Pediatric Pain Screening Identifies Youth at Risk of Chronic Pain in Sickle Cell Disease

Soumitri Sil, PhD[1,2], **Lindsey L. Cohen, PhD**[2,3], and **Carlton Dampier, MD**[1,2]

[1.]Aflac Cancer and Blood Disorders Center, Department of Pediatrics, Emory University School of Medicine

[2.]Children's Healthcare of Atlanta

[3.]Georgia State University, Department of Psychology

Abstract

Background: This study aimed to evaluate the preliminary validation and application of a pain screening tool to identify biopsychosocial risk factors for chronic pain in pediatric sickle cell disease (SCD) and classify youth with SCD into prognostic risk groups.

Method: Youth presenting to a pediatric SCD clinic completed the Pediatric Pain Screening Tool (PPST), a brief 9-item self-report questionnaire developed for rapid identification of risk in youth with pain complaints. Youth also completed a battery of standardized patient-reported outcomes, including pain characteristics, pain burden, functional disability, pain interference, depressive symptoms, pain catastrophizing, and fear of pain. Healthcare utilization was extracted from medical chart review.

Results: 73 8–18-year-olds (94% Black, 57% female) with SCD participated. The PPST demonstrated discriminant validity that ranged from fair to excellent (AUCs=0.74–0.93, $ps < .001$) for identifying significant pain frequency, disability, pain interference, and psychosocial distress. Receiver operating characteristic curve analyses indicated that previously established cutoff scores were appropriate for the SCD sample. Participants were classified into Low Risk (28.8%), Medium Risk (38.4%), and High Risk (32.9%) groups with significant group differences across measures, $F(18, 116) = 6.67$, $p < .001$. The High Risk group reported significantly higher pain intensity, pain frequency, pain burden, functional disability, pain interference, and depressive symptoms relative to both Low and Medium Risk groups ($ps<.005$).

Corresponding Author: Soumitri Sil, Ph.D., Emory University School of Medicine, Children's Healthcare of Atlanta, 2015 Uppergate Drive, Rm 426H, Atlanta, GA 30322, Phone: (404) 727-2712, Fax: (404) 727-4455, Soumitri.Sil@emory.edu.

Conclusions: The High Risk group demonstrated a pain and psychosocial profile consistent with chronic SCD pain. The PPST may be useful for efficiently identifying youth with chronic SCD pain or those at risk of poor outcomes.

Keywords

pediatric; sickle cell disease; chronic pain; screening; biopsychosocial; risk factors

As children with sickle cell disease (SCD) age into adolescence, pain frequency and severity increase along with the use of opioids[1–3]. There is increasing awareness that chronic pain is part of the pain experience for many adolescents with SCD[4]. The Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks – American Pain Society Pain Taxonomy (AAPT) identified core diagnostic criteria for chronic SCD pain, including ongoing pain present on most days over the past 6 months[5]. Although further validation is needed, the chronic SCD pain definition suggests the pain frequency characteristic of "most days" corresponds to 15 pain days per month and pain duration of at least 6 months. The AAPT also recommends classifying chronic pain along dimensions of psychological consequences and risk factors. Approximately 20% of children and adolescents report chronic pain consistent with AAPT criteria[4]. Common psychosocial risk factors and consequences of chronic SCD pain in youth include functional impairment, frequent school absences, elevated depressive symptoms, high levels of catastrophic thinking, and twice the number of inpatient admissions for pain relative to patients with SCD without chronic pain[4,6], which is consistent with other pediatric chronic pain conditions[7–9]. Thus, there is a pressing need to identify youth with SCD who are at risk for adverse outcomes to guide targeted treatments.

The treatment of chronic SCD pain remains challenging given the likely complex integration of vaso-occlusion and peripheral and central sensitization that is further complicated by biopsychosocial determinants[10]. The mechanisms that contribute to the transition from acute to chronic pain in SCD are not well-understood. Nonetheless, early identification of youth who may be at risk of developing chronic SCD pain is needed to help disrupt the onset and prevent the maintenance and exacerbation of chronic pain and its consequences. To date, there is no well-developed pain-related screening tool available to help identify youth with chronic pain in SCD. The Pediatric Pain Screening Tool (PPST) was recently adapted and validated in large samples of youth with mixed pain complaints (primarily musculoskeletal pain) as well as headaches[11,12]. Cutoff scores for the PPST were derived for grouping patients into categories to determine risk severity and allocation of treatment needs: low-risk (few prognostic risk factors), medium-risk (moderately unfavorable prognosis, high number of physical and low number of psychosocial risk factors), and high-risk (unfavorable prognosis, high levels of physical and psychosocial risk factors). Given the overlap in biopsychosocial factors (pain intensity, pain interference, depressive and anxiety symptoms) that can predict risk of poor outcomes in youth with different pain conditions including SCD[13], it is important to examine the utility of a brief screening tool in a sample of youth with SCD pain.

The primary aim evaluated the preliminary validation of the PPST compared to a standardized battery of well-validated patient-reported outcomes in a sample of youth with SCD. We expected the PPST would adequately discriminate patients with clinically significant levels (i.e., reference standard cases) on standardized pain and psychosocial measures from patients whose scores fell within the range that is not clinically significant (i.e., non-cases). Standardized measures included pain frequency, pain duration, functional disability, pain interference, healthcare utilization, depression, pain catastrophizing, and fear of pain. Next, we examined whether receiver operating characteristic (ROC) curve-derived cutoff score for the PPST in SCD was similar to the cutoff score derived from mixed chronic pain and headache samples used in previous validation studies. It was hypothesized that youth with SCD identified as "high risk" on the PPST would have the most impaired scores on pain characteristics (intensity, frequency, duration) and biopsychosocial risk factors (functional disability, pain interference, healthcare utilization, depressive symptoms, pain catastrophizing, fear of pain) consistent with a chronic pain profile.

