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Examining the prevalence of persistent postsurgical pain in pediatric spinal fusion surgery patients: a biopsychosocial approach

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BOSTON UNIVERSITY
SCHOOL OF MEDICINE

Thesis

**EXAMINING THE PREVALENCE OF PERSISTENT POSTSURGICAL PAIN IN
PEDIATRIC SPINAL FUSION SURGERY PATIENTS:
A BIOPSYCHOSOCIAL APPROACH**

by

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ABSTRACT

Objective: Despite extensive literature on chronic pain in surgical and nonsurgical adult patient populations and in the pediatric nonsurgical patient population, the acute to chronic postsurgical pain transition in children has been a largely neglected area of research. The purpose of this study was to examine the prevalence of persistent postsurgical pain in patients with adolescent idiopathic scoliosis who undergo spinal fusion surgery and to explore baseline differences between patients in varying longitudinal pain trajectories.

Methods: The Scoliosis Research Society Questionnaire-30, which includes pain, self-image, mental health, and activity subscales, was administered to 219 patients at a large Northeast children's hospital preoperatively and at one- and two-years postoperatively through their involvement in the Prospective Pediatric Scoliosis Study. A subset of these patients (n=77) also completed follow-up data at five-years post-surgery. Pain among this sample (in the past six months, in the past month, and at rest) was examined at each

of the time points. Longitudinal pain trajectories were identified using the SAS PROC TRAJ procedure, and trajectory groups were compared for baseline differences in age, self-image, and mental health functioning through one-way analysis of variance and post-hoc analyses.

Results: Preoperative pain was high in this sample, with 36% of patients prior to surgery reporting pain in the past month. The number of patients reporting pain in the past month postoperatively fell to 13% at one-year post-surgery but increased to 17% and 20% respectively at two- and five-years follow-up. A five-trajectory model emerged with a “no pain” group, a “pain improvement” group, a “short-term pain” group, a “delayed pain” group, and a “high pain” group with significant differences in baseline age ($p<.01$), self-image ($p<.01$), and mental health functioning ($p<.01$) found across groups.

Conclusions: The study suggests that pediatric persistent postsurgical pain is potentially a significant health concern. This study also provides preliminary evidence that baseline psychosocial factors may contribute to patients’ longitudinal pain experiences postoperatively. Efforts should be taken to better understand the role that these predictors play in the emergence of persistent postsurgical pain in pediatric surgical patients and to explore how biological factors affect somatosensory phenotypes in this patient population.

TABLE OF CONTENTS

Title	i
Reader's Approval Page	ii
Acknowledgements	iii
Abstract	iv
Table of Contents	vi
List of Tables	viii
List of Figures	ix
List of Abbreviations	x
Introduction	1
<i>Biological Components of Pain</i>	7
<i>Psychosocial Components of Pain</i>	9
<i>ALS and Spinal Fusion Surgery</i>	13
Objectives	18
Methods	19
<i>Participation</i>	19
<i>Measures</i>	19
<i>Procedures for Analysis</i>	22
Results	25
<i>Prevalence of Pain</i>	25
<i>Pain Trajectories</i>	27

Discussion	33
<i>Future Directions</i>	38
References	40
Vita	46

LIST OF TABLES

Table	Title	Page
1	Differences in baseline variables between pain trajectory groups.	32

LIST OF FIGURES

Figure	Title	Page
1	Biopsychosocial model of chronic pain.	6
2	The prevalence of participants reporting pain “in the past 6 months” and “in the past year” at each of the four time points.	26
3	BIC scores for various pain trajectory solutions.	28
4	Graphic representation of the five-trajectory solution ultimately chosen for further analysis.	30

LIST OF ABBREVIATIONS

AIS	Adolescent idiopathic scoliosis
ANOVA	One-way analysis of variance
BH4	Tetrahydrobiopterin
BIC	Bayesian information criterion
CIP	Channelopathy-associated insensitivity to pain
CMP	Chronic musculoskeletal pain
COMT	Catechol- <i>O</i> -methyltransferase
FDI	Functional disability inventory
GCH1	GTP cyclohydrolase
IRB	Institutional Review Board
LSD	Least significant difference
PE	Primary erythermalgia
PEPD	Paroxysmal extreme pain disorder
PPP	Persistent postsurgical pain
PPSS	Prospective Pediatric Scoliosis Study
QST	Quantitative sensory testing
SRS-30	Scoliosis Research Society Questionnaire-30
SRS-24	Scoliosis Research Society Questionnaire-24
SRS-22	Scoliosis Research Society Questionnaire-22

INTRODUCTION

Chronic pain is identified as a clinically significant problem with vast socioeconomic and humanitarian implications (Kehlet & Rathmell, 2010), and is consequently regarded as a valuable area of scientific investigation. Specifically, persistent postsurgical pain (PPP), has received heightened attention over the past 10 to 15 years, as surgical patients may be studied preoperatively and postoperatively, thereby providing researchers insight into the acute to chronic pain transition (Kehlet & Rathmell, 2010) and allow for the identification of risk factors and protective factors that influence the course of recovery for these patients (Katz & Seltzer, 2009). Due to the nature of surgery, whereby treatment involves damage to tissues, patients and their providers often expect that the patients will commonly experience acute pain postoperatively as a physiological response (Bruce & Quinlan, 2011). Alternatively, it is not expected that pain should persist once surgically damaged tissues have healed (Bruce & Quinlan, 2011). Nonetheless, it has been shown that between 10 and 50% of patients experience persistent pain following common surgical procedures (Kehlet, Jensen, & Woolf, 2006), and it has been further shown that as many as 5% of all surgical patients report severe and debilitating pain at one-year postoperatively (Bruce & Quinlan, 2011). While no one definition for PPP has been universally adopted in the pain literature (Katz & Seltzer, 2009), Macrae and Davies (1999) provide a four-component definition that effectively illustrates the acute to chronic postsurgical pain transition: 1) the patient's pain emerges postoperatively, 2) the pain lasts a duration of at least two months, 3) other possible

triggers for the pain have been excluded, and 4) the possibility that a pre-existing condition is perpetuating the pain has been excluded.

Over five million children undergo surgical procedures in the United States each year, and as acute postoperative pain is indicated in the majority of these patients, studying PPP in this patient population is warranted (Ahn, Fortier, & Kain, 2012). Despite the extensive literature that has been published on PPP in adults, few research efforts have been undertaken to assess its prevalence among the pediatric surgical population (Fortier et al., 2011). The surgeries typically encompassed in PPP literature are most commonly carried out in the adult patient population (e.g. mastectomy, coronary artery bypass surgery, caesarian section, limb amputation) (Kehlet et al., 2006). However, the current understanding of PPP cannot simply be applied to children, as a pediatric model of PPP may only emerge from investigations into pediatric-specific experiences and the surgeries that are more commonly carried out in children. Considering the devastating effects of chronic pain in children, which include but are not limited to diminished physical and psychological functioning (Hunfeld et al., 2001), sleep difficulties, increased utilization of health care resources (Roth-Isigkeit et al., 2005), frequent absence from school, diminished academic and athletic achievement (Fortier et al., 2011), anxiety, and depression (Walker & Greene, 1989), it is of critical importance that research on the acute to chronic postsurgical pain transition be extended to include pediatric patients, with the ultimate goal that providers might be able to more adequately screen patients at risk for developing chronic pain and subsequently implement effective therapeutic interventions for pain management.

