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## Trajectories of postsurgical pain in children: risk factors and impact of late pain recovery on long-term health outcomes after major surgery

Jennifer A. Rabbitts, M.B., Ch.B.<sup>a,d</sup>, Chuan Zhou, Ph.D.<sup>b,c</sup>, Cornelius B. Groenewald, M.B., Ch.B.<sup>a,c</sup>, Lindsay Durkin, B.A.<sup>c</sup>, and Tonya M. Palermo, Ph.D.<sup>a,b,c</sup>

<sup>a</sup>Department of Anesthesiology & Pain Medicine, University of Washington, Seattle, WA, USA

<sup>b</sup>Department of Pediatrics, University of Washington, Seattle, WA, USA

<sup>c</sup>Center for Child Health, Behavior and Development, Seattle Children's Hospital, Seattle, WA, USA

<sup>d</sup>Center for Clinical and Translational Research, Seattle Children's Hospital, Seattle, WA, USA

### 1. Introduction

Over one million children undergo inpatient surgery annually in the United States [9]. Emerging research indicates that many of these children have problems with pain after hospital discharge [21], with 80% of children experiencing moderate-severe pain at home two weeks after major surgery. Furthermore, recent studies suggest that pain may persist long-term for a sizeable portion of these children, with around 20% of children reporting significant pain beyond the expected healing period after major surgeries [4,7,17]. In the short-term, postsurgical pain significantly impacts children's recovery from surgery. While the majority of children recover to baseline health by one month after surgery, around 20% have persistent decline in health-related quality of life (HRQOL) at one month, which is associated with continued postsurgical pain [20].

While rates of persistent pain have been measured in a few studies in children 6 to 12 months after surgery [4,17], understanding of the course of postsurgical pain over time is limited. In adult populations, extensive research has examined the persistence of postsurgical pain [11,12] and recent research has identified distinct trajectory patterns in

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Corresponding author: Jennifer A. Rabbitts, M.B., Ch.B. Seattle Children's Hospital, 4800 Sand Point Way NE MB.11.500.3, Seattle WA 98105 Phone: (206) 987-2704, Fax: (206) 987-3935, jennifer.rabbitts@seattlechildrens.org.

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pain recovery after surgery [18]. For example, in the study conducted by Page et al., while the majority of adults had positive recovery with diminished pain over 12 months after surgery, a subgroup continued to have higher levels of persisting postsurgical pain [18]. The trajectory of this subgroup was distinct in the initial weeks to months after surgery, and was associated with poorer functional outcomes one year after surgery. It is also important to understand the course of postsurgical pain and whether distinct trajectory patterns exist in children recovering from major surgery. Little is known of the potential impact of persistent postsurgical pain on long-term health outcomes such as physical function, and HRQOL in children after surgery. These data are critical in order to identify children who are on a slower recovery trajectory, and to guide development of early intervention efforts to optimize outcomes for children having major surgery. Examining postsurgical pain trajectories over time also provides a unique opportunity to investigate the transition from acute to chronic pain in children, and the modifiable factors contributing to this process.

Therefore, the aims of this study were to address these research gaps by (1) prospectively characterizing pain trajectories using repeated assessments in the 12 months following surgery, (2) identifying presurgical child and parent psychological risk factors for late pain recovery, and (3) examining relationships between pain trajectories and long-term health outcomes. Based on recent adult studies [18], we hypothesized that a subgroup of children would follow a trajectory characterized by slower recovery of pain. Based on perioperative studies in children suggesting that child psychological factors [4] and parental factors [16] play a role in pain persistence, we hypothesized that greater child and parental pain catastrophizing would be associated with a late recovery trajectory. Finally we hypothesized that membership in a late pain recovery trajectory group would be associated with poorer HRQOL, and greater activity limitations over long-term.

## 2. Methods

### 2.1. Participants

Participants were 60 children ages 10–18 years undergoing major spine or chest wall surgery, and their parents. Following Institutional Review Board approval, children and parents were enrolled from general and orthopedic surgery clinics at a children's hospital in the northwestern United States over a 21 month period. Parents provided written consent and children provided written assent for participation in the study. Details of recruitment and retention statistics are presented in Figure 1. Children were eligible if they were (1) age 10–18 at the time of surgery, (2) undergoing spinal fusion or surgery for a pectus deformity, and (c) able to speak and read English. Children were excluded if they (a) had a serious comorbid health condition (e.g. requiring a daily medication, or prior major surgery), (b) did not live with their parent or guardian, or (c) their parent or guardian was not able to speak or read English.