Method

Recruitment

Participants were children and adolescents presenting to outpatient comprehensive SCD clinics at three campus locations of a tertiary care children's hospital over 14 months. Youth were eligible if they had SCD (any genotype), aged 8 to 18 years, and English-speaking. Patients receiving active treatment with hydroxyurea or transfusion for pain also were eligible for inclusion. Exclusion criteria included significant documented cognitive or developmental disabilities, chronic transfusions indicated for central nervous system complications (e.g., stroke), or comorbid medical condition in which pain is common (e.g., rheumatological or gastrointestinal conditions).

Study Procedures

Institutional Review Board approval was obtained prior to study initiation. Potentially eligible patients and parents were introduced to the study, and a trained research coordinator assessed eligibility and provided greater detail during clinic visits. Parents and youth provided written informed consent and assent. Patients completed web-based or pencil-and-paper measures while waiting for their provider. Families who previously expressed interest in research were contacted in clinic or by phone. Patients recruited by phone provided verbal consent and assent and either completed web-based or paper-and-pencil measures at home. Patients received a monetary incentive for participation time (about 30 minutes for survey completion).

Measures

Demographics—Detailed demographic and background information, including patient age, race, sex, annual family income, and common SCD treatment were collected from parents.

Pediatric Pain Screening Tool—The PPST is a 9-item self-report measure developed and validated among youth aged 8–18 with mixed pain complaints[11] and headaches[12]. Items

1 through 8 are answered dichotomously (no=0, yes=1), and item 9 is rated from "not at all" to "a whole lot" referencing the past 2 weeks. The ratings "a lot" and "a whole lot" are scored as 1, whereas ratings "not at all", "a little", and "some" are scored as 0. Total scores (range 0–9) include two subscales: physical (range 0–4) and psychosocial (range 0–5). In samples of youth with mixed pain complaints and headaches, cutoff scores for risk severity were: Low Risk (Total Score 2); Medium Risk (Total Score 3 and Psychosocial subscale 2); and High Risk (Total Score 3 and Psychosocial subscale 3).

Pain characteristics—Patients reported their average pain intensity over the last two weeks using a numeric rating scale (0 = no pain to 10 = worst possible pain). Patients reported the number of days they had pain in the past month (0–31 days), and how long (i.e., duration) they experienced the current level of pain frequency on a 5-point Likert rating (1=only this month to 5 = over 1 year)[4]. Per AAPT criteria, chronic SCD pain was defined as pain frequency 15 days per month with duration 6 months[5].

Sickle Cell Pain Burden—The Sickle Cell Pain Burden Interview (SCPBI) is a 7-item self-report of pain burden in the past month (0 = none, 1 = a few, 2 = some, 3 = many, 4 = every)[3]. Higher total scores (0–28) indicate severe pain burden. Clinical cutoff scores are not yet established. Therefore, item 1 "How many days have you had any pain [in the last month]?" was used to further evaluate pain frequency. Total scores were used in analysis to compare differences among PPST risk groups. Internal reliability for this study sample was 0.88.

Functional Disability—The Functional Disability Inventory (FDI) is a well-validated 15-item self-report of perceived difficulty performing daily activities across settings[14]. Items are rated from 0 (no trouble) to 4 (impossible) and totaled (range 0–60). Established clinical reference points are 0–12 (no/minimal disability), 13–29 (moderate disability), and 30–60 (severe disability)[15]. The FDI has high internal consistency, moderate to high test-retest reliability, and good predictive validity[14,16]. Internal reliability for this study sample was 0.96.

Pain Interference—The PROMIS Pediatric Pain Interference Short Form is a well-validated 8-item self-report of pain-related difficulties in the past 7 days[17]. Total scores (0–32) are transformed into T-scores. Higher T-scores indicate greater pain interference. Internal consistency for the sample was 0.96.

Depressive Symptoms—The Children's Depression Inventory-2 (CDI-2) is a well-validated 24-item self-report of depressive symptoms in the past two weeks[18] frequently used in pediatric pain research[19–22]. Total scores (0–54) are transformed into T-scores based on patient age and sex. Higher T-scores indicate greater symptom severity. Study coordinators immediately reviewed CDI results and informed a licensed psychologist of reports of suicidality. A risk assessment and safety plan were devised and mental health service referrals were provided, as appropriate. Internal reliability for the current sample was 0.90.

Pain Catastrophizing—The Pain Catastrophizing Scale – Child (PCS-C) is a well-validated 13-item questionnaire on thoughts and feelings about pain[23,24] commonly used in pediatric pain[24–26]. Items are rated from 0 (mildly) to 4 (extremely). Higher total scores (0–52) reflect greater catastrophic thinking about pain. Established clinical reference points include: low (0–14), moderate (15–25), and high (26)[25]. Internal reliability for the current sample was 0.95.

Fear of Pain—The Fear of Pain Questionnaire – Child (FOPQ-C) is a validated 24-item self-report of pain-related fear and avoidance[27]. Items are rated from 0 (Strongly Disagree) to 4 (Strongly Agree). Higher total scores (0–96) indicate higher fear. Internal consistency was 0.96.

Healthcare Utilization—Electronic medical record data were reviewed to gather the number of inpatient hospitalizations (admissions) and emergency department (ED) visits related to SCD pain within the last 12 months. Three or more admissions or 3 ED visits within the past 1 year were considered clinically significant[28–30].