While the few studies examining PPP in children exhibit notable methodological limitations, they do provide a preliminary basis for further exploring the subject. Wong and colleagues (2007) conducted a retrospective survey study to examine the prevalence of PPP among scoliosis patients treated with spinal fusion surgery. Among 105 patients who completed the survey, which included 85 patients with adolescent idiopathic scoliosis (AIS), seven patients with Marfan's syndrome, three patients with neurofibromatosis, and 10 patients with various rare syndromes, 52% reported prolonged postoperative pain—either isolated back pain, isolated pelvic pain, a combination of back and pelvic pain, or non-localized pain. Of the patients who reported persistent back pain, 40% reported that their pain lasted longer than three months, and half of this group indicated pain lasting longer than one year. Importantly, of the patients reporting back pain, 28 and 36%, respectively, indicated that their pain affected daily life and sleep. They also found that more severe perioperative pain was associated with higher susceptibility to developing PPP. Despite these concerning findings, methodological shortcomings of the study must be considered. For instance, the data combines survey results of patients with operative dates as far back as 1977 and as recently as 2001. While Wong and colleagues assert a relatively homogenous group of study participants with similar operative procedures, the wide range of operative dates provokes consideration of how surgical techniques have evolved over time and how differing techniques might variably affect patients. Furthermore, the study included an average time of 5.7 years between the date of surgery and date of survey, with a range of four months to 27 years. As Wong and colleagues note, a long duration between surgery and

survey might have led to pain recall difficulties for participants, while a short duration might have led researchers to underestimate the prevalence of patients exhibiting prolonged pain beyond 12 months.

Fortier and colleagues (2011) conducted a cross-sectional, preliminary study to examine the incidence of PPP in children. Of 113 surgical patients, with an age range of two to 17 years, 15 (13.3%) indicated chronic postoperative pain, with children reporting a median pain duration of 4.1 months and parents reporting a median pain duration of 4.0 months. Up to 30% of children interviewed indicated that their pain interfered with current normal functioning in areas including academic and extracurricular involvement, household activities, and sleep. Significant ethnic differences were also observed, with those reporting chronic postoperative pain more likely to be of Hispanic/Latino descent than participants not reporting chronic postoperative pain. While these findings also support the existence of PPP in children, procedural shortcomings include the wide age range of study participants and the diversity of surgical procedures encompassed in the results. Fortier and colleagues also note that the participants were recruited postoperatively, thus giving rise to the potential for recall bias. Researchers highlight the value in carrying out a prospective, longitudinal study with a less variable surgical population, narrower age range, and evaluation of preoperative pain and functioning (Fortier et al., 2011).

Examining the development of PPP in children is best carried out through a biopsychosocial framework, which asserts that biological, psychological, and social factors interact and contribute to the emergence of pain chronicity (Kehlet et al., 2006).

Figure 1 highlights the theorized interplay between biological and psychological components in the development of chronic pain (Gatchel et al., 2007).

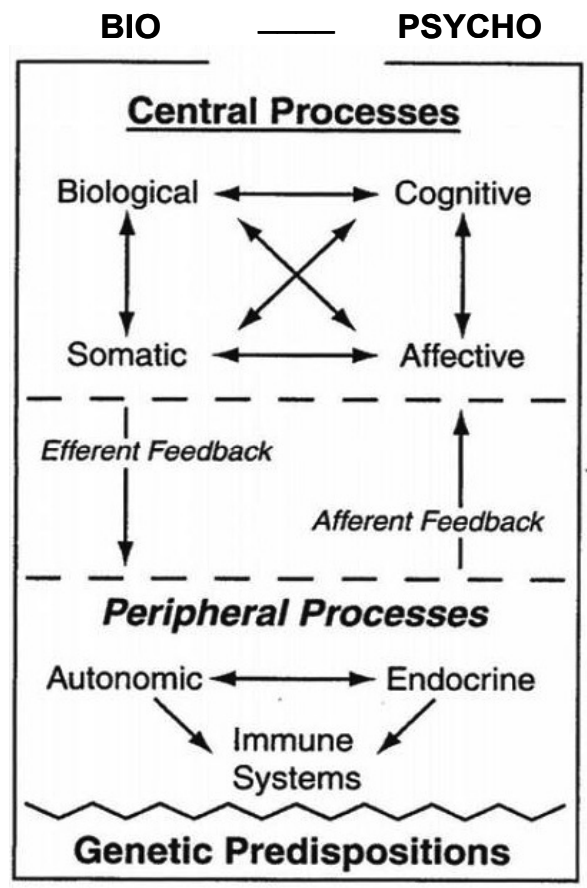


Figure 1. Biopsychosocial model of chronic pain. Pain chronicity is theorized to be the product of reciprocal relationships between central and peripheral neural processes, genetic predisposition, and psychological and social factors (Gatchel et al., 2007).

Biological Components of Pain

With regard to biological underpinnings of postsurgical pain chronicity, Kehlet, Jensen, and Woolf (2006) propose that PPP results either from persistent inflammation or more frequently, from neuropathic pain caused by surgical injury to major peripheral nerves. In the majority of surgeries associated with PPP, major nerves are exposed to the surgical field, and it is suggested that damage to these nerves is a critical element in the acute to chronic postsurgical pain transition (Kehlet et al., 2006). While nerve injury appears to be a prerequisite for PPP, it is not sufficient, as exemplified by such procedures as mandibular osteotomy, after which only around 10% of those experiencing severe intraoperative nerve damage ultimately suffer from clinically significant neuropathic pain (Kehlet et al., 2006). They further posit that in outlining effective strategies for pain alleviation, it is of critical importance that neuropathic causes of pain are distinguished from non-neuropathic causes, such as in the case of a patient whose persistent pain is perpetuated by a lasting inflammatory response.

In addition to the iatrogenic considerations for the emergence of postsurgical pain, genetic predisposition has also been investigated as a contributing biological factor. Recent findings suggest that heritable factors may be implicated in the variability in pain sensitivity between different individuals (Norbury et al., 2007). Schanberg and colleagues (2001) found that a large number of children reporting to a pediatric rheumatology clinic had parents who also exhibited pain histories, with 93% of children having family histories of at least one chronic pain condition. Furthermore, it was shown that the level of parent pain treatment-seeking behavior is positively correlated with

having children who report higher levels of pain and who exhibit poorer health status (Schanberg et al., 2001). It was also found that parents reporting more pain-related interference with activities are more likely to have children who experience higher levels of present pain (Schanberg et al., 2001). Bruehl and Chung (2006), in a study of chronic low back pain patients, showed that a positive parental chronic pain history is associated with heightened pain sensitivity and impairments in endogenous opioid analgesia. Twin studies have also highlighted the possible impact of heritability in pain sensitivity (Norbury et al., 2007). A study of monozygotic and dizygotic twin pairs has estimated the heritability for low back as between 52 and 68% and for neck pain as between 35 and 58% (MacGregor et al., 2004).

Specific gene mutations have been identified in studies of chronic pain. Three pain disorders have been found to be due to dysfunction in the voltage-gated sodium-channel type IX alpha subunit, $\text{Na}_v1.7$, which is encoded by the gene *SCN9A* (Drenth & Waxman, 2007). Primary erythralgia (PE) and paroxysmal extreme pain disorder (PEPD), two hereditary chronic pain disorders, have been shown to be due to a gain of function missense mutation in $\text{Na}_v1.7$, while channelopathy-associated insensitivity to pain (CIP) has been found to result from a nonsense mutation in the subunit (Drenth & Waxman, 2007). Catechol-*O*-methyltransferase (COMT), an enzyme involved in catecholamine metabolism, has been shown experimentally to be associated with increased pain sensitivity in rats (Nackley et al., 2007). Furthermore, tetrahydrobiopterin (BH_4), a cofactor in the production of catecholamine, serotonin, and nitric oxide, has been found to intrinsically regulate pain sensitivity and persistence (Tegeder et al., 2006).

