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Predictors of the transition from acute to persistent musculoskeletal pain in children and adolescents: a prospective study

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Abstract

Strategies directed at the prevention of disabling pain have been suggested as a public health priority, making early identification of youth at risk for poor outcomes critical. At present limited information is available to predict which youth presenting with acute pain are at risk for persistence. The aims of this prospective longitudinal study were to identify biopsychosocial factors in the acute period that predict the transition to persistent pain in youth with new-onset musculoskeletal (MSK) pain complaints. Participants were 88 children and adolescents (age 10–17 years) presenting to the emergency department (n=47) or orthopedic clinic (n=41) for evaluation of a new MSK pain complaint (< 1 month duration). Youth presented for two study visits (T1 = <1 month post pain onset; T2 = 4 month follow-up) during which they completed questionnaires (assessing pain characteristics, psychological factors, sleep quality) and participated in a lab task assessing conditioned pain modulation (CPM). Regression analyses tested T1 predictors of longitudinal pain outcomes (pain persistence, pain-related disability, quality of life). Results revealed approximately 35% of youth had persistent pain at 4-month follow-up, with persistent pain predicted by poorer CPM and female sex. Higher depressive symptoms at T1 were associated with higher pain-related disability and poorer quality of life at T2. Findings highlight the roles of depressive symptoms and pain modulation in longitudinally predicting pain persistence in treatment-seeking youth with acute MSK pain, and suggest potential mechanisms in the transition from acute to chronic MSK pain in children and adolescents.

1. Introduction

Strategies directed at the prevention of disabling pain have been suggested as a public health priority [1]. Persistent pain during childhood is associated with limitations in physical functioning, impaired quality of life, sleep disturbances, peer difficulties, and elevated depressive symptoms [6; 12; 17; 44]. In the United States alone, total expenditures for moderate to severe pediatric chronic pain are estimated at \$19.5 billion/year [14]. Moreover, chronic pain during childhood confers risk for pain and high health care use in adulthood [3]

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with onset of pain in childhood predicting widespread pain, higher anxiety and poorer functional status later in life [15]. There is a limited understanding of how biopsychosocial factors including pain responsiveness present in the acute pain period influence the transition from acute to chronic pain during childhood.

High prevalence of musculoskeletal (MSK) pain during childhood places a significant burden on children, families, and the health care system [18; 39]. Epidemiologic studies suggest MSK pain remits in many youth, however approximately 30% experience continued pain at 1 and 4-year follow-ups [8]. High pain-related impairment, psychological comorbidity, sleep disturbance, female sex and older age [7; 9; 25; 34] have been identified as predictors for MSK pain persistence or recurrence. Because this previous research was limited to survey data and included heterogeneous samples of youth with new and ongoing pain complaints, a thorough characterization of factors in the acute pain period that predict pain persistence was not possible.

Research with adults prospectively examining risk for persistent MSK pain after traumatic injury identified older age, high initial pain rating, psychological factors (anxiety, depression, cognitive avoidance), and low educational attainment as predictors (see review, [32]). Additional data suggests post-injury anxiety, depression, posttraumatic stress symptoms, and pain catastrophizing predict pain persistence after acute injury [2; 31]. The developmental and interpersonal factors unique to childhood may limit the generalizability of these adult findings, making it critical to conduct similar prospective studies of youth with new-onset MSK pain.

Alterations in pain processing may increase risk for chronicity in youth with acute pain. Deficits in endogenous pain inhibition increase risk for developing chronic neck pain [33] and chronic post-surgery pain in adults [19]. Prospective studies examining deficits in pain modulation as a mechanism for pain persistence in pediatric samples have not yet been conducted.

To our knowledge this is the first longitudinal investigation of factors that predict the transition from acute MSK pain to persistent MSK pain in treatment-seeking youth. Based on available literature, we hypothesized that at least 30% of youth would endorse persistent MSK pain at 4-month follow-up. Guided by the Biobehavioral Model of Pediatric Pain [45] and research suggesting pain inhibitory circuitry and biopsychosocial factors influence the pain trajectory, we hypothesized that sleep quality, depression, pain anxiety, and conditioned pain modulation (CPM) in the acute pain period (<1 month pain duration) would predict pain persistence and pain-related functioning (pain-related disability and quality of life) at four months.

