually modeled pain scores by time point for each cluster. The clusters have been colored coded across figures and numbered from least to greatest pain burden, defined as the area under the pain over time curve, at the beginning of the observation period with Cluster 1 having the lowest pain burden and Cluster 6 having the highest. Cluster 2 had the largest membership (26%) while Cluster 6 had the smallest

membership (6%). Note that there is a rough relationship between intercept (predicted pain score upon hospital discharge) and pain burden, but with considerable exceptions by clusters. For example, Clusters 4 and 6 started with nearly equivalent and high initial pain scores, yet the pain burden of Cluster 6 was over 3 times greater than Cluster 4.

Figure 5 shows individual trajectories as predicted by the change-point model by cluster overlaid with the mean trajectory for each cluster. The time to first change point was poorly related to pattern of recovery, being 16 ± 9 days for Cluster 1, 18 ± 7 days for Cluster 2, 26 ± 8 days for Cluster 3, 23 ± 7 days for Cluster 4, 26 ± 6 days for Cluster 5, and 26 ± 9 days for Cluster 6.

3.4. Predictors of cluster membership

Several univariate logistic regression models exploring predictors of cluster membership were performed in order to determine entry into the multinomial logistic regression model. These results are detailed in Table 2. The criteria for entry into the multinomial model was a p value $< .20$ univariately along with bivariate correlations with another predictor below $r = .60$. The predictors that met the p value threshold were PROMIS Depression Total Score, Perceived Stress Scale Total Score, number of previous cesarean deliveries, predicted pain score on the first postoperative day, smoking status and observed pain score on the first postoperative day. Two pairs of factors (PROMIS Depression Total Score and Perceived Stress Scale Total Score; predicted and observed pain score on the first postoperative day) were correlated at $r > 0.60$ (and possessed variation inflation factors > 10) so the predictor with the lowest p value univariately between the two was added to the multinomial model. The four predictors finally obtained for the multinomial model were Perceived Stress Scale Total Score, number of previous cesarean deliveries, observed pain score on the first postoperative day and smoking status.

The final model (Table 3) statistically significantly predicts cluster membership better than an intercept-only model ($X^2 = 121.946$, $df = 20$, $p < .001$, data not shown). The independent variables that were statistically significant were Perceived Stress Scale Total Score ($X^2 = 16.078$, $df = 5$, $p = .007$) and pain score on the first postoperative day ($X^2 = 80.337$, $df = 5$, $p < .001$). For these models, several predictors were similarly weighted across cluster groups (i.e., worst pain 24 hours after surgery), while several others were weighted quite differently across clusters (e.g., PSS score, previous C-sections). These predictors could be used to make predictions for which participants might belong to each cluster. However, the model had only fair positive predictive value, correctly predicting membership in the low pain burden groups Clusters 1 and 2 (61% and 69% correct assignment, respectively) but was poor at predicting membership in the highest pain group, Cluster 6 (4% correct assignment).

4. Discussion

We utilized the data collected during this study to evaluate three main objectives: feasibility of an SMS text-based approach to daily diary assessments after cesarean delivery, generalizability of the Bayesian change-point approach to modeling recovery from pain after surgery to a large population, and initial exploration of predictors for pain recovery using modeled parameters as primary outcome measures. The results provide a unique description

of the dynamic change in pain once patients leave the hospital after this surgery. They also provide guidance and identify challenges to application of these methods to large observational and interventional studies.

4.1. Feasibility of SMS text-based approach to daily diaries

This analysis of 435 subjects confirms the exploratory analysis of the first 157 subjects in this study [9], that women after cesarean section overwhelmingly prefer text-messaging using their smartphones rather than direct entry into REDCap or paper data entry. We also confirmed a high compliance rate, with over 82% of subjects who provided data completing daily diaries for 2 months with enough data to be included in the analysis. This is a higher completion rate than the 63% success rate for daily telephone calls in a small study of 56 women after cesarean delivery [13] or the 72% success rate for a mobile app in a study of 494 day surgery patients which only included two assessments in the first two weeks after surgery [10]. Advantages of Web-or mobile phone-based methods for daily diaries include time stamping of data entries and ability for study personnel to assess compliance in real time and provide reminders as needed.