### 2.2. Procedures

Longitudinal repeated assessments were conducted at five time-points: presurgery, in-hospital, two weeks, four months and one year postsurgery. At presurgery, children and parents completed a seven-day assessment at home during the week leading up to surgery.

Children completed measures assessing baseline pain catastrophizing, pain characteristics, HRQOL, and activity limitations. Children also completed daily monitoring with an electronic pain diary. Parents completed baseline measures reporting socio-demographics, and parental pain catastrophizing. Participants were instructed to complete measures independently. Study materials were couriered to the participants' homes and collected by study staff on the day of surgery. The in-hospital assessment consisted of collection of clinical data and pain ratings from the medical records by study staff. Children repeated the seven-day daily pain diary, as well as pain, HRQOL, and activity limitations questionnaires at home at two weeks, four months and again one year after surgery. Study materials for follow-up assessments were couriered to and from the participants' homes. Children and parents received gift cards in the amounts of \$20 and \$10 respectively on completion of each home assessment. Data were collected over a 3 year period from March 2012 to February 2015. The acute outcomes (two weeks) after surgery have been described in two prior manuscripts reporting predictors of poorer acute postsurgical outcomes [21] and predictors of memories of acute postsurgical pain [13]. The present report is the first to report the long-term (four month and 12 month) outcomes in this sample. Actigraphy data were also collected as part of this study and will be reported separately.

### 2.3. Measures

**2.3.1. Pain intensity**—Pain intensity was rated using a standard 11-point numerical rating scale (NRS), with anchors of 0 'No pain' and 10 'Worst possible pain'. Children reported on their daily pain intensity once a day in the evening for seven days at baseline and each follow-up home assessment. Time-stamped entries were made electronically via a PDA device. Children reported on their postsurgical pain intensity in the hospital using the same 11-point numerical rating scale (NRS, 0–10) used in the daily electronic diary. In the hospital, the child's bedside nurse recorded child self-reported pain intensity ratings into the medical record at least every four hours, as well as when medically indicated. These were collected from the electronic medical record by research staff. Numeric rating scales have demonstrated construct validity including sensitivity to change for measuring postsurgical pain intensity in children of this age range both in the hospital and at home after surgery [14].

**2.3.2. Pain characteristics**—Children reported on additional characteristics of pain experienced in the preceding seven days on a pain questionnaire at baseline and at each follow-up home assessment. Children reported on pain frequency and duration on Likert-type scales with five response options for frequency ranging from 'Not at all' to 'Daily' and four response options for duration from 'Less than 1 hour' to 'All day'.

**2.3.3. Child pain catastrophizing**—Prior to surgery, children self-reported on their thoughts and feelings in response to pain on the Pain Catastrophizing Scale, child version (PCS-C). Children rate their responses to pain on a five point Likert-type scale ranging from 'Not at all' to 'Extremely', for 13 items (e.g. 'When I have pain I keep thinking about how much it hurts', 'When I have pain I wonder whether something serious may happen'). Items are summed, yielding a maximum possible score of 52, and three subscale scores (rumination, magnification, helplessness) with higher scores indicate greater pain

catastrophizing. The PCS-C has shown good internal consistency ( $\alpha = 0.87 - 0.90$ ) in schoolchildren with and without pain, and strong correlations with pain intensity ( $r = 0.49$ ) and disability ( $r = 0.50$ ) in those with chronic pain [5]. The PSC-C has been used in prior pediatric surgical samples [6,15].

**2.3.4. Parental pain catastrophizing**—Prior to surgery, parents reported on their own thoughts and feelings in response to their child's pain on the Pain Catastrophizing Scale, parent version (PCS-P). Parents rate their responses when their child is in pain on a similar five point Likert-type scale to the child version ('Not at all' to 'Extremely'), on 13 items (e.g. 'When my child is in pain, I keep thinking about how much he/she is suffering', 'When my child is in pain, I wonder whether something serious may happen'). The PCS-P has shown good internal consistency ( $\alpha = 0.81 - 0.93$ ) in parents of children with and without chronic pain, and is significantly associated with parenting stress and functional disability in children with pain [8]. The PCS-P has been used in prior pediatric surgical samples [6].