Increased BH4 levels are seen following axonal injury and peripheral inflammation, and GTP cyclohydrolase (GCH1) has been implicated as the rate-limiting enzyme for its synthesis (Tegeder et al., 2006). Healthy individuals homozygous for a haplotype of the GCH1 gene have been found to experience reduced pain sensitivity, and studies show that immortalized leukocytes retrieved from carriers for this gene variant exhibit a lower level of GCH1 upregulation than do controls (Tegeder et al., 2006). It is important that future research efforts focus on how genetic factors may play into the acute to chronic pain transition, specifically in children and adolescents who have undergone surgical procedures, as the gene environment interaction may differ in a pediatric sample as compared to in an adult sample.

Psychosocial Components of Pain

While biological factors certainly contribute to acute phase pain, and studies also suggest that these factors may also play a role in the emergence of PPP, psychosocial factors must also be considered for how they contribute to the development of chronic pain postoperatively. Some researchers have even suggested that among spine surgery patients, psychological variables have a stronger impact on chronic pain than medical ones, with placebo effect studies demonstrating the influence of emotional and cognitive factors on pain (Anke Hinrichs-Rocker et al., 2009). In one such study, Moseley and colleagues (2002) compared pain and functional outcomes among patients with osteoarthritis of the knee who were randomly selected to receive either one of two arthroscopic procedures or a placebo procedure. Researchers ultimately found no significant difference in pain between the two groups and similarly no significant

differences in functioning (Moseley et al. 2002). Further highlighting the biopsychosocial interplay in the postsurgical pain experience, a low level of optimism preoperatively has been shown to independently put patients at risk for PPP four months postoperatively and also to affect pain intensity at four months postoperatively (Powell et al., 2012). Brander and colleagues (2003) carried out a prospective, observational study to examine factors contributing to long-lasting postoperative pain in patients undergoing total knee arthroplasty. They found that preoperative depression and anxiety were associated with increased pain at one-year postoperatively, and that one-eighth of patients still exhibited moderate to severe pain at this time point despite normal clinical or radiographic findings (Brander et al., 2003).

Among the non-surgical chronic pain population, socioeconomic, psychological, and environmental factors have also been found to contribute to how individuals respond to noxious stimuli (Kehlet et al., 2006). For instance, patients with chronic musculoskeletal pain (CMP) have been found to have heightened sensitivity to pain when depression and anxiety are present (Olaya-Contreras & Styf, 2013).

Despite pharmacologic advances in pediatric postoperative pain management, existing knowledge of psychological factors in the emergence of pediatric postsurgical pain has lagged behind (Logan & Rose, 2005). According to Logan and Rose (2005), identifying psychological factors associated with pain and analgesic use will be valuable for implementing methods to more effectively carry out postoperative pain management in children via non-pharmacological means. PPP and associated psychosocial predictors have not been adequately studied in children, but such variables have been studied in the

context of acute postsurgical pain. When controlling for surgical and demographic variables, psychosocial variables such as distress related to an upcoming surgery and child coping behaviors have been shown to be predictive of acute postoperative pain (Palermo, Drotar, & Lambert, 1998).

When examining a pediatric population, it is also important to consider how parent behaviors and responses affect children's pain and functional outcomes, especially considering that parents of children with chronic pain have been shown to exhibit higher degrees of anxiety and depression as compared to parents of children who are not in pain (Walker, Garber, & Greene, 1991) and that parents have been found to engage in protective responses when their child is experiencing pain (Connelly et al., 2010). Moreover, it is necessary to better understand how parents view their child's pain and how they view children's pain in general prior to establishing methods to enhance parental support for pediatric chronic pain treatment regimens (Gaughan et al., 2012). One study on children with chronic neuropathic pain found that parents' lack of understanding regarding their child's treatment, doubts about treatment efficacy, and concerns over the demands of treatment influence a child's lack of compliance toward a treatment regimen (Butterworth, 2008). It is also valuable to consider not only how child distress but also how parent distress, both globally and in the context of a child's pain, influences pediatric pain and functioning (Sieberg, Williams, & Simons, 2011). The manner by which children learn to respond to their pain is influenced by seeing how their parents react to distress and by witnessing their parents' protective behaviors in response to their children's pain, such as in the case of parent having a child skip school when in

pain (Connelly et al., 2010). Simons and colleagues (2008) conducted a study to investigate how parent responses to pain and adolescent pain coping strategies influence adolescent pain behaviors. Adolescent chronic pain patients at a multidisciplinary clinic and their parents were asked to complete survey measures that assessed the child's pain, functional disability, responses to pain, somatization, and parental responses (Simons, Claar, & Logan, 2008). It was found that when children refrain from active coping strategies, such as seeking out support for pain, and passive coping strategies, such as distancing oneself from pain stressors through self-isolation or catastrophizing, parent protective response may result in heightened functional disability and increased pain complaints in adolescents (Simons et al., 2008).

Sieberg and colleagues (2011) investigated how parent protective responses (e.g. allowing a child to miss school or offering special treats to the child when in pain) to their child's pain mediate the relationship between parent distress—both global psychological distress and distress in the context of a child's pain—and child functional disability. Of the parent participants, 30% reported clinically significant distress, though global distress in this population was not found to correlate with pediatric functional disability (Sieberg et al., 2011), consistent with prior literature (Kashikar-Zuck et al., 2008; Eccleston et al., 2004). Nevertheless, parent distress in the context of a child's chronic pain was found to be associated with child functional disability, thus underscoring the potential value in screening parents of pain patients for the nature of their distress and examining the degree to which parent distress might influence a child's functioning (Sieberg et al., 2011). Moreover, parent protective behaviors were found to

mediate the relationship between parent distress in the context of a child's pain (e.g. depression, catastrophizing, and feelings of helplessness) and functional disability (Sieberg et al., 2011). Thus, in improving chronic pain treatment regimens, parent protectiveness, in addition to pain-specific distress, should also be considered for how it affects functioning in pediatric chronic pain patients (Sieberg et al., 2011).

AIS and Spinal Fusion Surgery

Turk and Okifuji (1996) assert that chronic pain patients fall into one of two groups based on their recollection of pain onset. The first group includes patients who report their pain as immediately associated with a particular event such as an injury or accident. The second group includes patients whose onset of pain can best be characterized as insidious, such that these individuals are unable to identify any specific event as directly associated with their pain. Turk and Okifuji posit that while previous research has often treated chronic pain patients homogenously, subsequent literature suggests that the specific nature of pain onset may in fact contribute to substantially different experiences in chronic pain and corresponding disability. Greenfield and colleagues (1992) carried out a study in which fibromyalgia patients were placed into one of two categories. Those patients whose clinical symptoms could be tied to a precipitating event such as trauma, surgery, or a particular medical illness were classified as having reactive fibromyalgia, and this group was found to experience higher levels of disability than fibromyalgia patients with insidious onset (Greenfield, Fitzcharles, & Esdaile, 1992; Turk & Okifuji, 1996). Another study found that among headache patients, those whose pain was posttraumatic more frequently experienced pain and had a

worse prognosis than did patients whose pain emerged insidiously (Turk & Okifugi, 1996). Such research highlights the importance of studying surgical patients with persistent pain as a unique group separate from their nonsurgical counterparts.