There are also challenges to the use of text messaging for diary entry. During peak enrollment, study personnel were spending 3–4 hr per daily (including weekends and holidays), sending reminders, entering data from text message to the REDCap database, and making follow up phone calls. In an ongoing study examining patterns of recovery after lower extremity total joint arthroplasty (NCT 02685735) we have reduced time demand on study personnel by utilizing a daily email with a link for computer-, tablet- or phone-based direct entry into a secure REDCap site (data not shown). An initial study in this older patient population showed that they greatly preferred paper methods [9], but this digital method has been well accepted.

Despite the high success rate, 7% of consented patients provided no data at all and a sizeable proportion of subjects who did provide data missed too many diary entries to be included in the analysis. These individuals differed in several important ways from those who were included. We excluded women with chronic pain or taking chronic analgesics from this initial study, and it is conceivable that the methods used to acquire data in the current study would have a high failure rate in this population which is vulnerable to prolonged recovery [21].

4.2. Pattern of recovery in the population as a whole

As in the exploratory analysis of the first 157 women in this sample [9], analysis of the 3-fold greater final dataset confirmed that change in pain intensity over time in women after cesarean delivery is best modeled by an initial log(time) decline followed by a change point, determined by a sequential Bayesian method, to another pattern. The large majority (81%) of women in this study showed one change point, typically from a log(time) decline to a linear pain intensity score of 0. The proportion of women predicted by this model to have pain 2 months after surgery (9%) was equivalent to that measured by telephone interview in our previous multi-center study in 287 women after cesarean delivery [6].

In addition to better modeling the actual data, use of the change-point analysis may provide clues regarding the timing of the “transition” of acute to persistent pain and guide future study design. The first change point occurred on average 22 days after surgery in the entire population and was poorly related to patterns of recovery, ranging over a narrow time period from an average of 18 days in the fastest recovering cluster to 26 days after surgery in the slowest recovering one. These data are consistent with a recovery process experienced by all patients in the 2–4 week period after cesarean delivery leading to complete recovery or a more persistent pain process.

4.3 Clusters of recovery patterns within the population

Non-biased methods to identify groups with common trajectories have been applied to change in pain intensity ratings over time in patients with chronic pain [4] and in those after surgery [2; 14]. Chapman and colleagues identified 3 patterns of recovery from pain during a 6-day hospitalization after surgery [2] but did not assess patients beyond this period. Miaskowski and colleagues identified 4 patterns of recovery from pain over a one year period after breast surgery for cancer [14]. The first post-surgery data point in that study, however, was 2 months after surgery and, notably, within clusters there was minimal (<10%) change in pain intensity rating between 2 months and 1 year after surgery [14]. Similarly, a study of nearly 500 patients after total knee arthroplasty identified 3 clusters of recovery patterns and noted that there was minimal change in pain from the first observation one year after surgery to the last, 5 years after surgery. These studies agree with the observation that presence and intensity of persistent pain 2 months after surgery is a strong risk factor (Odds Ratio 18.4) for pain lasting years [19] and suggest that clusters of recovery in the initial 2 month period strongly predict pain presence and intensity 1 and 5 years later.

4.4. Predictors of cluster membership

This study was designed to determine feasibility, challenges, and generalizability of the data acquisition and modeling methods previously described [9] to a large, homogeneous surgical population and as such included only a few, simple list of biopsychosocial factors which might predict speed of recovery in the first two months after this surgery. Nonetheless, it is encouraging, given the associations mentioned in the previous paragraph between pain presence 2 months after surgery and persistent pain much later that the predictive factors for class membership for pattern of recovery in the current study after cesarean delivery (severity of acute pain, stress, smoking, surgical intervention) are also observed in studies of risk factors for persistent pain 1–2 years after surgery [1; 12; 20; 21]. These data provide a strong rationale for future, more extensive studies of predictors of early recovery after surgery and for the use of growth curve modeled parameters rather than pain presence as primary outcome measures in future interventional clinical trials.