**2.3.5. Health-related quality of life**—Children completed self-report of their HRQOL during the preceding seven days on the Pediatric Quality of Life Scale, Short-Form (PedsQL™), a 15-item questionnaire assessing physical, emotional, social, and school function. Children rate difficulty with each item on a Likert-type scale with five response options ranging from 'Never' to 'Almost always'. Responses are reverse scored and transformed to a 0 to 100 range. These are then summed for each scale and divided by the corresponding number of items, to yield a Total Score, and Psychosocial and Physical Health Summary subscale scores, with higher scores indicating better HRQOL. The PedsQL™ has been used broadly in pediatric samples as well as in postsurgical pediatric populations [20], and the PedsQL™ Short-Form has been shown to be comparable to the full-length version [3].

**2.3.6. Activity limitations**—Children completed the Child Activity Limitations Interview (CALI), a 21-item scale measuring activity limitations due to pain [19]. Items include physical, social, and routine daily life activities (e.g. 'Playing with friends', 'Riding a bike or scooter', 'Schoolwork'). Children rate 'how difficult or bothersome doing these activities was for you because of pain' over the past 7 days. Response options are on a five-point Likert-type scale ranging from 'Not very difficult' to 'Extremely difficult'. Scores are then summed (possible range from 0 to 84) with higher scores indicating greater activity limitations (greater functional impairment). This measure has shown good internal consistency ( $\alpha = 0.95$ ), and high cross-informant reliability with parent reported activity limitations ( $r = 0.73$ ) [19].

**2.3.7. Sociodemographic and clinical data**—Parents reported on child race, ethnicity, and family income. Several variables including child age, sex, procedure type, duration of surgery, and hospital length of stay were collected from the electronic medical record by study personnel.

## 2.4. Statistical analyses

All analyses were conducted using STATA Statistics/Data Analysis (Version 12.1 S.E., StataCorp, College Station, TX). To characterize pain trajectories over 12 months following surgery, pain trajectory analyses were conducted using the “traj” procedure in STATA [1,2], a STATA equivalent of “proc traj” in SAS. This procedure implements a longitudinal data analysis methodology for estimating group-based trajectory models. Group-based trajectory modeling is a specialized form of finite mixture modeling, which analyzes repeated-measures data using maximum likelihood to identify distinct clusters of individuals following statistically similar progressions of outcomes over time [10]. We assumed the number of groups to be tested a priori at 2 and quadratic shaped trajectories for both groups. Based on prior postsurgical pain trajectory studies in adult populations [18], baseline pain was considered as a predictor of postsurgical pain, and in-hospital assessment was the starting point of the trajectories. Mean pain intensity and 95% confidence bound for each of the four postsurgical time-points was used to describe pain trajectories. Testing for skewness/kurtosis was non-significant, and therefore mean pain intensity was used in the postsurgical pain trajectory analysis. Mean pain was calculated from pain scores (NRS, 0–10) obtained from the 7 day diary for the two-week, four-month, and one year time-points, and for the first three postoperative days after surgery for the in-hospital time-point.

To identify risk factors for late recovery of pain, a logistic regression analysis was conducted examining baseline psychosocial factors (child and parental pain catastrophizing) associated with trajectory group membership, controlling for age, sex, and baseline pain. To investigate relationships between late recovery of pain and long-term health and functional outcomes, a multivariate regression analysis was conducted examining associations between trajectory group membership and HRQOL and activity limitations, controlling for age and sex. Surgical procedure type was examined and found to not significantly relate to postsurgical pain intensity or health and functional outcomes at 12 months in our sample and therefore was not included in the models.

## 3. Results

### 3.1. Descriptive statistics

Participants included 60 children, 10 to 18 years of age (mean = 14.7 years, SD = 1.9), and their parent or guardian. Children were predominantly female (66.7%), and white (83.4%). Demographic and surgical characteristics are shown in Table 1. At baseline, children reported average pain intensity over 7 recorded days from daily diaries of 2.8 (SD = 2.5). Surgeries took an average of 5.2 hours (SD = 1.6), and children stayed in the hospital for 4.5 days (SD = 1.1) on average. During the first three postoperative days in hospital, children reported an average pain intensity of 3.9 (SD = 1.5). Longitudinal data collected on daily pain diaries indicated average pain intensity for the sample of 3.8 (SD = 2.2) at two weeks, 1.2 (SD = 1.7) at four months, and 1.1 (SD = 1.3) at one year after surgery.