The AIS patient population undergoing spinal fusion surgery represents a valuable one in the research mission to better understand how children and adolescents may suffer from PPP. AIS is a condition defined by an abnormal lateral spine curvature in otherwise healthy individuals, with a typical age of onset of 10 years, a higher incidence among Caucasian females (Goldberg, Mayo, Poitras, & Hanley, 1994), and a 7:1 female to male ratio (Kleiber et al., 2007). Spinal curvature up to 10 degrees is considered normal with further curve progression unlikely (Kleiber et al., 2007). Though researchers have not pinpointed the specific cause of AIS, theories include hormonal and muscle imbalances and asymmetric growth, and 30% of AIS patients have a family history of the condition, thus giving rise to speculation of genetic predisposition (Scoliosis Research Society). Though not a verified measure, a genetic test known as the ScoliScoreTM has been utilized in young patients with mild curvature (below 25 degrees), in addition to clinical tests and x-ray images, to evaluate risk of curve progression to greater than 40 degrees (Scoliosis Research Society). Prevalence studies show that between 2 and 3% of children below the age of 16 exhibit idiopathic scoliosis with 10 degrees or less of curvature, while between 0.3 and 0.5% of children in that age range are estimated to have 20 degrees or more of curvature (Nachemson, Lonstein, & Weinstein, 1982; Weinstein, 1999). Though other forms of scoliosis exist such as congenital scoliosis, due to abnormal formation of ribs or spine, and neuromuscular scoliosis, due to nervous system

disorders such as spina bifida, cerebral palsy, and muscular dystrophy (A.D.A.M. Medical Encyclopedia), scoliosis of an idiopathic nature represents approximately 65% of all cases (United States Preventive Services Task Force, 2004).

AIS is the most common and deforming orthopedic condition from which children and adolescents suffer (LeMontagne, Hepworth, Cohen, & Salisbury, 2003), and given the most widely accepted definition of PPP as offered by Macrae and Davies (1999), wherein pain must emerge postoperatively, AIS is an appropriate condition to study, as chronic pain is not always present preoperatively (Scoliosis Research Society). Moreover, AIS patients are an appropriate focus for the present study, as despite their spinal curvature, the majority of these patients are otherwise healthy. In addition to the fact that pain does not frequently result from AIS, neurologic symptoms are also typically absent (Scoliosis Research Society). Furthermore, spinal curvature in AIS patients does not place added pressure on organs, and shortness of breath is not seen (Scoliosis Research Society). Focusing on AIS patients undergoing spinal fusion surgery allows researchers to more effectively focus in on postsurgical outcomes and to more clearly identify the exact timing of injury to the patient's body (Katz & Seltzer, 2009).

Spinal fusion surgery is indicated as a preventive measure for further spinal curvature and pulmonary dysfunction in late adulthood (Kleiber et al., 2007). The procedure, which depending on the location of curvature may be anterior and/or posterior, involves implanting a bone graft and placing hardware to stabilize the graft until fusion occurs (Kleiber et al., 2007). Spinal fusion surgery is identified as one of the most invasive orthopedic procedures performed in the pediatric surgical arena (Kotzer,

2000), with an average operating room time of five hours and typical length of hospital stay between five and six days (Kleiber et al., 2007). While spinal fusion surgery patients may generally resume regular activities within three to four weeks, often times, these patients cannot fully participate for three to six months postoperatively (Kotzer, 2000). Studies have been undertaken to examine the psychosocial correlates of recovery outcomes in this patient population. LaMontagne and colleagues (2004) examined the coping styles of spinal fusion surgery patients preoperatively and at nine months postoperatively and found that those patients with “vigilant coping strategies” toward distressing situations, versus those with “avoidant coping strategies,” had greater recovery outcomes, participating in more activities and performing more strongly academically. Older adolescents and patients with a greater internal locus of control were also found to have more favorable recovery outcomes (LaMontagne et al., 2004). Such findings support the importance of examining the associations of psychosocial factors in long-term pain and functioning outcomes of patients undergoing surgical treatment for AIS.

While research on the postoperative chronic pain phenomena of AIS patients undergoing spinal fusion surgery is largely lacking, it has been shown that these patients report high levels of pain in the acute postoperative phase, despite use of opioid treatments (Kotzer, 2000), consistent with findings that children experience clinically significant pain more commonly following orthopedic procedures than other types of surgery (Karling, Renstrom, & Ljungman, 2002). Nevertheless, scoliosis has been shown to be a risk factor for depression in adolescents, as self-esteem and life-satisfaction have

been found to be significantly higher among patients receiving surgical treatment for their spinal curvature as opposed to those patients who refrain from surgical intervention (Zhang et al., 2011).

In spite of perceived positive outcomes of spinal fusion surgery, long-term pain in this patient population remains a concern. Landman and colleagues (2011) showed that at one- and two-years follow-up, 68.8% and 64.4% respectively of spinal fusion surgical patients exhibiting preoperative pain experienced postoperative pain. These findings, in addition to existing knowledge of the complex biological and psychosocial interactions in the development of chronic pain, highlight the need to better understand why certain children experience clinically significant pain beyond the acute phase. Furthermore, as it has previously been shown that pain among the AIS patient population treated with spinal fusion surgery may in fact increase between two- and five-years postoperatively (Upasani et al., 2008), examining five-year outcomes represents a necessary avenue of scientific exploration.

OBJECTIVES

While PPP among adults has been studied extensively in recent years, the acute to chronic postsurgical pain transition has yet to be examined adequately among the pediatric surgical patient population. As over five million children undergo surgical procedures annually, and as 25% of adult patients reporting to chronic pain clinics identify surgery as the antecedent to their pain (Crombie, Davies, & Macrae, 1998), better understanding the factors associated with children exhibiting a heightened propensity to developing chronic pain postoperatively is critical. The purpose of the present study was to investigate the prevalence of PPP in AIS patients treated with spinal fusion surgery and to examine the factors associated with chronic postoperative pain and varying longitudinal pain trajectories in this patient population. It was hypothesized that in a substantial proportion of children presenting for spinal fusion surgery as treatment for AIS, pain would persist at one- and two-years post-surgery and potentially increase between two- and five-years post-surgery (Upasani et al., 2008). It was further hypothesized that individuals in trajectories in which pain persists postoperatively would report less favorable baseline mental health functioning and self-image as compared to those in trajectories in which patients experience no pain or in which pain diminishes longitudinally.

METHODS

Participation

Participants were patients from a large Northeast children's hospital who are enrolled in the Prospective Pediatric Scoliosis Study (PPSS), a multicenter study with a primary goal of assessing current practices in the surgical treatment of AIS. The PPSS began in 2003 with the following eligibility requirements: The participants must be at least eight years of age, have been diagnosed with thoracic scoliosis, lumbar scoliosis, and/or thoracolumbar scoliosis, and undergo posterior spinal fusion surgery. The patients are followed longitudinally—preoperatively and at one-, two-, and five-years postoperatively. The sample for the present study was extracted from a national database of all participating patients and analyzed retrospectively. The extracted sample included 459 patients who had completed preoperative measures, including 219 (48%) who completed follow-up measures at one- and two-years post-surgery and 77 (17%) who also completed measures at the five-year time point. As measures were completed at follow-up appointments or submitted via mail, failure to attend appointments and/or return measures are cited as reasons for the significant drop-off in participation from the completion of the measures preoperatively to one-, two-, and five-years post-surgery.