Statistical Analyses

Data were analyzed using SPSS version 23. ROC curve analysis was used to evaluate the potential utility of the PPST to detect diagnostically or clinically significant levels of risk or disorder and develop cutoff scores to allocate patients into a risk group[31]. Utility was determined by the PPST's ability to be both sensitive and specific to detecting risk, as determined by the area under the curve (AUC) metric.

Discriminant Validity—ROC curves calculated the AUC for the PPST total score and psychosocial subscale score by comparing scores against reference standard cases, defined as patients met criteria for clinically significant symptoms based on pre-existing, established cutoffs for each measure. Each standardized measure was dichotomized based on established cutoffs to determine "cases" and "non-cases." Case or non-case was determined for each measure independently. Established reference standard cases were defined as: Pain frequency 15 days/month[5] or SCPBI item 1 3 (i.e., "many" or "every" days/month); Pain duration 6 months[5]; FDI 13[15]; Pain Interference T-Score 65[32]; CDI-2 T-score 65[33]; PCS-C 26[25]; FOPQ-C 51[27]; Admissions 3[30]; or ED visits 3[28]. Responses that did not meet the established cutoff for a measure were categorized as non-cases for that measure. PPST total and psychosocial subscale scores were compared to all measures. Consistent with previous work[11,12], cases reflective of "psychosocial distress" also were classified based on patients who were cases on two or more of the psychosocial measures (i.e., depression, catastrophizing, and fear of pain). Strength of discrimination criteria of the AUC was classified based on the following standards: poor (<0.70), fair (0.70–0.79), good (0.80–0.89), and excellent discrimination (0.90)[31].

Validating High-Risk Cutoff Scores—PPST cutoff scores were previously recommended and validated using pediatric samples of musculoskeletal pain and headaches[11,12]. First, ROC curves for PPST total scores were examined against reference standard cases of disability. Classification into the high-risk group is primarily driven by

psychosocial factors. Therefore, ROC curve analysis examined the PPST psychosocial subscale score against cases for psychosocial distress to compare the data-driven cutoff for the SCD sample with the established cutoff score. Sensitivity was considered more important than specificity to support the goal of the PPST as a screener to avoid missing cases that truly have chronic SCD pain[31].

Concurrent Validity—Chi-square and multivariate analysis of variances (MANOVA) examined differences across the PPST risk groups based on frequency of cases and continuous scores on pain and psychosocial measures.

Results

Recruitment

Of the 124 eligible participants approached for the study, 93 provided consent (75% enrollment rate). Most patients who did not consent (n=26, 21%) expressed interest in the study but were unable to enroll due to time constraints (e.g., arrived late to clinic). Only 5 families (4%) refused to participate. Of the 93 who consented, 73 patients completed study procedures (78.5% participation rate). Primary barriers to participation were completing and returning surveys after completing verbal consent. There was no significant difference in child age or sex between those who completed participation and those who consented but did not complete study procedures.

Participants

Patients were on average 14.3 years old ($SD = 2.61$, range 8–18). Detailed sample characteristics are presented in Table I. Patients reported mild average pain intensity of 3.38 ($SD = 2.93$, range 0–10) with an average of 8.61 pain days ($SD = 9.41$, range 0–31) in the past month. There were no significant differences in patient or parent demographics by campus or recruitment method (clinic vs. phone).

PPST Item Endorsement

Descriptive statistics of measures revealed skewness and kurtosis within the limits of normal distribution. PPST total scores averaged 4.15 ($SD = 2.65$) with full possible range (0–9). Frequency of PPST item endorsement is presented along with the previous validation pain samples[11,12] to support comparison across conditions in Table II. In the SCD sample, "My pain is in more than one body part" was the most frequently endorsed item whereas "It is not really safe for me to be physically active" was the least frequently endorsed item. For the validation samples, "How much has pain been a problem in the last 2 weeks" and "It is difficult for me to be at school all day" were most frequently endorsed for mixed pain and headache samples, respectively. In contrast, "I feel that my pain is terrible, and it is never going to get any better" and "It is not really safe for me to be physically active" were least frequently endorsed by mixed pain and headache samples, respectively.

Discriminant Validity

The AUC for the PPST total score significantly discriminated cases from non-cases for most measures (AUCs = 0.74–0.93, ps < .001), indicative of fair to excellent discrimination.

Primary exceptions included poor discrimination for ED visits (AUC=.69, $p<.05$) and non-significant discrimination for pain duration (AUC=0.63, $p=.06$, see Table III). The AUC for the PPST psychosocial subscale revealed fair to good discrimination of cases from non-cases for most measures (AUCs = 0.72–0.86, $ps < .001$). The PPST psychosocial subscale demonstrated poor discrimination for pain duration and ED visits (AUCs = 0.65–0.67, $ps < .05$).

Validating High-Risk Cutoff Score

ROC curve analyses for the PPST total score and psychosocial subscale against cases for disability and psychosocial distress are illustrated in Figure 1. Comparable to previous validation studies, a PPST total score 5 was the best predictor of cases of moderate to severe functional disability. A psychosocial subscale score 3 was the best concurrent predictor of cases of psychosocial distress. These two cutoff scores are similar to previously established PPST cutoff scores in mixed pain and headache samples. Therefore, the following cutoff criteria were used based on previously established values: Low Risk (Total Score 2); Medium Risk (Total Score 3 and Psychosocial subscale 2); and High Risk (Total Score 3 and Psychosocial subscale 3). For the current sample, 28.8% were classified as Low Risk, 38.4% were Medium Risk, and 32.9% were classified as High Risk.