### 3.2. Postsurgical pain trajectories

Group-based trajectory modeling was used to identify groups of individuals with similar pain trajectories. The parameter estimates for the model are presented in Table 2. Baseline

pain and postsurgical trajectories for the 2 groups identified are shown in Figure 2. The largest group (Group 1,  $n = 49$ ), labeled “Early Recovery”, was characterized by decreasing pain from in-hospital to two weeks, and four months, which subsequently remained at low intensity until one year after surgery. The second group (Group 2,  $n = 11$ ), labeled “Late Recovery”, was characterized by increasing pain from in-hospital to two weeks after surgery, followed by decreasing pain to four months and one year after surgery. The observed pain scores for individuals at each time-point, separated by trajectory group membership are presented in Figure 3. Pain characteristics and health and functional outcomes at 12 months by trajectory group are presented in Table 3. Children in the late recovery group reported higher pain intensity (mean = 2.9, SD = 1.5) than children in the early recovery group (mean = 0.6, SD = 0.8) at 12 months after surgery ( $t = -5.86$ ,  $P < 0.001$ ). These children also reported significantly greater pain frequency (Fisher’s exact test,  $P < 0.05$ ), and longer pain duration (Fisher’s exact test,  $P < 0.05$ ).

### 3.3. Risk factors associated with pain trajectory group membership

A logistic regression analysis was conducted to examine baseline child and parent pain catastrophizing as predictors of trajectory group membership, controlling for age, sex, and baseline pain. Results are shown in Table 4. Parental pain catastrophizing was significantly associated with trajectory group membership. As hypothesized, greater parental catastrophizing about child pain predicted greater likelihood of membership in the late recovery group (O.R. = 1.11,  $P < 0.05$ ). Contrary to hypotheses, child pain catastrophizing was not significantly associated with trajectory group membership (O.R. = 0.89,  $P = 0.12$ ). Baseline pain (O.R. = 1.27,  $P = 0.21$ ), age (O.R. = 0.75,  $P = 0.25$ ), and sex (O.R. = 1.48,  $P = 0.72$ ) were not significantly associated with trajectory group membership.

### 3.4. Impact of pain trajectory group membership on health and functional outcomes

A multivariate regression analysis was conducted examining associations between trajectory group membership and long-term health outcomes at 12 months (HRQOL and activity limitations), controlling for age and sex. The results are presented in Table 5. Trajectory group membership was significantly associated with both HRQOL and activity limitations (CALI) at 12 months after surgery. As hypothesized, membership in the late recovery group was associated with poorer HRQOL ( $\beta = -10.7$ ,  $P = 0.02$ ), and greater activity limitations ( $\beta = 3.6$ ,  $P = 0.04$ ) at 12 months.

## 4. Discussion

This is the first study to comprehensively measure pain and health outcomes in children from baseline to one year after major surgery. Using group-based trajectory models we characterized pain trajectories over 12 months following surgery, finding two distinct trajectories of postsurgical pain in children. While the majority of children followed a favorable trajectory (early recovery) with pain decreasing progressively after surgery, a significant subgroup of children followed a trajectory pattern characterized by slower recovery of pain (late recovery), which was already distinct at two weeks after surgery. Parent pain catastrophizing, but not child pain catastrophizing, significantly predicted late

recovery of postsurgical pain. Membership in the late pain recovery trajectory group was associated with poorer patient-reported health and functional outcomes at 12 months.