Measures

At each time point, patients completed the Scoliosis Research Society Questionnaire-30 (SRS-30) (Scoliosis Research Society), a measure assessing health-related quality-of-life in AIS patients treated with spinal fusion surgery. The SRS-30 is a combination of the Scoliosis Research Society Questionnaire-22 (SRS-22) and the

Scoliosis Research Society Questionnaire-24 (SRS-24), both of which have been determined to be reliable and valid measures (Asher et al., 2003; Rothenfluh et al., 2012). The SRS-30 is made up of 30 questions, including 23 questions to be answered by all patients and seven questions to be answered only by postoperative patients. Included in the questionnaire are four subscales: *pain*, *self-image*, *mental health*, and *activity*. Most questions have five choices with items scored from 1 to 5, where a higher score on each item and the higher total score for a given subscale indicate a better patient outcome. For instance, possible responses to questions range from “Severely” = 1 to “None” = 5 and “Very unhappy” = 1 to “Very happy” = 5.

Prior to analyzing the data, each of the four subscales was tested for internal consistency at each time point, where a larger Cronbach’s alpha (alpha) indicates stronger consistency among items within a given subscale.

Pain

As pain was the primary outcome variable in this study, subscales and individual items were examined. The following questions are included in the pain subscale:

- 1) “Which one of the following best describes the amount of pain you have experienced during the past 6 months?”
- 2) “Which one of the following best describes the amount of pain you have experienced over the last month?”
- 3) “Do you experience back pain when at rest?”
- 4) “Which of the following best describes your medication usage for your back?”

- 5) “In the last 3 months have you taken any sick days from work/school due to back pain, and if so, how many?”
- 6) “Has your back treatment [increased/not changed/decreased] your back pain?”

Internal consistencies for the pain subscale were as follows: preoperative $\alpha = 0.68$, one-year postoperative $\alpha = 0.79$, two-years postoperative $\alpha = 0.84$, and 5-years post-operative $\alpha = 0.87$.

Self-Image

The following questions are included in the self-image subscale:

- 1) “If you had to spend the rest of your life with your back shape as it is right now, how would you feel about it?”
- 2) “How do you look in clothes?”
- 3) “Which of the following best describes the appearance of your trunk; defined as the human body except for the head and extremities?”
- 4) “Has your treatment changed your confidence in personal relationships with others?”
- 5) “Do you feel attractive with your current back condition?”
- 6) “On a scale of 1 to 9, with 1 being very low and 9 being extremely high, how would you rate your self-image?”
- 7) “Has your treatment changed your self-image?”

Internal consistencies for the self-image subscale were as follows: preoperative $\alpha = 0.75$, one-year postoperative $\alpha = 0.71$, two-years postoperative $\alpha = 0.75$, and five-years postoperative $\alpha = 0.78$.

Mental Health

The following questions are included in the mental health subscale:

- 1) “During the past 6 months have you been a very nervous person?”
- 2) “In the past 6 months have you felt so down in the dumps that nothing could cheer you up?”
- 3) “Have you felt calm and peaceful during the past 6 months?”
- 4) “In the past 6 months have you felt down-hearted and blue?”
- 5) “Have you been a happy person during the past 6 months?”

Internal consistencies for the mental health subscale were as follows: preoperative alpha = 0.77, one-year postoperative alpha = 0.81, two-years postoperative alpha = 0.87, five-years postoperative alpha = 0.86.

Activity

The activity subscale includes questions about current levels of activity and financial issues related to the patient’s condition. As this subscale did not demonstrate acceptable internal consistency, it was not analyzed further.

Procedures for Analysis

The Institutional Review Board (IRB) approved secondary analysis of data extracted from the PPSS national database. All statistical analyses were carried out using SPSS Software Version 19 and SAS.

Descriptive statistics were conducted for all demographic and study variables. One-way analyses of variance (ANOVAs) were carried out to compare participants with preoperative data but without follow-up data and participants with both preoperative and

follow-up data. Frequencies were calculated for each item in the pain subscale to reflect the patient's pain experiences longitudinally. Pain variables were dichotomized to reflect patient experiences of pain and frequency of pain at rest. Pain responses were separated into one of two groups: either "moderate to severe pain" or "mild to no pain." Participant responses regarding frequency of pain at rest were also separated into one of two groups: either "often to very often experience pain at rest" or "rarely to never experience pain at rest."

For the purpose of analyzing longitudinal pain trajectories across the preoperative and postoperative time points, the SAS PROC TRAJ procedure (Jones, Nagin, & Roeder, 2001) was utilized. The PROC TRAJ procedure enables researchers to estimate a regression model for each discrete group within the overall population and therefore to provide insight into the different trajectory paths that individual participants follow across the multiple time points (Jones et al., 2001). The PROC TRAJ procedure generates fit estimates, which indicate the probability that a given patient belongs to a particular trajectory. An average probability of $\geq .70$ among members of a given trajectory group is recommended (Cote et al., 2002). In the PROC TRAJ procedure, model complexity and overall fit are determined partly on the Bayesian information criterion (BIC), which are negative values, where values closer to zero indicate a better fit (Jones et al., 2001). Using the PROC TRAJ procedure, even those individuals with missing data may be grouped into a trajectory path, as the procedure uses the existing values from each case to estimate a participant's timeline (Jones et al., 2001).

Once distinct trajectory groups were established using this procedure, one-way ANOVAs were carried out to compare groups for preoperative characteristics including age, pain, self-image, mental health and days of school/work missed. Post-hoc Least Significant Difference (LSD) tests were used to further compare mean results across the different trajectories. Specifically, these tests are used to identify where mean differences lie following an ANOVA that has yielded a significant result.

RESULTS

The mean age of enrollment in the present study was 14.28 years. Consistent with existing literature on AIS prevalence (Goldberg et al., 1994), the majority of the sample in the present study was female (79%) and Caucasian (83%). No significant differences in age, gender, race/ethnicity, or preoperative pain were found between those patients who completed follow-up data and those who only completed preoperative data. However, significant differences in preoperative pain were found between patients with follow-up data at one-year, two-years, and five-years post-surgery and those with follow-up data only at one-year and two-years post-surgery. Patients with five-year follow-up data reported significantly less pain preoperatively than patients without five-year follow-up data ($F(1, 219) = 6.17, p < .05$).

Prevalence of Pain

In the Past Six Months

In response to the question regarding pain experienced in the past 6 months, approximately 38% of participants reported moderate to severe pain preoperatively. At the one-year postoperative time point, approximately 18% of the participants reported moderate to severe pain in the past six months. At the two-year time point, approximately 17% of participants reported pain in the moderate to severe range. At five-years follow-up, approximately 20% of the 77 responding participants reported pain in the moderate to severe range. See Figure 2.

In the Past Month

Responding to the amount of pain experienced in the past month, around 36% of participants reported pain in the moderate to severe range preoperatively. At one-year post-surgery, approximately 13% of participants reported pain in the moderate to severe range. Approximately 17% of participants reported moderate to severe pain at the two-year time point. At five-years follow-up, approximately 20% of responding patients reported pain in the moderate to severe range. See Figure 2.