2. Method

This study was conducted at an academic medical center in the northwestern United States. All study procedures were approved by the Institutional Review Board, and all participants provided consent or assent prior to participating. Child and adolescent participants were 88 youth ages 10–17 years recently evaluated in an emergency department or orthopedic clinic

for an acute MSK pain complaint (e.g., limb, back or neck pain). Inclusion criteria at time of study enrollment required MSK pain duration of less than one month, and current pain at the MSK location for which the child sought medical care. Participants were excluded if serious pathology (e.g., infection, disease process) was associated with the source of the pain complaint or participants had a surgical procedure (including reductions) conducted or planned at the identified pain site. Youth were also excluded if they had another ongoing pain problem (e.g., frequent headaches, recurrent abdominal pain) or a history of chronic pain or surgery at the site of the acute pain complaint. Youth and their participating parent were required to be able to independently complete written questionnaires and be proficient in English to participate. A previous manuscript reported on pain characteristics in the new-onset pain sample compared to youth with chronic MSK pain and healthy youth [22], and a second paper described widespread pain in a subsample [29]. This is the first paper to report the study's longitudinal findings and describe factors that predict the persistence of MSK pain.

2.1. Procedures

Potential participants were identified by research or clinical staff familiar with the study either during children's medical appointment/emergency department visit or through review of daily clinic schedules. The study's IRB permitted this review of electronic medical records for the purposes of identifying participants. An informational flyer was given in clinic to potentially eligible families or sent to the child's home. Families were then contacted via phone to undergo additional screening and if eligible, were invited to participate in the study.

88 families were enrolled in the study. 131 families declined to participate. The majority of families who declined cited time involved for the two in-person laboratory visits, located a significant distance from the medical center where the child sought care, as the reason. Further, 124 families were not eligible with the most common reasons being: child no longer had pain at time of phone screening for study enrollment, presence of a comorbid health condition/chronic pain problem, or primary parent was non-English speaking.

Participating families provided written assent/consent before undergoing any study procedures. Youth and their parents attended an in-person laboratory visit at T1 (<1 month post-pain onset) and four month follow-up. Assessment at both time points consisted of comprehensive measurement of pain characteristics, psychological functioning, pain-related disability, sleep quality, and conditioned pain modulation. All procedures were administered by trained research assistants and scripted instructions were read to the child or adolescent to insure uniform experimental conditions. The conditioned pain modulation assessment took approximately 20 minutes, with total assessment procedures (including consent and measure administration) approximately one hour for each of the two visits. Families were provided with gift cards as incentives for completion of study assessments. Participants were also reimbursed for parking costs and provided bus passes (if needed) to limit any financial barriers associated with participation.

2.2. Questionnaire Measures

2.2.1. Demographics—Parents reported on their child’s age, sex, race/ethnicity and family income.

2.2.2. Body mass index (BMI)—Study staff collected children’s height and weight measurements during their laboratory visits. Height and weight information was entered into the Center for Disease Control’s online calculator (<https://nccd.cdc.gov/dnpabmi/calculator.aspx>) to calculate BMI corrected for age and sex.

2.2.3. Pain characteristics—Pain characteristics were assessed using child report of pain intensity and pain frequency. Specifically children were asked to report on their “usual pain intensity” over the past 7 days using a Numerical Rating Scale (11 point NRS 0–10) [24; 46]. Children reported on pain frequency using a 6 point ordinal scale (0–4; 0 = “not at all” to 4 = “daily”) to describe how often pain occurred over the last 7 days.

2.2.4. Pain location(s)—Pain locations were documented in two ways, *primary acute MSK location* (T1) and *total locations of pain* (both T1 and T2). Location of primary acute MSK pain complaint was reported verbally by participants at study enrollment and coded into 1 of 6 MSK pain locations: hand/arm, leg/foot, back, shoulder, neck, hip, or chest. In addition, youth used a body diagram at both T1 and T2 to indicate all location(s) of pain (MSK and non-MSK pain) over the past week. Body diagrams were coded into 9 locations representing MSK and non-MSK pain (hand/arm, leg/foot, back, shoulder, neck, hip, chest, head, and abdomen); locations were summed for the *total number of pain locations* at T1 and T2.