The mean values for postsurgical pain for the whole sample showed pain recovering rapidly after surgery, with mean pain intensity at four and 12 months after surgery lower than baseline levels. This is similar to the findings of Connelly et al., who also found that children reported high levels of pain prior to surgery, which worsened immediately after surgery and then declined progressively over 6 months after spine surgery in children [4]. However, our analytic approach using group-based pain trajectories enabled us to identify and examine a subgroup of children whose recovery was delayed after surgery. Interestingly, this late recovery subgroup already showed a different pattern of postsurgical pain at 2-weeks; their pain had increased further from levels reported in-hospital, distinguishing children in this subgroup from the early recovery group. The late recovery subgroup showed a decrease in pain by 4 months, and at 12 months after surgery, however pain intensity was still significantly greater at 4 and 12 months compared to children in the early recovery group. In contrast, the early recovery group had reached low levels of pain by 4 months, which did not change further over long term follow up. Our findings are also consistent with those of Sieberg et al., who used data from a surgical registry to examine pain trajectories after spinal fusion [22]. While they were limited by the measures used in the registry, their data suggested that subgroups of children exist with poorer recovery. Early identification of children who are on a trajectory of delayed recovery would allow opportunity for early intervention, possibly preventing persistence of pain. Future research is needed to develop and evaluate such interventions in the pediatric surgical population.

In addition we extended the findings of previous research by examining the impact of postsurgical pain trajectories on health outcomes at one year after surgery. Despite the high number of surgeries performed in children, up until now there have been very little data on patient-reported health outcomes in these children over the longer term. In a previous study, we found that pain during the initial weeks at home after surgery significantly impacted recovery of HRQOL in the short-term [20]. Our present finding that pain trajectories impact health outcomes over the longer term underscores the importance of pain control not only during the early postoperative period, but also in the subsequent months after surgery. It is critical that research focus on optimizing pain recovery in order to improve outcomes in higher risk children or children following a slower recovery trajectory.

In this same sample, we previously reported that parents have a significant impact on their children's acute postsurgical pain, as well as on their subsequent memories of acute postsurgical pain [13,21]. The present study revealed that parent behaviors and cognitions may continue to exert an influence on their children's long-term pain recovery after surgery. These findings extend those of Page et al [16] who found that parents' catastrophizing about pain after their child's surgery predicted children's pain 12 months after surgery [16]. Our study was able to address measurement flaws of prior studies by assessing risk factors in the week *prior* to children's surgery, and measuring parent's catastrophizing specifically about *their child's* pain, as opposed to catastrophizing in response to their own pain experiences. Identifying risk factors before surgery provides an opportunity to screen populations and apply targeted interventions. Our findings suggest that the powerful impact of parents on

their child's pain recovery may be harnessed by developing interventions targeting parents' cognitions and behaviors around their children's pain. Not only can this potentially improve children's postsurgical pain outcomes, but also their health outcomes over the year following surgery.

Our findings should be interpreted in light of several limitations. It is possible parents may have influenced their child's self-report, despite our steps to minimize this potential source of bias. Our study included a limited range of major surgical procedures and therefore results may be less generalizable to a broad pediatric surgical population. The sample size of our study was small and therefore we chose a less complex mixture modeling procedure and limited our analysis to two trajectory groups. It is likely that with a larger sample size we would be able to identify additional trajectory patterns. In addition, the small sample size may also have limited our power to detect some associations such as that between baseline child catastrophizing and pain recovery profiles. Future research is needed to examine postsurgical pain trajectory patterns in larger samples of children having major surgeries in order to extend our results. In addition, future studies could consider daily measurement of additional pain characteristics in addition to pain intensity to further characterize pain trajectories.

In conclusion, we identified two distinct trajectories of postsurgical pain in children having major surgeries. While the majority of children had early recovery of pain, a subgroup of children had late recovery of pain, which was associated with poorer health and functional outcomes at 12 months. Parental pain catastrophizing before surgery predicted a late recovery, suggesting that preventive strategies targeting parents' cognitions and behaviors around their child's pain may improve pain and health outcomes in children having major surgeries. Given the significant impact of pain on these children's health outcomes after surgery, progress in children's pain management after surgery is critically needed.