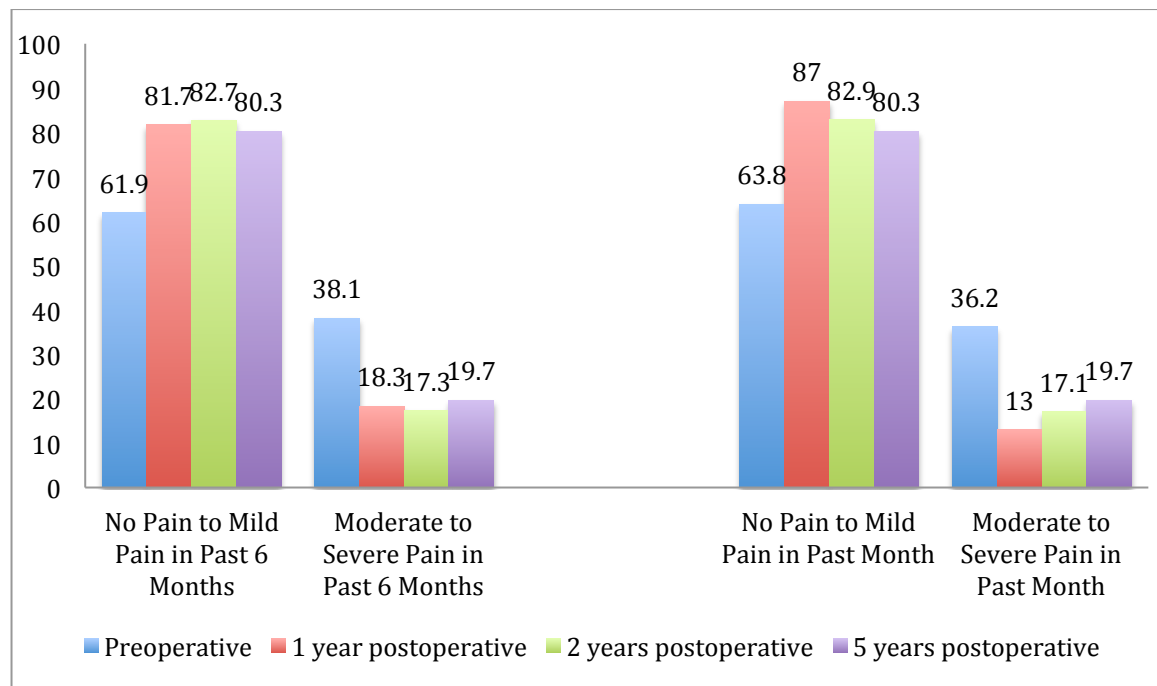


Figure 2: The prevalence of participants reporting pain “in the past 6 months” and “in the past year” at each of the four time points.

At Rest

Prior to surgery, around 43% of patients reported pain “often to very often” when at rest. Postoperatively, this number dropped substantially, with around 6% of patients

reporting pain “often to very often” at rest at one- and two-years follow-up and around 7% of patients reporting pain “often to very often” at five-years follow-up.

Medication Usage for Back

Across all time points, narcotics usage was low, with less than 1% of participants reporting their use of narcotics as “daily” and 1% of participants reporting their use of narcotics as “weekly or less.” Preoperatively, 3% of patients reported their use of non-narcotics as “daily.” Daily non-narcotic usage increased slightly postoperatively, with 3%, 4%, and 5% of patients respectively reporting “daily” usage of non-narcotics at the one-year, two-years, and five-years postoperative time points. “Weekly or less” usage of non-narcotics increased from 22% preoperatively to 28% at each of the postoperative time points.

Days Missed from Work/School Due to Back Pain

Preoperatively, 9% of patients reported one or more day of work/school missed in the past three months due to back pain. Postoperatively, the number of patients missing work/school increased slightly with 14%, 13%, and 12% respectively missing one or more days of school in the past three months at one-year, two-years, and five-years follow-up.

Pain Trajectories

The SAS PROC TRAJ procedure was used to generate between one and seven trajectory solutions for the purpose of determining which set of trajectories most appropriately and parsimoniously demonstrated the longitudinal pain experiences of the participants across each of the time points. Graphic model curves that illustrated the

different trajectory solutions were examined and judgment was used in selecting the most appropriate number of trajectories to analyze. Despite there being no statistical test to determine differences in BIC scores (Singer and Willett, 2003), BIC scores were calculated for all trajectory solutions other than the one-trajectory solution and were found to be similar (See Figure 3), thus offering no indication that any one of the trajectory solutions was superior to the others. Average probabilities among members of each trajectory group ranged from 0.69 (SD=.19) in the case of the “delayed pain” group to as high at 0.90 (SD=.15) for the “high pain” group, suggesting adequate to excellent average model fit for the five trajectories.

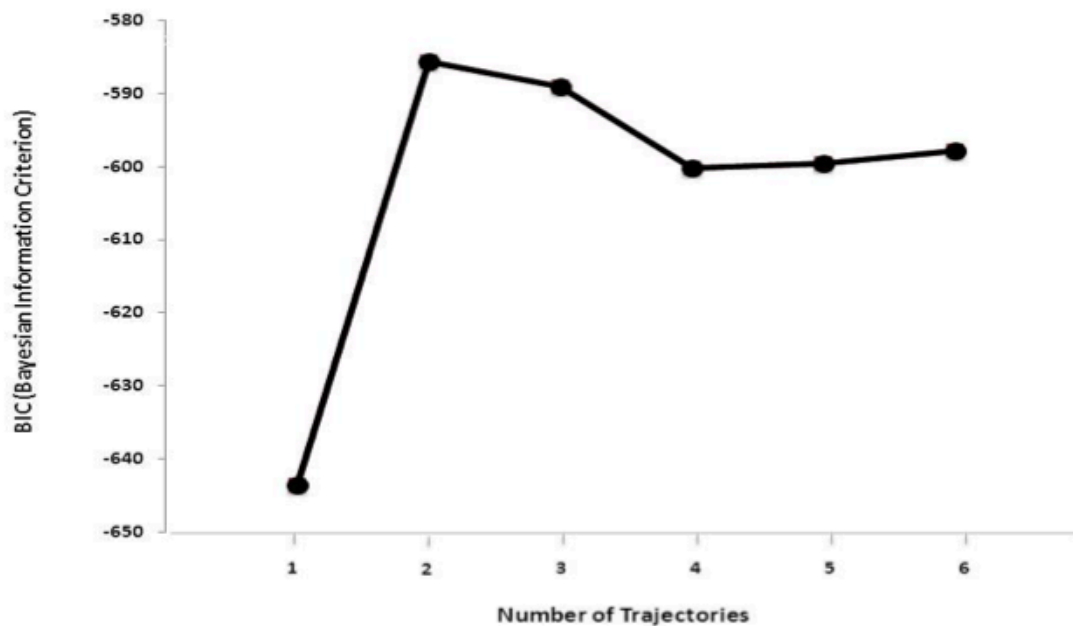


Figure 3: BIC scores for various pain trajectory solutions.

Ultimately, a five-trajectory solution was selected for analysis (See Figure 4), as each trajectory group appeared to be clinically distinct and relevant. When a larger number of trajectory groups were considered for analysis, understanding the clinical significance of each group proved difficult. When a smaller number of trajectory groups were considered for analysis, valuable information appeared to be lost, as participants who followed substantially different longitudinal paths preoperatively and postoperatively might have been inappropriately grouped together.

Each of the five trajectories was assessed and labeled based on the longitudinal pain experience of the patients belonging to the respective group. The five trajectory groups were classified as follows:

- 1) “*No pain*” group: This trajectory included patients who experienced little to no pain preoperatively and continued on this path with little pain at each of the three postoperative time points. 17% of patients were grouped in this trajectory (n=23).
- 2) “*Pain improvement*” group: This trajectory included patients who indicated moderate pain preoperatively and then reported little to no pain at each of the three postoperative time points. This was the most common trajectory with 44% of patients (n=123).
- 3) “*Short-term pain*” group: This trajectory included patients whose pain worsened from pre-surgery to one-year post-surgery and then reported lower pain at two-years follow-up and further improvements at five-years follow-up. 14% of patients were grouped in this trajectory (n=34).