2.2.5. Pain persistence—Persistence of MSK pain at four months was coded using a two-step process. First, the participant’s report of their *primary acute MSK pain location* at T1 was compared with their completed body diagram at T2. Second, using a standard definition of clinically significant improvement in pain intensity (50% reduction), pain intensity (0–10 NRS) reported at T2 was subtracted from reported pain intensity at T1. Youth were coded as having “persistent pain” if they endorsed pain on the T2 diagram that matched their primary pain location at T1 and they *did not achieve at least 50% improvement in pain intensity* from T1 to T2. Youth were coded as “recovered” if they did not report pain at the same primary pain location, or if they did report pain at the same primary pain location but reported *at least 50% improvement in pain intensity* from T1 to T2. This stringent definition of persistent pain was chosen in order to provide an estimate of clinically meaningful pain persistence at T2.

2.2.6. Depressive symptoms—Adolescents completed the 20-item Center for Epidemiological Studies Depression Scale (CES-D) to assess depressive symptoms. Item responses on the CES-D range from 0 (Rarely or none of the time; less than 1 day) to 3 (Most or all of the time; 5–7 days) and are summed to create a total score ranging from 0–60, with higher scores indicating greater depressive symptoms. A CES-D score of 16 or greater indicates clinically significant depressive symptoms [30]. The CES-D is widely used to assess depressive symptoms in children and adolescents, and has demonstrated acceptable

1-week test-retest reliability and validity in relationships with other measures of internalizing symptoms [30].

2.2.7. Pain-related disability—The Child Activity Limitations Interview (CALI-21) was used to assess pain-related disability in children and adolescents [26]. This 21-item measure assesses ability to participate in physical and functional activities over the previous 4 weeks, using 5 response options ranging from 0 ‘not difficult’ to 4 ‘extremely difficult’. A total score is calculated by summing ratings for all 21 items (range from 0 – 84), with higher scores indicating greater functional disability due to pain. The CALI-21 child version has demonstrated reliability and validity in assessing pain-related disability in school aged children and adolescents [26].

2.2.8. Fear of pain—Youth reported fear and avoidance related to pain using the Fear of Pain Questionnaire (FOPQ-C) [37]. The 24 items on the scale are rated on a 5-point scale ranging from 0 ‘strongly disagree’ to 4 ‘strongly agree’ and items are summed for a total score, with higher scores indicating more pain-related fear. The FOPQ-C has excellent reliability and construct validity and the measure has been used to assess pain-related fear in diverse pain samples [35; 36].

2.2.9. Pain catastrophizing—The Pain Catastrophizing Scale for Children (PCS-C) was used to assess catastrophizing about pain symptoms in children and adolescents [4]. The measure’s standard instructions were used which prompt children to reflect on past painful experiences (“Below are some things that happen to you when you have pain”) and to indicate the degree that they experienced ruminating, magnifying, or helpless thoughts or feelings. Response options are on a 5-point scale (0–4) ranging from 0 ‘not at all’ to 4 ‘extremely’. This scale shows good internal consistency and reliability and has been validated for use with 8 to 16 year old children [4]. The total score was calculated using the updated 11 item scoring system (eliminating items 7 and 8) with clinical reference points being 0–14 (low); 15–25 (moderate); and 26 and greater (high) catastrophizing symptoms [28].

2.2.10. Sleep quality—The 28 item Adolescent Sleep-Wake Scale (ASWS) was used to assess children’s perceptions of their sleep quality [20]. Youth reported on their sleep during the previous month along a 6-point scale (range from 1 ‘always’ to 6 ‘never’) with higher scores indicating better sleep quality. The ASWS measures five behavioral dimensions of sleep (going to bed, falling asleep, maintaining sleep, reinitiating sleep, returning to wakefulness). The ASWS total score was used in analyses. The ASWS is a valid and reliable assessment tool that has been used extensively in both pain and non-pain populations [21; 27].