4.5. Limitations

We studied relatively healthy women for elective surgery from a single center where approximately half of the cesarean deliveries are performed by the university teaching service, limiting generalizability. Additionally, the complete dataset lacked much of the diversity of the population recruited into the study. One can argue, based on these observations and others by our group [5; 6], that chronic pain after cesarean delivery is rare

and of minor public health concern. On the other hand, cesarean delivery is one of the most common major surgical procedures performed globally [7] and other investigators utilizing appropriate methods have observed a quite high (22%) incidence of pain one year after cesarean delivery [11]. We did not contact women in this study beyond the 2 month study period, so cannot determine from these data the relationship between individual or cluster pattern of recovery and long term persistence of pain. And we did not include preoperative assessment of many factors which might predict persistent pain after surgery. Finally, we recognize that pain is but one aspect of suffering and dysfunction after surgery, and knowing the time course of recovery from pain alone is incomplete. Future studies should include assessments of other domains, including sleep and physical dysfunction.

4.5. Conclusions

Although over 82% of women after cesarean delivery provided enough daily diary entries over 2 months for analysis, this presented considerable demands on study personnel 7 days a week. Pain declines initially in a log(time) fashion after this surgery for 2–4 weeks, followed by change in pattern, most commonly to complete resolution of pain. Cluster analysis reveals 6 patterns of recovery and an anticipated prevalence of pain 2 months after surgery (9%) similar to that previously observed. Factors which predict cluster membership were the same as those associated with chronic persistent pain after surgery, although the predictive model was poor. These approaches inform women and caregivers of expected patterns of recovery from pain after cesarean delivery and provide data necessary for future study for observational, forecasting, and interventional clinical trials.

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Figure 1. Subject disposition

Number of subjects are in parentheses. The two datasets discussed in this study are the complete dataset used for the primary analysis and the missing embedded dataset used for the sensitivity analysis.

Figure 2. Missing data

Proportion of subjects in the complete dataset (blue) and missing embedded dataset (red) with each of the possible number of daily diary data points missing.

Figure 3. Pattern of recovery from pain in the study population

A) Heat map of worst daily pain over the 2 month study period for the 435 subjects in the complete dataset. For depiction of typical recovery, the black line is smoothed from the mean value for all subjects on that day. **B)** Proportion of subjects changing from one function of recovery to another as a function of postoperative day. All subjects in the complete dataset ($n=435$) had at least one change point, shown in red. Fewer had at least 2 change points, shown in green, and only 20 subjects had a 3rd change point, shown in blue.

Figure 4. Cluster analysis of group patterns of recovery in the complete dataset

Modeled worst daily pain over the two month period assigned to 6 clusters, depicted in a rainbow pattern from most rapid recovery in purple to most slowest recovery in red. Number of members in each class in parentheses.

Figure 5. Individual data within clusters

Modeled data from all individuals within each of the 6 clusters, depicted in a rainbow pattern from most rapid recovery in purple to most slowest recovery in red. Thin lines are individual subjects and thick line is the modeled pattern for that cluster.

Table 1.**Demographic and Obstetric Characteristics**

	Complete Dataset (n=435)	Missing Embedded Dataset (n=95)
Age (years)	30.7 (5.5)	28.8 (6.4)
Height (cm)	164 (7.0)	165 (6.4)
Weight (kg)	95 (23)	92 (20)
Race *		
African-American	99 (23)	39 (41)
Asian/Pacific Islander	3 (1)	0
Caucasian	304 (70)	52 (55)
Hispanic	24 (5)	4 (4)
Other	5 (1)	0
Smoker *		
Yes	42 (10)	28 (29)
No	393 (90)	67 (71)
ASA Physical Status		
1	19 (4)	4 (4)
2	371 (85)	79 (83)
3	45 (11)	12 (13)
Gravida *		
1	35 (8)	8 (8)
2	158 (36)	23 (24)
3	112 (25)	18 (19)
4	66 (15)	16 (17)
>4	64 (15)	30 (32)
Para *		
1	221 (51)	35 (37)
2	110 (25)	27 (28)
3	38 (9)	18 (19)
4	13 (3)	7 (7)
>4	5 (1)	0
Number of previous CD		
0	83 (19)	16 (17)
1	224 (52)	44 (46)
2	97 (22)	20 (21)
3	26 (6)	14 (15)
4	4 (1)	1 (1)
Estimated gestational age (wk)	39 (1.0)	39 (1.4)
Neonatal weight (kg)	3.5 (0.5)	3.2 (0.6)
Apgar score at 1 minute	8 [8,8]	8 [8,8]
Apgar score at 5 minutes	9 [9,9]	9 [9,9]

All values are n (%) except age, height, weight and estimated gestational age, which are mean (standard deviation) and Apgar scores which are median [1st, 3rd quartiles.