- 4) “*Delayed pain*” group: This trajectory included patients who reported little pain prior to surgery and at one and two-years follow-up but then reported high levels of pain at five-years follow-up. 19% of patients were grouped in this trajectory (n=28).
- 5) “*High pain*” group: This trajectory included patients who reported moderate pain preoperatively and who, despite some improvements at one-year follow-up, ultimately went on to experience worsened pain at two-years follow-up and a further decline into the severe pain range at five-years follow-up. This was the least common trajectory with just 6% of patients (n=11).

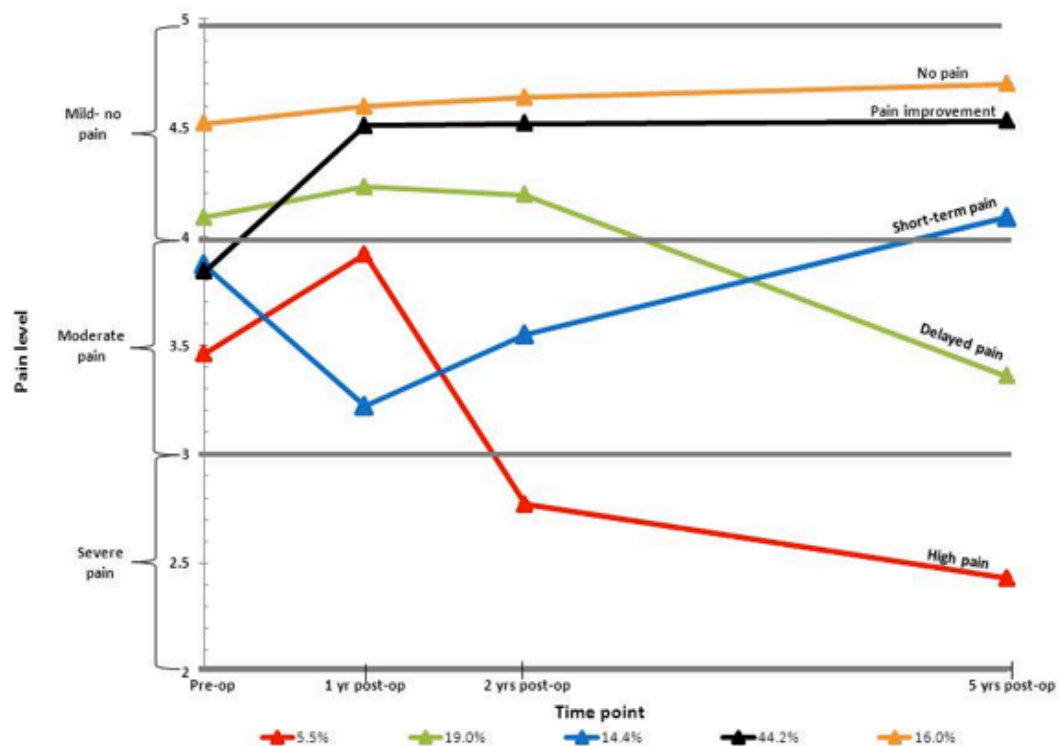


Figure 4: Graphic representation of the five-trajectory solution ultimately chosen for further analysis.

Table 1 shows the means levels of the baseline variables on which each of the trajectory groups were compared: age at enrollment, pain, self-image, mental health, and school or work missed. For each of those variables, significant differences were found between the different trajectory groups. Post-hoc LSD tests showed that the average age of enrollment for children in the “no pain” group was significantly lower than that of the “delayed pain” group (difference, -2.27, $p=.01$), the “pain improvement” group (difference, -1.99, $p=.01$), and the “short-term pain” group (difference, -2.14, $p=.004$). Preoperative pain among patients in the “high pain” group was significantly higher than among patients in the “no pain” group (difference, -1.3, $p=.000$) and the “delayed pain” group (difference, -.70, $p=.000$). Preoperative self-image was significantly higher in the “delayed pain” group than in the “pain improvement” group (difference, .42, $p=.03$). Mental health was also significantly better in the “delayed pain” group as compared to the “pain improvement” group (difference, .61, $p=.003$) and the “short-term pain” group (difference, .4, $p=.04$).

Table 1: Differences in baseline variables between pain trajectory groups.

<i>Variable</i>	Total (<i>n</i> =219) Mean (SD)	“No pain” (<i>n</i> =23) Mean (SD)	“Delayed pain” (<i>n</i> =28) Mean (SD)	“Pain improvement” (<i>n</i> =123) Mean (SD)	“Short -term pain” (<i>n</i> =34) Mean (SD)	“High pain” (<i>n</i> =11) Mean (SD)	<i>F</i> Ratio
Age at enrollment	14.28 (2.28)	12.48 (2.06) ^a	14.75 (1.96) ^b	14.47 (2.23) ^b	14.62 (2.40) ^b	13.64 (2.16) ^{a,b}	4.82 **
Preoperative pain	3.99 (.53)	4.81 (.20) ^a	4.21 (.47) ^d	3.86 (.37) ^{b,c}	3.86 (.50) ^c	3.50 (.77) ^e	30.9 **
Preoperative self-image	3.49 (.59)	3.67 (.56) ^a	3.81 (.40) ^a	3.40 (.58) ^b	3.35 (.68) ^b	3.76 (.63) ^{a,b}	4.02 **
Preoperative mental health	3.98 (.61)	4.06 (.52) ^{a,c}	4.35 (.34) ^c	3.95 (.66) ^{a,b}	3.74 (.54) ^b	3.95 (.71) ^{a,b,c}	4.33 **
Preoperative frequency of missed work/school days	.14 (.46)	0 (0) ^a	.04 (.19) ^a	.14 (.45) ^a	.18 (.52) ^a	.55 (.93) ^b	3.21 *

Note. Within rows, different superscripts indicate significant differences at $p < .05$; * $p < .05$; ** $p < .01$

DISCUSSION

While chronic pain has been studied widely among the adult and pediatric populations, and while PPP, in recent years, has become a focus of investigation among adult surgical populations, the study of the acute to chronic postsurgical pain transition in children and adolescents has been largely neglected. Considering the millions of children who undergo surgical procedures in the United States annually and the many adult chronic pain patients who identify surgery as the antecedent for their pain, better understanding the incidence of PPP in the pediatric patient population and its biopsychosocial correlates is imminently important.

The objectives of the present study were to examine the incidence of PPP among children and adolescents who have undergone spinal fusion surgery as treatment for AIS as well as to explore the longitudinal pain trajectories in this patient population across four time points—prior to surgery and at one-year, two-years, and five-years post-surgery. AIS was selected as a valuable sample in which to study surgical pain experiences, as chronic pain is not typically present preoperatively, thus allowing researchers to more effectively examine postoperative pain outcomes. It was hypothesized that a substantial proportion of patients would develop pain persisting at one- and two-years post-surgery and that a subset of these patients would report worsened pain at five-years follow-up.

It should be noted that based on the most widely accepted definition of PPP as posited by Macrae and Davies (1999), a patient's pain must emerge postoperatively and must not have resulted from any other underlying condition distinct from the surgery

itself. Therefore, the postoperative pain experienced by many of the patients in the present study sample may not strictly abide by that definition, as preoperative pain was ultimately found to be more of a problem than expected, based on the assumption that pain would not be prevalent among AIS patients prior to spinal fusion surgery. Moderate to severe levels of pain were reported preoperatively in the “pain improvement” group, in the “short-term pain” group, and in the “high pain” group. Thus, the results of this study suggest that pain in the preoperative AIS population might be more of a concern than previously imagined. While overall, the proportion of patients reporting pain in the past six months and past month fell substantially between the preoperative time point and the follow-up time points, pain was still persistent in a significant percentage of patients at one- and two-years follow-up, with a slight increase in pain prevalence at five-years follow-up.