2.3. Laboratory assessment of conditioned pain modulation

Children and adolescents participated in a hot and cold thermal task to assess conditioned pain modulation. Procedures are based on methods used in an adult study examining risk for post-surgical pain [13] and in a study of children with irritable bowel syndrome (IBS) [48]. During the laboratory task, youth underwent a series of heat sensations applied to their

dominant inner forearm, first alone, and then in conjunction with the child's non-dominant hand in a cold water bath. Heat stimuli were produced by a Thermal Sensory Analyzer (Medoc) with a 30mm × 30mm surface stimulator. Baseline heat temperature started at 32.0°C with an increasing temperature rate of 1.5°C and a cooling rate of 8°C/s. For safety, a maximum temperature was set at 52°C. After each heat sensation the thermode was moved to an adjacent location on the child's forearm to prevent sensitization. Cold stimulus was produced with an 8°C circulating water bath (cold pressor).

2.3.1. Test stimulus—First, youth underwent a brief training phase (a series of 2 heat sensations) to familiarize them with the heat stimuli device, instructions and perceived sensations. Participants were then administered a series of 4 heat sensations and were instructed to push a button on a controller “when the heat becomes painful” (baseline heat pain threshold; B-HPT). Instructions explicitly stated that assessment was for a pain threshold, not how much heat the child could tolerate.

2.3.2. Conditioning stimulus—Next, youth were instructed to immerse their non-dominant hand (just above wrist) in the 8°C circulating water bath. After their non-dominant hand was in cold water for 10 seconds, youth underwent a series of 3 heat pain sensations on the dominant arm. As they had done previously during the B-HPT task, participants were instructed to push a button on a controller “when the heat becomes painful” (conditioning heat pain threshold; C-HPT). Participants were instructed to keep their hand in the water throughout the duration of this task with total immersion time approximately 60 seconds.

2.3.3. Calculating conditioned pain modulation index—A conditioned pain modulation (CPM) index score was calculated using the ratio of the C-HPT with the conditioning stimulus (cold pressor) to the B-HPT multiplied by 100. A greater index score indicates a larger CPM effect. This method of calculation of CPM has been used in other laboratory tasks examining pain sensitivity in clinical pain samples [23].

2.4 Data analysis

Data were analyzed using SPSS v.22. Summary statistics were used to describe characteristics of the sample and are reported for the total sample in Tables 1 and 2. Means and standard deviations were used for continuous data, and categorical items were described using frequency statistics. To identify the proportion of youth who reported persistent MSK pain at 4 month follow-up, percentages of youth with/without persistent pain were computed using information from two variables, pain location and clinically significant reduction in pain intensity from T1 to T2. Further, for descriptive purposes t-tests and chi-square analyses were conducted to compare T1 variables (pain characteristics, pain-related disability, quality of life, depressive symptoms, pain cognitions, sleep quality, and CPM Index) by T2 pain status (persistent pain versus recovered) and participant sex.

To test biopsychosocial predictors of the transition from acute to chronic MSK pain, separate regression models were conducted for three outcomes: pain persistence, pain-related disability, and quality of life. Biopsychosocial predictors included pain intensity, depression, pain anxiety, sleep, and CPM in the acute pain period (<1 month). Associations among

individual demographic factors (T1 age, sex, BMI, and fracture status) and outcomes were tested before running each regression to identify potential covariates. The linear regression models also controlled for the T1 value of the relevant outcome variable (e.g., controlling for T1 pain-related disability in model examining pain-related disability at T2).

2.4.1. Considerations for lab task data—All 88 youth participated in the laboratory pain assessment. Six participants could not be exposed to the conditioning stimulus (cold pressor) due to having a non-removable cast on their non-dominant arm or hand so only data from the test stimulus (B-HPT) were available for 82 youth. Further, 1 child elected to stop the experimental pain task before receiving the conditioning stimulus (cold pressor) due to not tolerating the heat stimuli. Based on those limitations, T1 CPM could be calculated for $n=81$ youth.