Concurrent Validity

The percentages of patients meeting clinically significant or elevated levels of pain and psychosocial measures across the 3 PPST risk groups were examined (see Table IV). As expected, a low percentage of cases meeting clinically significant levels on standard measures (0–7%) fell into the Low Risk group, a moderate percentage of cases (24–45%) across measures were classified as Medium Risk, and the largest percentage of cases (48–71%) across measures were classified into High Risk. Consistent with discriminant validity analyses, PPST risk groups did not significantly differ in the distribution of cases meeting clinically significant levels for pain duration or ED visits and thereby excluded from further analysis.

MANOVA analysis examining pain intensity, pain frequency, pain burden, disability, pain interference, pain admissions, depressive symptoms, pain catastrophizing, and pain-related fear as continuous variables revealed significant PPST risk group differences across measures (Wilks' $\lambda = 0.24$, $F(18, 116) = 6.67$, $p < .001$, see Table V). Post-hoc analysis with Bonferroni correction ($p < .005$) revealed the High Risk group reported significantly higher pain intensity, pain frequency, pain burden, functional disability, pain interference, and depressive symptoms relative to both Low and Medium Risk groups. The High Risk group had significantly more admissions, higher pain catastrophizing and fear of pain compared to the Low Risk group. The Medium Risk group reported significantly higher levels of pain catastrophizing and fear of pain relative to Low Risk, but no significant differences emerged between the Medium and High Risk group on these two psychosocial measures. One-way ANOVA and chi-square analyses revealed no significant differences between PPST Risk Groups by demographic characteristics (i.e., child age, sex, annual family income, hemoglobin type, or treatment with hydroxyurea or chronic transfusions; all p's > .05).

Discussion

There is preliminary evidence that the PPST may be a valid and useful screening tool to identify youth at risk for chronic SCD pain who also demonstrate a psychosocial profile consistent with chronic pain in SCD[4] and other pain conditions[7–9]. The PPST performed well in identifying prognostic factors commonly associated with adverse outcomes among a sample of youth with SCD and classified pediatric patients with SCD into risk groups that may efficiently inform treatment decision-making.

The PPST adequately identified patients who met clinically significant levels of pain frequency, functional disability, pain interference, inpatient admissions, depressive symptoms, pain catastrophizing, and pain-related fear. The data-derived cutoff score for the PPST "high risk" classification was both sensitive and specific for identifying youth with elevated psychosocial distress and was comparable to the cutoff score resulting from two prior validation samples of pediatric musculoskeletal pain[11] and headaches[17]. Therefore, previous recommendations for the PPST cutoff scores for classifying patients into risk groups may be meaningfully applied to youth with SCD. Use of a single, universal pain screening tool (rather than multiple disease-specific measures) offers several potential benefits, including ease of comparison and interpretation across chronic pain conditions, generalization of findings that advance the field of pediatric SCD and chronic pain, and implementation into busy clinical practice.

As expected, the PPST performed well on discriminating patients with high pain frequency. The High Risk group reported an average of 15.5 pain days per month, consistent with the AAPT chronic SCD pain diagnostic criteria (i.e., pain on most days [15] per month)[5]. However, the PPST did not adequately discriminate cases of pain duration (i.e., pain frequency lasting 6 months). Study findings indicate that pain duration is relatively stable across varying pain frequency, with up to 60% of youth in each risk group reporting pain duration of over 1 year. The PPST was developed and originally administered in pain clinics where typical referrals are patients with chronic pain; thus, the screening tool may not have been designed to capture pain duration as a diagnostic criterion or risk factor for poor prognostic outcomes. Although pain duration is a key component used to distinguish chronic from episodic SCD pain, the larger chronic pain literature suggests that how long a patient has experienced chronic pain has no significant or reliable relation with pain or functional outcomes[34]. Therefore, pain duration may not be critical for identifying youth at risk for poor functional outcomes but remains important for diagnosing chronic SCD pain.

The clinical utility and applicability of the PPST as a brief screening tool in pediatric SCD is promising. The screener, which takes 1–2 minutes to complete, may offer a brief overview that is consistent with a more detailed battery of well-established, standardized patient-reported outcome measures that can take up to 30 minutes to complete to identify psychosocial risk factors indicative of poor prognostic outcomes. Use of a single screening tool may offer improved time efficiency and reduce patient burden in completing patient-reported outcomes while offering clinically useful data to guide further assessment and treatment decision-making. Furthermore, brief, routine screening offers a key opportunity for risk stratification that can help inform a stepped care model for allocating treatment and

resources based on patient need. For example, youth in the Low Risk group may be responsive to medication and standard care that integrates education about SCD self-management whereas the Medium Risk group may require targeted education about the biopsychosocial impact on pain and introduction to coping skills to facilitate improved functioning. Youth in the High Risk group may require more intensive, interdisciplinary treatment that combines medical care; psychological services such as cognitive-behavioral therapy; physical therapy; and integrative treatments such as acupuncture, yoga, or tai-chi[35]. Therefore, brief and routine screening can allow for early identification of youth experiencing SCD pain and co-morbid psychosocial risks and may facilitate early, targeted intervention to help improve pain and functioning.

Focused attention on the Medium Risk group may help identify youth transitioning from acute to chronic pain. The biopsychosocial model of pain describes pain and disability as a multidimensional and dynamic bi-directional interaction among physiological, psychological, and social factors resulting in chronic pain[13]. Youth in the Medium Risk group report subclinical levels of many functional and psychosocial factors commonly associated with chronic pain, including mild functional disability, depressive symptoms, pain catastrophizing, and pain-related fear. These elevated psychosocial factors combined with physiological changes can play essential roles in the transition to chronic SCD pain. Thus, the PPST may facilitate identification of youth in need of closer monitoring and early intervention to prevent the development of chronic SCD pain.