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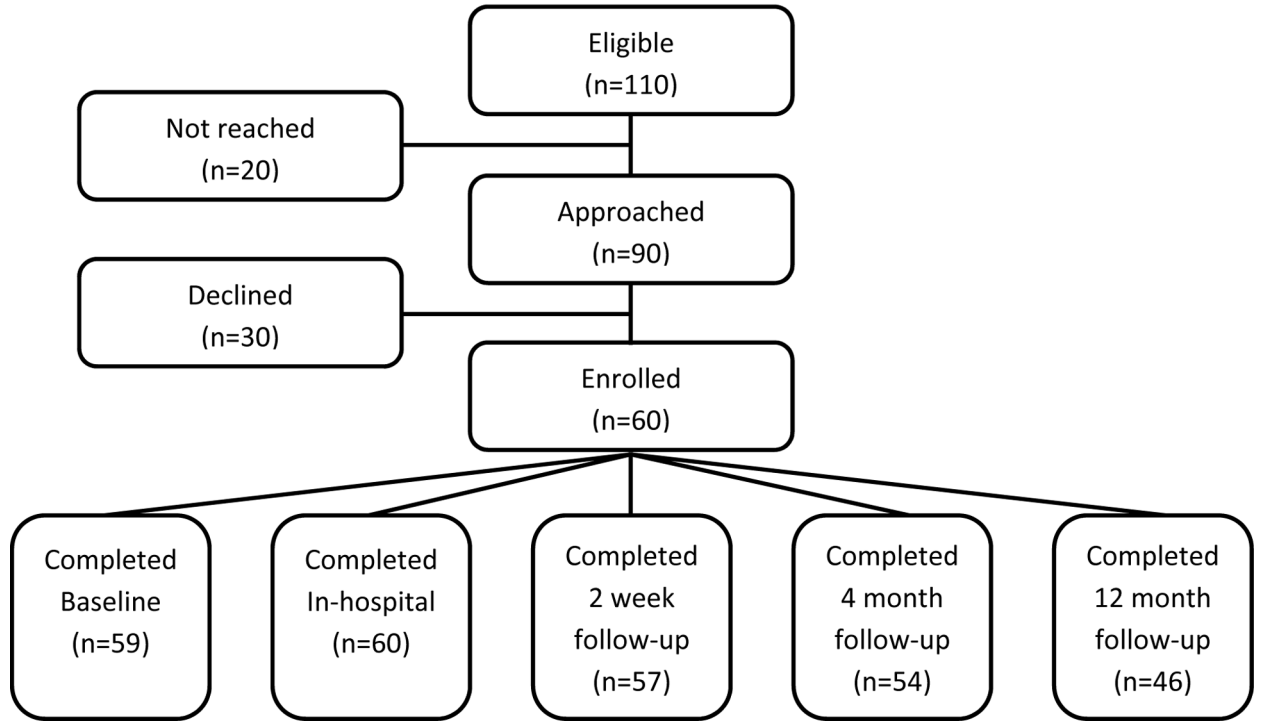
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**Figure 1.**



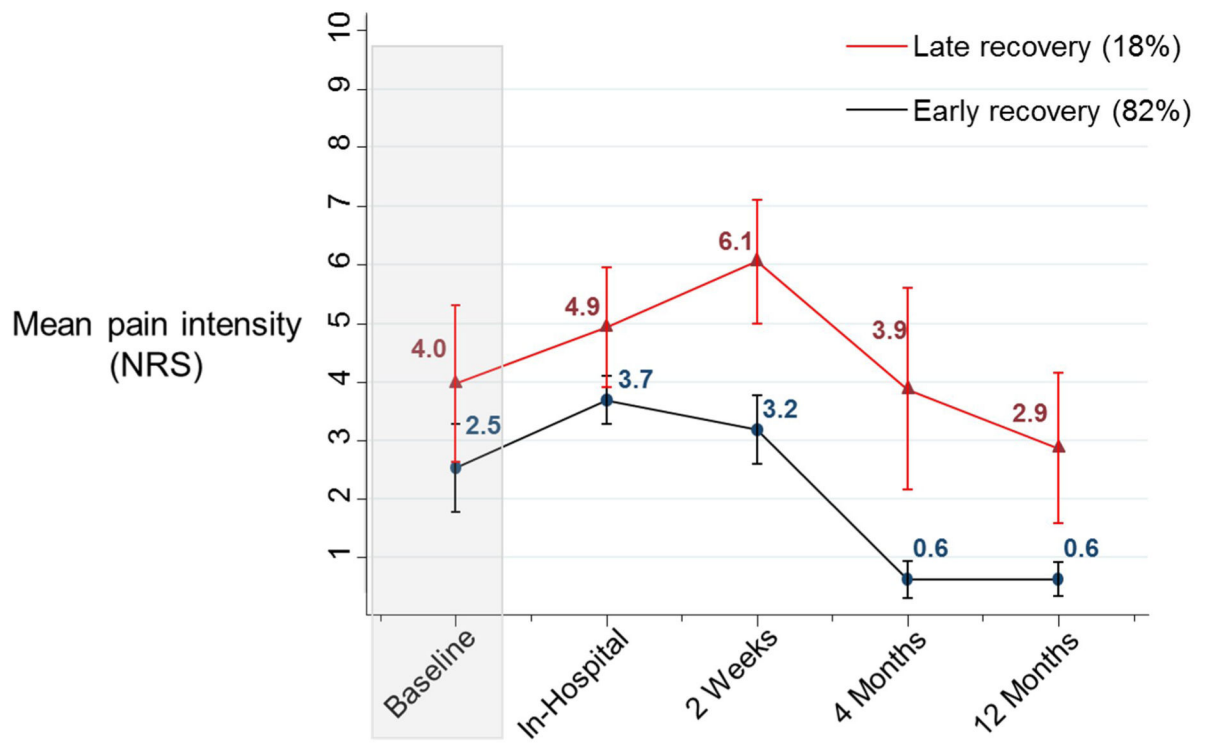
**Figure 1.**  
Recruitment statistics.