Of these 81 youth, the majority ($n=72$, 88.9%) completed the whole CPM task. Nine participants did not complete all 3 heat stimuli during the concurrent cold pressor (C-HPT) outlined by the protocol. Specifically 7 youth received only 2 heat sensations and 2 youth received only 1 heat sensation during the C-HPT. A priori we elected to use the mean of available data for each participant when calculating the C-HPT rather than eliminating youth who did not complete all 3 heat pain sensations. This was decided to maximize data available for CPM analyses.

3. Results

3.1. Descriptives

88 youth (M age = 13.8 yrs, SD = 1.9; 60.2% female) with new onset MSK pain participated in the study. Sociodemographic and pain characteristics of the sample at T1 are presented in Table 1. Study participants had sought care in the emergency department ($n=47$) or orthopedic clinic ($n=41$) with most frequently occurring primary acute MSK pain locations being leg/foot, hand/arm and back pain. Youth reported an average of 1.7 (SD=1.2) pain locations at T1 with 27 youth ($n=30.7\%$) having sustained a fracture. Average pain intensity at T1 was 4.8 (SD=2.2, 0–10 NRS) and this was not different by sex, referral source, or in youth who sustained a fracture versus no fracture. Sports injuries were reported to be the primary etiology of pain complaints, followed by non-sports accidents and spontaneous onset/no identified cause.

Given prior findings showing sex differences in risk for MSK pain, we examined possible sex differences on biopsychosocial factors. Results revealed no T1 sex differences on pain intensity, activity limitations, psychological variables (depression, catastrophizing, pain-related fear), sleep or CPM. Differences in T1 pain frequency were significant at the trend level, with females reporting more frequent pain than males, $t(83) = -1.97$, $p = .053$.

3.2. Transition from acute to persistent MSK pain at follow-up

The majority of youth completed T2 assessments ($n=71$, 80.7%). Those lost to follow-up reported either being unable to come in for the lab visit or were not able to be contacted. Of the 71 youth who completed the T2 assessment, 38 continued to have pain at the same MSK location at 4 month follow-up. Of these 38 participants, 7 achieved clinically significant

reduction in pain ($\geq 50\%$ reduction) at T2 making the number of youth identified as having persistent pain $n=31$. Conservatively calculating pain persistence using the total sample size at T1 ($n=88$), 35.2% youth had persisting pain at the same location. Primary pain location of youth with persistent pain was leg/foot pain, followed by back and hand/arm pain.

Youth with persistent pain at T2 reported an average of 2.2 ($SD=1.4$) pain locations and reported moderate usual pain intensity ($M=4.5$, $SD=1.9$). Chi-square and t-tests were used to examine T1 demographic factors (listed in Table 1) by T2 persistent pain status. Results revealed sex differences by persistent pain status at T2; 87.1% of youth with persistent pain were female while only 12.9% of youth with persistent pain were male, $\chi^2(1, N = 71) = 12.0$, $p = .001$. Findings showed youth with persistent pain versus those who recovered did not differ by any of the other T1 demographic characteristics.

For descriptive purposes, differences in T1 biopsychosocial factors by pain status at T2 (persistent pain versus recovered) are presented in Table 2. The groups differed solely on CPM index score such that youth with persistent pain at 4 month follow-up had lower T1 CPM index scores (indicating poorer pain modulation).

3.3. Biopsychosocial predictors of T2 pain persistence

Three separate regressions (1 logistic, 2 linear) tested T1 biopsychosocial predictors of pain persistence, pain-related activity limitations, and quality of life at four months. Results are presented in Tables 3 and 4. Preliminary analyses examined the association between sex, BMI, fracture status, and T1 age with the outcomes to determine inclusion of covariates. Sex emerged as a significant predictor in all four models so it was entered as a covariate in all of the regression models. Non-significant covariates were trimmed from all models.

The same model of T1 biopsychosocial predictors was used in the 3 regression models predicting pain persistence, pain-related disability and quality of life. The predictors were: pain intensity, depressive symptoms, pain anxiety (fear of pain and pain catastrophizing), sleep quality and CPM index. In all three regressions, T1 values of the T2 outcome variable (e.g., T1 pain-related disability in the model predicting T2 pain-related disability; T1 QOL in the model predicting T2 QOL) were included as a covariate on the 1st step of the regression model (along with sex) to account for T1 values.