The interpretation of study findings should be considered within the context of a few limitations. The cross-sectional study design, convenience sample, and modest sample size limit the ability to examine the predictive validity of the screening tool on long-term pain and biopsychosocial outcomes. Additional validation of the PPST with a larger representative sample is needed to further support the validation of the screening tool among youth with SCD, which may support future studies in the development of a diagnostic measure for chronic SCD pain. Healthcare utilization data may be under-represented if families sought emergent care from medical settings outside of our healthcare system and may account for PPST scores being invariant by ED visits. Future validation studies may consider collecting additional reports of healthcare use, opioid consumption, amending or adding an item to capture pain duration for diagnostic benefit, and exploring the development of parent proxy report.

Despite these limitations, study findings provide preliminary evidence that the PPST can efficiently and effectively identify modifiable biopsychosocial factors that classify youth based on risk for poor pain and functional outcomes. The PPST may be a useful tool to identify youth who are at risk of transitioning from acute to chronic SCD pain as well as identify youth who have chronic pain and present with a biopsychosocial profile consistent with chronic SCD pain. Future research is warranted to evaluate the utility of the PPST to inform targeted patient needs and guide treatment decision-making.

Acknowledgments

## Abbreviation: Full term or phrase:

AAPT	Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks – American Pain Society Pain Taxonomy
AUC	Area under the curve
CDI-2	Children's Depression Inventory – 2
FDI	Functional Disability Inventory
FOPQ-C	Fear of Pain Questionnaire – Child
M	Mean
PCS-C	Pain Catastrophizing Scale – Child
PPST	Pediatric Pain Screening Tool
ROC	Receiver operating characteristic
SCD	Sickle cell disease
SCPBI	Sickle Cell Pain Burden Interview
SD	Standard deviation

References Cited

1. Dampier C, Ely B, Brodecki D, O'Neal P. Characteristics of pain managed at home in children and adolescents with sickle cell disease by using diary self-reports. J Pain. 2002;3(6):461–70. Epub 2003/11/19. PubMed PMID: 14622732. [PubMed: 14622732]

2. Shapiro BS, Dinges DF, Orne EC, Bauer N, Reilly LB, Whitehouse WG, Ohene-Frempong K, Orne MT. Home management of sickle cell-related pain in children and adolescents: natural history and impact on school attendance. Pain. 1995;61(1):139–44. 10.1016/0304-3959(94)00164-A. PubMed PMID: 7644237. [PubMed: 7644237]

3. Zempsky WT, O'Hara EA, Santanelli JP, Palermo TM, New T, Smith-Whitley K, Casella JF. Validation of the Sickle Cell Disease Pain Burden Interview–Youth. The Journal of Pain. 2013;14(9):975–82. doi: 10.1016/j.jpain.2013.03.007. [PubMed: 23701707]

4. Sil S, Cohen LL, Dampier C. Psychosocial and Functional Outcomes in Youth With Chronic Sickle Cell Pain. Clin J Pain. 2016;32(6):527–33. 10.1097/ajp.0000000000000289. PubMed PMID: 26379074. [PubMed: 26379074]

5. Dampier C, Palermo TM, Darbari DS, Hassell K, Smith W, Zempsky W. AAPT Diagnostic Criteria for Chronic Sickle Cell Disease Pain. J Pain. 2017 10.1016/j.jpain.2016.12.016. PubMed PMID: 28065813.

6. Sil S, Dampier C, Cohen LL. Pediatric Sickle Cell Disease and Parent and Child Catastrophizing. J Pain. 2016;17(9):963–71. 10.1016/j.jpain.2016.05.008. PubMed PMID: 27263990. [PubMed: 27263990]

7. Gauntlett-Gilbert J, Eccleston C. Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning. Pain. 2007;131(1–2):132–41. doi: 10.1016/j.pain. 2006.12.021. [PubMed: 17267129]

8. Kashikar-Zuck S, Goldschneider KR, Powers SW, Vaught MH, Hershey AD. Depression and Functional Disability in Chronic Pediatric Pain. The Clinical Journal of Pain. 2001;17(4):341–9. [PubMed: 11783815]

9. Palermo TM. Impact of recurrent and chronic pain on child and family daily functioning: a critical review of the literature. Journal of Developmental & Behavioral Pediatrics. 2000;21(1):58–69. [PubMed: 10706352]

10. Darbari DS, Ballas SK, Clauw DJ. Thinking beyond sickling to better understand pain in sickle cell disease. European journal of haematology. 2014;93(2):89–95. 10.1111/ejh.12340. PubMed PMID: 24735098. [PubMed: 24735098]

11. Simons LE, Smith A, Ibagon C, Coakley R, Logan DE, Schechter N, Borsook D, Hill JC. Pediatric Pain Screening Tool: rapid identification of risk in youth with pain complaints. Pain. 2015;156(8): 1511–8. 10.1097/j.pain.0000000000000199. PubMed PMID: 25906349; PubMed Central PMCID: PMCPmc4504741. [PubMed: 25906349]

12. Heathcote LC, Rabner J, Lebel A, Hernandez JM, Simons LE. Rapid Screening of Risk in Pediatric Headache: Application of the Pediatric Pain Screening Tool. J Pediatr Psychol. 2018;43(3):243–51. 10.1093/jpepsy/jsx123. PubMed PMID: 29048551. [PubMed: 29048551]

13. Edwards RR, Dworkin RH, Sullivan MD, Turk DC, Wasan AD. The Role of Psychosocial Processes in the Development and Maintenance of Chronic Pain. J Pain. 2016;17(9 Suppl):T70–92. 10.1016/j.jpain.2016.01.001. PubMed PMID: 27586832; PubMed Central PMCID: PMCPmc5012303. [PubMed: 27586832]