* **Bold** items indicate group differences (Chi-Square; $P < 0.001$)

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Table 2.

Univariate predictors of cluster membership (n=435)

Predictor factor variables	P-value
PROMIS depression instrument total score	0.001 [*]
Perceived stress scale total score	<0.001 [*]
Maternal weight	0.442
Age	0.372
Height	0.482
Gravida	0.239
Para	0.470
Estimated gestational age	0.478
ASA status	0.412
Number of prior cesarean deliveries	0.121
Smoking status	0.039
Indication for cesarean delivery	0.414
Race/ethnicity	0.356
Predicted pain score on the first postoperative day	0.010 [*]
Observed worst pain score on the first postoperative day	<0.001 [*]
Neonatal weight	0.873
Neonatal Apgar score at 1 minute	0.417
Neonatal Apgar score at 5 minutes	0.305

^{*} P<0.05 statistically significant

Table 3.

Summary of multinomial logistic regression

Cluster	Predictor	B	SE	Wald	p	OR	95% CI (OR)	
							Lower	Upper
1	(reference)							
2	Intercept	-2.824	0.596	22.438	<.001			
	PSS Total Score (0–31)	0.067	0.031	4.798	0.028	1.07	1.007	1.136
	Number of previous cesarean sections (0–4)	0.113	0.209	0.29	0.591	1.119	0.743	1.687
	Worst pain in the first 24 hrs after surgery (0–100)	0.044	0.007	34.827	<.001	1.045	1.03	1.06
	Smoker (non-smoker as reference)	0.154	0.617	0.062	0.803	1.167	0.348	3.911
3	Intercept	-2.443	0.619	15.592	<.001			
	PSS Total Score (0–31)	0.036	0.033	1.185	0.276	1.036	0.972	1.106
	Number of previous cesarean sections (0–4)	0.242	0.22	1.219	0.269	1.274	0.829	1.959
	Worst pain in the first 24 hrs after surgery (0–100)	0.037	0.008	22.311	<.001	1.037	1.022	1.053
	Smoker (non-smoker as reference)	-1.176	0.883	1.776	0.183	0.308	0.055	1.74
4	Intercept	-4.652	0.729	40.678	<.001			
	PSS Total Score (0–31)	0.072	0.035	4.357	0.037	1.075	1.004	1.151
	Number of previous cesarean sections (0–4)	0.292	0.233	1.567	0.211	1.339	0.848	2.116
	Worst pain in the first 24 hrs after surgery (0–100)	0.058	0.009	42.718	<.001	1.06	1.042	1.078
	Smoker (non-smoker as reference)	0.565	0.65	0.757	0.384	1.76	0.493	6.289
5	Intercept	-4.701	0.698	45.29	<.001			
	PSS Total Score (0–31)	0.097	0.033	8.616	0.003	1.102	1.033	1.177
	Number of previous cesarean sections (0–4)	0.343	0.223	2.359	0.125	1.409	0.91	2.184
	Worst pain in the first 24 hrs after surgery (0–100)	0.057	0.008	45.938	<.001	1.059	1.042	1.077
	Smoker (non-smoker as reference)	-0.006	0.668	0	0.992	0.994	0.268	3.683
6	Intercept	-7.935	1.108	51.31	<.001			
	PSS Total Score (0–31)	0.152	0.045	11.547	0.001	1.165	1.067	1.271
	Number of previous cesarean sections (0–4)	0.61	0.288	4.49	0.034	1.841	1.047	3.236

Cluster	Predictor	B	SE	Wald	p	OR	95% CI (OR)	
							Lower	Upper
	Worst pain at 24 hours post delivery (0–100)	0.069	0.012	30.147	<.001	1.071	1.045	1.098
	Smoker (non-smoker as reference)	0.528	0.775	0.463	0.496	1.695	0.371	7.742

PSS=Perceived Stress Scale; PROMIS Depression=PROMIS Depression short form instrument