3.3.1. Predictors of pain persistence at T2—Results of the logistic regression testing predictors of pain persistence revealed CPM index score ($B = -.15$, $p = .046$) and sex ($B = 3.49$, $p = .003$) were significant predictors of MSK persistence. Specifically females and those with lower T1 CPM index scores were more likely to have persistent pain at T2. See Table 3.

3.3.2. Predictors of pain-related disability at T2—Results of the linear regression testing predictors of T2 pain-related disability revealed depressive symptoms ($\beta = .39$, $p = .02$) and CPM Index score ($\beta = -.37$, $p = .005$) were the only significant predictors of pain-related disability at T2. Youth with higher depressive symptoms and lower CPM index scores at T1 had greater pain-related disability at T2. See Table 4.

3.3.3. Predictors of quality of life at T2—Results of the linear regression testing predictors of T2 quality of life revealed above and beyond T1 QOL, T1 depressive symptoms ($\beta = -.44$, $p = .001$) predicted poorer QOL at T2. Pain catastrophizing emerged as a predictor at the trend level ($\beta = -.29$, $p = .066$), with youth who had greater pain catastrophizing at T1 having poorer QOL at T2. See Table 4.

4. Discussion

To our knowledge, this is the first prospective study of treatment-seeking youth with new onset MSK pain to investigate within a longitudinal design the transition from acute to chronic MSK pain. Specifically we conducted comprehensive assessments of pain, psychological functioning, sleep, and conditioned pain modulation to identify factors that predict MSK pain persistence and inform mechanisms in the transition from acute to MSK chronic pain. Findings revealed approximately 35% of youth had persistent pain at 4-month follow-up, with persistence predicted by poorer conditioned pain modulation and female sex. Depressive symptoms during the acute pain period also served as an important predictor of pain-related disability and quality of life at four months.

Two biopsychosocial factors, female sex and impairment in inhibitory pain modulation, predicted the transition from acute to chronic MSK pain. Conditioned pain modulation during the acute pain period predicted both MSK pain persistence and limitations at 4-month follow-up, suggesting that impairment in inhibitory pain modulation may predict children's non-recovery from acute MSK pain. This finding extends adult research implicating CPM scores as risk factors for the development of chronic pain [5; 19; 33] and suggests CPM may be a mechanism in the transition from acute to chronic MSK pain in youth.

Depressive symptoms emerged as the only psychological factor assessed at T1 that predicted pain-related functioning at T2. Previous research has demonstrated that negative mood can amplify pain and impair one's ability to cope [47]. Moreover, prior work with adolescents has identified depression as an early risk factor for chronic pain, with a strong temporal association between depression and subsequent chronic pain onset [40]. Linking findings from this study to opportunities for improving clinical care, the US Preventive Services Task Force recommends depression screening of youth in health care systems [38]. Our data suggest that leveraging this recommendation and conducting depression screening in children and adolescents with new-onset pain complaints might help identify youth at risk for poor pain-related functioning who may need targeted interventions or additional monitoring.

Findings from this study showing sex differences in risk for persistent pain at T2 are in line with a large body of research showing increased prevalence of chronic pain in females versus males in both children and adults [11]. While female participants in the current study had more frequent pain at T1, there were no sex differences on other T1 biopsychosocial factors (pain intensity, CPM, psychological factors, sleep) that may heighten risk for persistent pain. Future studies examining the transition from acute to chronic pain should monitor symptoms more frequently to capture potential sex differences in trajectories of pain, mood, and disability over time. Also relevant, sex differences in rates of chronic pain

emerge in adolescence around the time of pubertal development [39]. In addition to these pubertal changes, children experience substantial developmental and psychosocial changes, which might impact pain perception differently by sex. Examining risk for transition from acute to persistent pain by sex across stages of pubertal development is an important direction of future research.