14. Walker LS, Greene JW. The functional disability inventory: measuring a neglected dimension of child health status. Journal of Pediatric Psychology. 1991;16(1):39–58. PubMed PMID: 1826329. [PubMed: 1826329]

15. Kashikar-Zuck S, Flowers SR, Claar RL, Guite JW, Logan DE, Lynch-Jordan AM, Palermo TM, Wilson AC. Clinical utility and validity of the Functional Disability Inventory (FDI) among a multicenter sample of youth with chronic pain. Pain. 2011;152(7):1600–7. [PubMed: 21458162]

16. Claar RL, Walker LS. Functional assessment of pediatric pain patients: psychometric properties of the functional disability inventory. Pain. 2006;121(1–2):77–84. 10.1016/j.pain.2005.12.002. PubMed PMID: 16480823; PubMed Central PMCID: PMCPmc3144698. [PubMed: 16480823]

17. Dampier C, Jaeger B, Gross HE, Barry V, Edwards L, Lui Y, DeWalt DA, Reeve BB. Responsiveness of PROMIS(R) Pediatric Measures to Hospitalizations for Sickle Pain and Subsequent Recovery. Pediatric blood & cancer. 2016;63(6):1038–45. 10.1002/pbc.25931. PubMed PMID: 26853841. [PubMed: 26853841]

18. Kovacs M Children's Depression Inventory Available from Multi-Health systems, Inc., 908 Niagara Falls Blvd., North Tonawanda, N.Y. 14120–2060; 1992.

19. Conte P, Walco G, Kimura Y. Temperament and stress response in children with juvenile primary fibromyalgia syndrome. Arthritis and Rheumatism. 2003;48(10):2923–30. [PubMed: 14558099]

20. Eccleston C, Crombez G, Scotford A, Clinch J, Connell H. Adolescent chronic pain: patterns and predictors of emotional distress in adolescents with chronic pain and their parents. Pain. 2004;108(3):221–9. 10.1016/j.pain.2003.11.008S0304395903004585 [pii]. PubMed PMID: 15030941. [PubMed: 15030941]

21. Kashikar-Zuck S, Goldschneider KR, Powers SW, Vaught MH, Hershey AD. Depression and functional disability in chronic pediatric pain. Clinical Journal of Pain. 2001;17(4):341–9. PubMed PMID: 11783815. [PubMed: 11783815]

22. Logan DE, Claar RL, Guite JW, Kashikar-Zuck S, Lynch-Jordan A, Palermo TM, Wilson AC, Zhou C. Factor Structure of the Children's Depression Inventory in a Multisite Sample of Children and Adolescents With Chronic Pain. The Journal of Pain. 2013;14(7):689–98. doi: 10.1016/j.jpain. 2013.01.777. [PubMed: 23642409]

23. Goubert L, Eccleston C, Vervoort T, Jordan A, Crombez G. Parental catastrophizing about their child's pain. The parent version of the Pain Catastrophizing Scale (PCS-P): A preliminary validation. PAIN. 2006;123(3):254–63. doi: 10.1016/j.pain.2006.02.035. [PubMed: 16644128]

24. Crombez G, Bijttebier P, Eccleston C, Mascagni T, Mertens G, Goubert L, Verstraeten K. The child version of the pain catastrophizing scale (PCS-C): a preliminary validation. Pain. 2003;104(3): 639–46. doi: 10.1016/S0304-3959(03)00121-0. [PubMed: 12927636]

25. Pielech M, Ryan M, Logan D, Kaczynski K, White MT, Simons LE. Pain catastrophizing in children with chronic pain and their parents: Proposed clinical reference points and reexamination of the Pain Catastrophizing Scale measure. PAIN®. 2014;155(11):2360–7. doi: 10.1016/j.pain. 2014.08.035. [PubMed: 25180013]

26. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychological assessment. 1995;7(4):524. doi: Doi 10.1037//1040-3590.7.4.524. PubMed PMID: WOS:A1995TL18000014.

27. Simons LE, Sieberg CB, Carpino E, Logan D, Berde C. The Fear of Pain Questionnaire (FOPQ): Assessment of Pain-Related Fear Among Children and Adolescents With Chronic Pain. The Journal of Pain. 2011;12(6):677–86. doi: 10.1016/j.jpain.2010.12.008. [PubMed: 21354866]

28. Aisiku IP, Smith WR, McClish DK, Levenson JL, Penberthy LT, Roseff SD, Bovbjerg VE, Roberts JD. Comparisons of high versus low emergency department utilizers in sickle cell disease. Annals of emergency medicine. 2009;53(5):587–93. 10.1016/j.annemergmed.2008.07.050. PubMed PMID: 18926599. [PubMed: 18926599]

29. Carroll CP, Haywood C, Lanzkron S. Prediction of onset and course of high hospital utilization in sickle cell disease. Journal of Hospital Medicine. 2011;6(5):248–55. doi: 10.1002/jhm.850. [PubMed: 21661098]

30. Epstein K, Yuen E, Riggio JM, Ballas SK, Moleski SM. Utilization of the office, hospital and emergency department for adult sickle cell patients: a five-year study. Journal of the National Medical Association. 2006;98(7):1109–13. Epub 2006/08/10. PubMed PMID: 16895280; PubMed Central PMCID: PMCPMC2569470. [PubMed: 16895280]

31. Youngstrom EA. A primer on receiver operating characteristic analysis and diagnostic efficiency statistics for pediatric psychology: we are ready to ROC. J Pediatr Psychol. 2014;39(2):204–21. 10.1093/jpepsy/jst062. PubMed PMID: 23965298; PubMed Central PMCID: PMCPmc3936258. [PubMed: 23965298]