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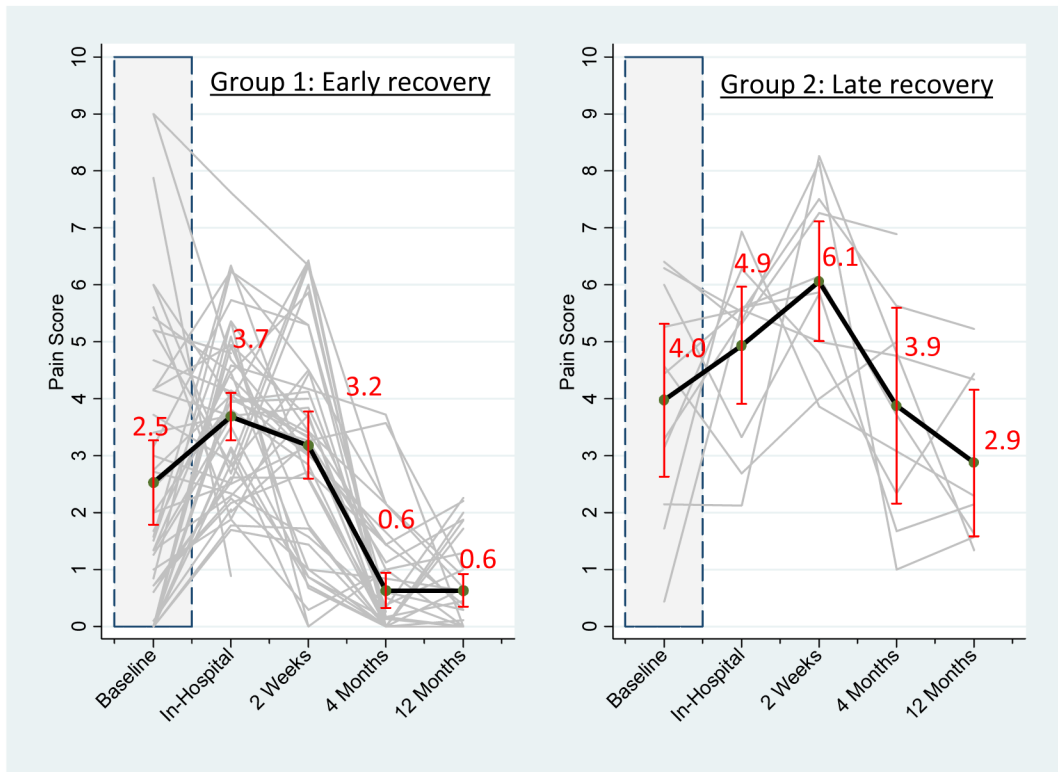
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**Figure 2.**

Group-based trajectory analysis of postsurgical pain intensity, showing mean pain intensity for two trajectory groups: early recovery (n = 49), and late recovery (n = 11).