We were able to obtain a clearer illustration of the participants’ distinct longitudinal pain experiences through use of the SAS PROC TRAJ procedure. Through this method, participants were grouped into one of five longitudinal paths describing their pain across the preoperative and postoperative time points. These included, a “no pain” group, a “pain improvement” group, a “short-term pain” group, a “delayed pain” group, and a “high pain” group. To predict risk and protective factors associated with different pain trajectories, the five groups were compared for baseline characteristics including age at the time of surgery, preoperative pain, self-image, mental health, and days missed of school/work. Consistent with literature on the role of age in chronic pain experiences (Evans et al., 2010), age was found to be protective against pain preoperatively and at

each time point postoperatively, with members of the “no pain” group being significantly younger at time of surgery than members of the “pain improvement” group, the “short-term pain” group, and the “delayed pain” group. Therefore, investigating how hormonal changes and developmental milestones associated with altered psychological stress and/or social experiences are involved in the initiation and persistence of postoperative pain may be valuable.

It was hypothesized that patients in persistent pain trajectories would report worse self-image and mental health functioning. The findings of this study partially substantiated this hypothesis:

Of particular interest were our findings on baseline differences in self-image and mental health across the “delayed pain” group and the “pain improvement” group. Contrary to what one might logically predict, lower self-image prior to surgery was actually associated with more favorable pain outcomes. Unique to the present study, as opposed to a longitudinal study of chronic pain in a non-surgical patient population, is the fact that the patients in this study have undergone an invasive procedure that may have substantially altered their physical appearance. It is possible that if a patient’s spinal curvature has contributed substantially to his or her lowered self-image, then such a patient might have the most to gain aesthetically through spinal fusion surgery. Postoperatively, these patients, who prior to surgery have lower self-image scores, might feel such a sense of improvement in appearance that those positive feelings might contribute to milder pain outcomes or higher pain tolerance. Alternatively, those patients who preoperatively exhibit higher self-image scores might have less to gain aesthetically

through spinal fusion surgery, so it is conceivable that postoperatively, these patients experience a less dramatic sense of physical improvement, fewer positive feelings associated with their spinal correction, and therefore a worse degree of pain or lower pain tolerance.

Preoperatively, the “delayed pain” group was also found to exhibit better mental health functioning than both the “pain improvement” group and the “short term” pain group. Thus, better mental health functioning was found to be protective against pain preoperatively and at one- and two-years follow-up but not at five-years follow-up. One consideration is that the SRS-30 presents too general a subscale to effectively assess mental health functioning. While the subscale asks questions relating to a patient’s recent feelings of nervousness, peacefulness, and sadness, perhaps having the patient answer questions that more narrowly assess those feelings, especially as those feelings relate to their pain and/or operation, would be a more effective means of accurately illustrating their mental health functioning. Specifically, pain acceptance, fear of pain, and pain catastrophizing are regarded in literature as important factors in children’s experiences with pain and associated disabilities (Simons, Sieberg, & Kaczynski, 2010). The mental health subscale of the SRS-30 also neglects to ask questions regarding the patient’s social relationships and interactions—important avenues for future research considering the extensive findings concerning the effects of parent distress and parent behavioral responses on pain and functioning outcomes in children (Sieberg et al., 2011).

Functional disability is another important area of consideration, having previously been demonstrated to be intimately associated with children’s chronic pain experiences

and social encounters (Hunfeld et al., 2001; Simons et al., 2008; Sieberg et al., 2011). Unfortunately, functioning could not be appropriately assessed among the patients in the present study, as the activity subscale did not demonstrate acceptable internal consistency. Since the pain subscale includes a question regarding the number of days of work/school missed in the past three months due to back pain, that question was analyzed independently, as absence from school and/or work may be regarded as an effective representation of how pain impacts daily functioning. Overall, this sample did not indicate much school or work missed in the past three months due to pain across the preoperative and postoperative time points. This is contrary to existing literature in the non-surgical chronic pain population, where heightened pain frequency and intensity have been shown to be associated with worsened psychological and physical functioning (Hunfeld et al., 2001). Future research endeavors could benefit by using a measure such as the Functional Disability Inventory (FDI) (Walker & Green, 1991), which has been demonstrated to be reliable and valid in assessing functioning in pediatric chronic pain patients (Claar & Walker, 2006).

Interestingly, the patients in the “high pain” trajectory, who exhibited moderate to severe pain preoperatively and at two- and five-years postoperatively did not differ significantly from patients in the other four trajectories on baseline self-image or mental health. While this may be attributed to the SRS-30 subscales, which include questions that are arguably too general to fully capture the self-image and mental health statuses of the patients, it is also possible that the pain outcomes among patients in the “high pain” group are more heavily influenced by biological factors than by psychosocial factors.

This consideration underscores the need to further explore biological predictors of chronic pain in children and adolescents. In light of scientific findings on the heritable nature of pain sensation variability (Norbury et al., 2007), chronic pain conditions (Schanberg et al., 2001), and impairments in endogenous opioid analgesia (Bruehl & Chung, 2006), biological factors must be examined for how they play a direct role in the pediatric acute to chronic pain transition and how they interact with psychological stressors and social variables to influence varying pain trajectories in children. Furthermore, quantitative sensory testing (QST), a technique that has been utilized in recent years to identify somatosensory phenotypes associated with chronic pain susceptibility (Rolke et al., 2006), should be implemented into future research methodologies for studies of the acute to chronic postsurgical pain transition in children.

The findings of this study confirm our hypothesis that a substantial percentage of patients undergoing spinal fusion surgery as treatment for AIS would experience persistent pain postoperatively. More surprising was our finding that this patient population actually exhibited a high prevalence of pain preoperatively. It would be valuable to further explore the high incidence of preoperative pain among this sample, perhaps as compared to a healthy control arm, as chronic pain is not typically associated with an AIS diagnosis (Scoliosis Research Society).

Future Directions

In line with our assertion that improved methodologies should be implemented to better assess the incidence of PPP among AIS patients undergoing spinal fusion surgery, to better capture the mental health statuses of these patients, and to study the biological

factors associated with chronic pain in pediatric surgical patients, we have obtained approval and have begun recruitment for a prospective longitudinal study examining the biopsychosocial predictors of PPP in this patient population. The target sample size is 300 patients over the next three years. As opposed to the present study in which patients only completed the SRS-30, the prospective study involves both children and their parents completing various measures that have been shown to be valid and reliable in assessing such psychosocial variables as pain catastrophizing, fear of pain, acceptance of pain, and quality of life. Patients and their parents complete these measures preoperatively and at one-month, six-months, and 12-months postoperatively. It is our belief that by administering more reliable and extensive psychosocial measures, we will better capture the psychological and social experiences of these patients and gain greater insight into how parent factors interact with child pain and functioning. This prospective study is also more involved in its investigation into biological components of chronic pain. Somatosensory phenotypes are being compared through QST sessions that patients undergo preoperatively and at six months postoperatively. Moreover, 5 ml of blood are being drawn from each consenting patient preoperatively to be stored for later genetic analysis. It is our goal that through better understanding the complex phenomena involved in chronic pain among pediatric surgical patients, that more effective means of psychosocial intervention and pain management might be implemented to influence more favorable outcomes.

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Vita

The diagram consists of 10 horizontal bars of varying lengths and positions, arranged in a staggered fashion. The bars are arranged in a sequence that suggests a timeline or a sequence of events. The bars are arranged in a staggered fashion, with some starting and ending at different points along a horizontal axis. The bars are arranged in a sequence that suggests a timeline or a sequence of events.

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