32. Morgan EM, Mara CA, Huang B, Barnett K, Carle AC, Farrell JE, Cook KF. Establishing clinical meaning and defining important differences for Patient-Reported Outcomes Measurement Information System (PROMIS((R))) measures in juvenile idiopathic arthritis using standard setting with patients, parents, and providers. Qual Life Res. 2017;26(3):565–86. 10.1007/s11136-016-1468-2. PubMed PMID: 27913986; PubMed Central PMCID: PMCPmc5311023. [PubMed: 27913986]

33. Kovacs M Chidlren's Depression Inventory. North Tonawanda, NY: Multi-Health Systems Inc.; 1992.

34. McCracken LM, Turk DC. Behavioral and cognitive-behavioral treatment for chronic pain: outcome, predictors of outcome, and treatment process. Spine (Phila Pa 1976). 2002;27(22):2564–73. 10.1097/01.Brs.0000032130.45175.66. PubMed PMID: 12435995. [PubMed: 12435995]

35. Tick H, Nielsen A, Pelletier KR, Bonakdar R, Simmons S, Glick R, Ratner E, Lemmon RL, Wayne P, Zador V. Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care: The Consortium Pain Task Force White Paper. Explore (New York, NY). 2018;14(3):177–211. 10.1016/j.explore.2018.02.001. PubMed PMID: 29735382.
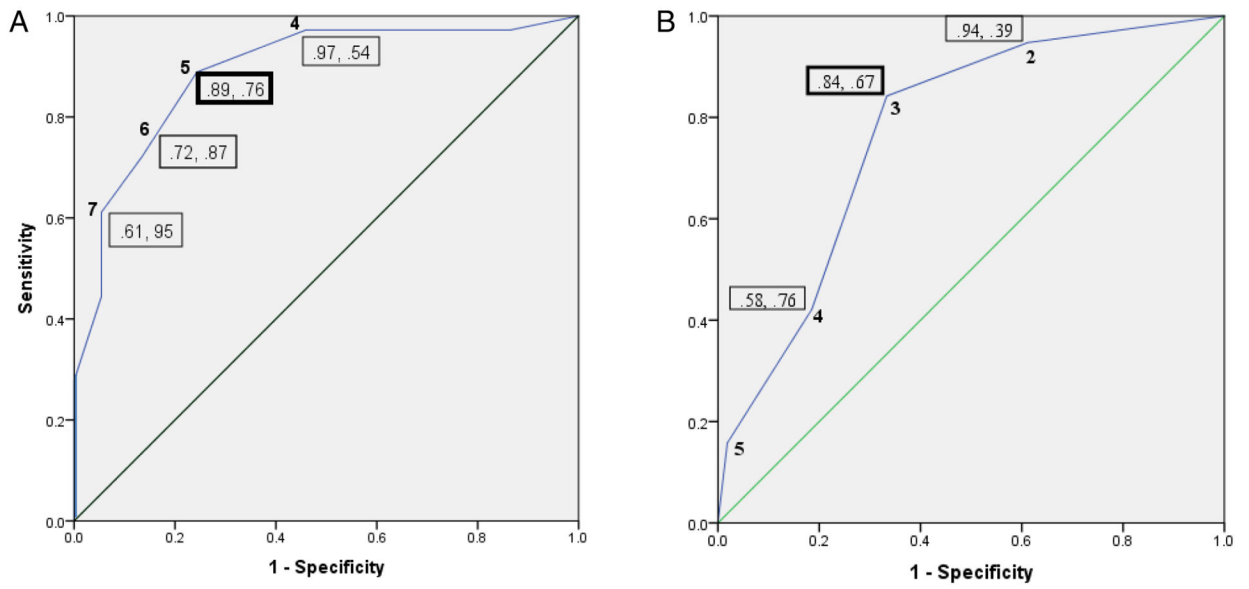
Figure 1.
Receiver operating characteristic (ROC) curves for the (A) PPST total score against reference standard cases for disability, and (B) PPST psychosocial subscale score against reference standard case for psychosocial distress defined using depression, pain catastrophizing, and fear of pain. Boxed numbers indicate sensitivity and specificity values. The straight line signifies the null.

TABLE 1.

Sample characteristics (n=73)

Child	
Mean Age (SD)	14.3 (2.6), range 8–18
Sex (% Female)	57.5
Race (% Black or African American)	94.3
Hemoglobin Type (%)	
HbSS	75.0
HbSC	13.9
HbSβ$^+$	8.3
HbSβ^0	1.4
HbSO-Arab	1.4
SCD Treatments (%)	
Hydroxyurea	81.7
Chronic Transfusions	15.7
Parent	
Reporter (mother/stepmother)	93.1
Race (% Black or African American)	88.9
Marital Status (%)	
Married/Partnered	40.8
Single	32.4
Divorced/Separated	21.1
Widowed	2.8
Prefer not to answer	2.8
Highest grade completed (%)	
High School or GED	24.7
Some college or trade	27.4
College or trade degree	35.6
Graduate or Professional degree	12.3
Annual family income (%)	
$10,000	3.1
$10,001–20,000	26.2
$20,001–30,000	15.4
$30,001–50,000	23.1
$50,001–75,000	13.8
$75,001	15.4
Prefer not to answer	3.1

TABLE 2.