**Figure 3.** Observed pain scores for individuals, displayed by trajectory group membership.

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**Table 1**

Sociodemographic and surgical characteristics of children having major surgery

Characteristics	N (%) / M (SD)
Age (years)	14.7 (1.9)
Sex	
Female	40 (66.7%)
Male	20 (33.3%)
Child race	
White	50 (83.4%)
African-American	2 (3.3%)
Asian	2 (3.3%)
Other/not reported	6 (10%)
Child ethnicity	
Hispanic	1 (1.7%)
Non-Hispanic	53 (88.3%)
Not reported	6 (10%)
Annual household income	
< \$ 29,999	8 (13.3%)
\$ 30,000–\$69,999	15 (25.1%)
> \$ 70,000	33 (55.8%)
Not reported	4 (6.6%)
Surgical procedure	
Posterior spinal fusion	48 (80%)
Anterior-posterior spinal fusion	2 (3.3%)
Nuss procedure for pectus deformity	9 (15.0%)
Ravitch procedure for pectus deformity	1 (1.7%)
Length of surgery (hours)	5.2 (1.6)
Length of hospital stay (days)	4.5 (1.1)

**Table 2**

Group-based trajectory model for postsurgical pain trajectories

Trajectory group	Probability of group membership	Standard error	Parameter	Estimate	Standard error
1	78.0	10.5	Intercept	5.53	0.84
			Linear	-1.69	0.82
			Quadratic	0.06	0.17
2	22.0	10.5	Intercept	3.73	1.90
			Linear	1.79	1.78
			Quadratic	-0.54	0.34

**Table 3**

Pain characteristics and health outcomes at 12-month follow-up across pain trajectory groups and for the total sample

	Trajectory groups		Total sample
	Early recovery	Late recovery	
Pain intensity, M (SD)	0.6 (0.8)	2.9 (1.5)	1.1 (1.3)
Pain frequency, n (%)			
Not at all	12 (34.3)	0 (0.0)	12 (27.9)
Once per week	10 (28.6)	2 (25.0)	12 (27.9)
2 to 3 times per week	9 (25.7)	2 (25.0)	11 (25.6)
3 to 5 times per week	3 (8.6)	1 (12.5)	4 (9.3)
Daily	1 (2.9)	3 (37.5)	4 (9.3)
Pain duration, n (%)			
Less than 1 hour	30 (85.7)	4 (50.0)	34 (79.1)
A few hours	2 (5.7)	0 (0.0)	2 (4.7)
Half of the day	3 (8.57)	3 (37.5)	6 (14.0)
All day	0 (0.0)	1 (12.5)	1 (2.3)
Activity limitations, M (SD)	2.4 (3.6)	6.3 (7.3)	3.1 (4.7)
Health-related quality of life, M (SD)			
Total quality of life	86 (10.8)	74.8 (15.3)	83.9 (12.4)
Psychosocial quality of life	85.9 (12.5)	76.3 (13.8)	84.1 (13.1)
Physical quality of life	86.1 (14.0)	71.9 (25.2)	83.5 (17.2)

Logistic regression examining demographic and psychosocial factors associated with membership in the late recovery trajectory group

**Table 4**

Predictors	Odds ratio	Standard error	Z	P	Confidence interval
Parental pain catastrophizing	1.11	0.05	2.1	0.03	1.01 – 1.22
Child pain catastrophizing	0.89	0.06	-1.57	0.12	0.78 – 1.03
Baseline pain	1.27	0.25	1.26	0.21	0.87 – 1.86
Age	0.75	0.19	-1.15	0.25	0.45 – 1.23
Sex	1.48	1.58	0.37	0.72	0.18 – 12.0



Multivariate regression model examining trajectory group membership as a predictor of functional limitations and health-related quality of life

**Table 5**

Predictors	Coefficient	SE	T	P	Confidence interval
<b><u>Activity limitations</u></b>					
Late recovery trajectory	3.63	1.79	2.03	0.04	0.01 – 7.26
Age	0.03	0.39	0.07	0.95	-0.77 – 0.82
Sex	2.23	1.61	1.39	0.17	-1.02 – 5.48
<b><u>Health-related quality of life</u></b>					
Late recovery trajectory	-10.7	4.74	-2.26	0.03	-20.3 – (-1.15)
Age	0.14	1.04	0.13	0.89	-1.96 – 2.24
Sex	-3.68	4.25	-0.86	0.39	-12.3 – 4.93