Frequency of PPST Item Endorsement

PPST items	Current sample (sickle cell)	Validation sample [a] (mixed pain)	Validation sample [b] (headache)
	Agree (%)	Agree (%)	Agree (%)
Physical subscale			
My pain is in more than one body part	83.6	69.4	40.9
I can only walk a short distance because of my pain	50.7	56.8	25.6
It is difficult for me to be at school all day	52.1	73.1	76.9
It is difficult for me to fall asleep and stay asleep at night	49.3	63.6	54.5
Psychosocial subscale			
It is not really safe for me to be physically active	30.1	45.9	19.4
I worry about my pain a lot	52.1	48.3	54.5
I feel that my pain is terrible and it is never going to get any better	31.5	36.6	45.9
In general, I do not have as much fun as I used to	32.9	61.7	54.5
Overall, how much has pain been a problem in the past 2 weeks? [c]	32.8	79.2	73.1

Note. PPST=Pediatric Pain Screening Tool.

[a] Data taken from Simons et al (2015)

[b] Data taken from Heathcote et al (2017)

[c] Item responses include "not at all," "a little," "some," "a lot," and "a whole lot." Responses of "a lot" and "a whole lot" are coded as endorsement of bothersomeness for the total score and are reflected in the Agree column.

TABLE 3.

Discriminant Validity: area under the curve (AUC) for screening tool total scores and psychosocial subscale scores against reference standard cases

Reference standards	Case definition		Total scores, AUC (95% CI)	Psychosocial subscale scores, AUC (95% CI)
High pain frequency	Pain frequency	15 days/month	.82 (.71 - .93) ***	.81 (.68 - .93) ***
	SCD Pain Burden Days	many	.83 (.74 - .92) ***	.82 (.71 - .93) ***
Persistent pain duration	Duration	6 months	.63 (.50 - .77)	.65 (.52 - .78) *
Moderate to severe disability	FDI	13	.93 (.87 - .98) ***	.86 (.78 - .95) ***
High pain interference	Pain Interference T-score	65	.80 (.68 - .93) ***	.80 (.66 - .94) ***
High inpatient admissions	Admissions for pain	3	.74 (.62 - .86) **	.77 (.66 - .89) ***
High ED visits	ED visits for pain	3	.69 (.55 - .82) *	.67 (.53 - .82) *
Elevated depressive symptoms	CDI T-score	65	.76 (.63 - .88) ***	.69 (.53 - .85) *
High pain catastrophizing	PCS-C	26	.75 (.64 - .86) ***	.72 (.60 - .84) ***
High pain-related fear	FOPQ	51	.83 (.73 - .92) ***	.80 (.70 - .90) ***
Psychosocial distress index (CDI, PCS, FOPQ)	Case on two or more psychosocial variables †		.78 (.67 - .89) ***	.76 (.64 - .88) ***

Note: FDI = Functional Disability Inventory; ED = emergency department; CDI = Children's Depression Inventory-2; PCS-C = Pain Catastrophizing Scale for Children; FOPQ = Fear of Pain Questionnaire.

† Psychosocial variables include depressive symptoms, catastrophizing, and fear of pain

*
$p < .05$,

**
$p < .01$,

***
$p < .001$

TABLE 4.

Chi-Square Results for Risk Group across Clinically Significant or Elevated Pain Characteristics and Pain-Related Outcomes

	PPST Risk Group			
	Low	Medium	High	χ^2 value
High pain frequency	0% (n=0)	29% (n=4)	71% (n=10)	13.52 ***
Burden days frequency	0% (n=0)	30% (n=7)	70% (n=16)	23.96 ***
Persistent pain duration	22% (n=7)	31% (n=10)	47% (n=15)	3.97
Moderate to severe disability	0% (n=0)	39% (n=13)	61% (n=20)	31.43 ***
High pain interference	6% (n=1)	24% (n=4)	71% (n=12)	14.89 ***
High admissions for pain	5% (n=1)	37% (n=7)	58% (n=11)	9.84 **
High ED visits for pain	7% (n=1)	43% (n=6)	50% (n=7)	4.45
Elevated depressive symptoms	0% (n=0)	40% (n=6)	60% (n=9)	9.67 **
High pain catastrophizing	7% (n=2)	45% (n=14)	48% (n=15)	13.17 ***
High pain-related fear	3% (n=1)	44% (n=14)	53% (n=17)	20.56 ***

**
p<.01,

***
p<.001

TABLE 5.

Univariate Analysis of Variance Results for Risk Group across Pain Characteristics and Pain-Related Outcomes

Variable (range of scores)	PPST Risk Group			F-value
	Low M (SD) N=21	Medium M (SD) N=28	High M (SD) N=24	
Pain intensity (0–10)	1.20 (1.47)[a]	2.77 (2.42)	5.78 (2.58)[c]	23.46[**]
Pain frequency (0–31)	2.60 (2.89)[a]	7.46 (8.17)[b]	15.52 (10.35)[c]	14.62[**]
SCD Pain Burden (0–28)	2.20 (2.04)[a]	9.65 (4.48)[b]	14.82 (4.87)[c]	51.29[**]
Functional disability (0–60)	1.85 (2.35)[a]	15.19 (12.21)[b]	27.30 (12.21)[c]	32.16[**]
High pain interference	43.23 (11.27)[a]	55.47 (11.50)[b]	66.36 (9.67)[c]	22.25[**]
Admissions for pain (0–18)	0.30 (0.73)[a]	2.04 (3.98)	3.22 (3.41)	4.57[*]
Depressive symptoms (40–100)	48.05 (6.84)[a]	54.85 (9.88)[b]	61.04 (11.07)[c]	9.89[**]
Pain catastrophizing (0–54)	12.80 (10.63)[a]	25.31 (11.99)[b]	31.26 (11.63)	14.23[**]
Pain-related fear (0–96)	18.70 (16.53)[a]	50.31 (15.33)[b]	55.96 (22.64)	25.20[**]

Note: Superscripts represent significant group differences using Bonferroni-corrected post-hoc comparisons between

[a] Low-High,

[b] Low-Medium,

[c] Medium-High

[*] p<.01,

[**] p<.001