Despite previous research indicating associations between pain cognitions, (particularly pain-related fear and pain catastrophizing) and pain-related functioning in adolescents with chronic pain [43; 50], these factors did not emerge as significant predictors of pain persistence or pain-related functioning in the current study. It is possible that pain-related fear and catastrophizing have a stronger association with pain symptoms later in the course of a pain condition rather than during the acute period. Prospective studies assessing changes in pain-related fear and catastrophizing in youth who transition from acute to chronic pain will help to answer this question. Future research can also examine how age and stage of cognitive development may impact associations among catastrophizing and pain outcomes in youth with acute pain. Recent data within a pediatric chronic pain sample found pain catastrophizing was more strongly associated with disability in adolescents compared to younger children [10].

The definition of persistent pain in this study also warrants discussion, as there is currently no standard method for determining pain persistence. For the current study we used a conservative approach for defining pain persistence, including pain location and clinically significant improvement in pain intensity. Using this definition approximately 1/3 of youth continued to have persistent pain at 4-month follow-up. These results are consistent with previous epidemiologic research reporting 32% had persistent MSK pain at one year, and 31% had recurrence at four years [8]. Moving forward it will important to consider standardizing practices for reporting pain persistence in both children and adults. This will make it easier to pool research in this area, and to calculate the number of youth who transition from acute to chronic pain across studies.

Our findings should be interpreted in light of several limitations. First, this study is limited by a small sample size and attrition and will require replication in a larger cohort of children. In addition, participants were exclusively youth experiencing acute MSK pain. While MSK pain is one of the most prevalent pain problems experienced by children and adolescents, risk factors for pain persistence may be different for youth with other pain conditions. In addition, locations and etiology of MSK pain complaints was varied in our sample and youth had a combination of injury and non-injury etiologies. Additional studies recruiting youth with different types of acute pain problems will be needed to identify risk factors for pain persistence in those samples. Moreover, it will be important for future research to include additional assessment of clinical factors (e.g. proper healing of fractures) at follow-up to determine if they play any role in pain persistence.

Because study follow-up was limited to 4 months the longer term outcomes of participants is unknown. Extending the time period of follow-up will be important in future prospective studies particularly for understanding whether T1 risk factors influence pain beyond four months. Consideration should also be given to study designs and sampling that might allow

for assessment of CPM prior to acute pain onset. Because CPM was assessed after MSK pain onset it was not possible to determine if poorer CPM preceded the acute pain experience or if CPM declined in the context of a new MSK pain problem.

Expanding laboratory assessment of pain responsiveness to other modalities and approaches is also needed [49]. This could include CPM assessment using different locations on the body, pressure pain assessed via algometer, or tests of temporal summation. Previous research has shown pain responsiveness or sensitivity can be impacted by pain location and body site on which testing is conducted [41; 42]. Using a protocol that involves pain assessment on multiple body locations (including painful and non-painful body sites) in follow-up studies is recommended. With this additional research, the potential contributions of brief and feasible “bedside” pain testing protocols can be examined. This could potentially make assessment of CPM possible in the clinical setting, particularly if these methods continue to show promise in predicting pain outcomes.

A host of factors that could potentially predict pain outcomes were not explored in this study. These include regular tobacco use and joint hypermobility, which have been identified as potential predictors in other research [16]. Additionally, more information about the context in which the acute pain occurred (e.g., initial pain ratings, injury severity) and assessment of factors relevant to injury-related pain (e.g., post-traumatic stress) may be valuable. For example, research in adults hospitalized after traumatic injuries has identified post-traumatic stress and injury variables as relevant to pain outcomes [31].

In conclusion, despite the compelling data that adolescents are at risk for developing chronic MSK pain, prevention strategies are lacking. Data from this study identified that biopsychosocial factors (particularly female sex, poor conditioned pain modulation and depressive symptoms) place youth with acute MSK pain at risk for poor recovery. Targeted interventions or closer monitoring of youth with elevated symptomatology at time of injury may be considered. Taken together, our preliminary findings suggest it is possible to identify predictors of the transition from acute to persistent MSK pain in youth, information that may support early identification of at-risk youth who may benefit from targeted intervention.

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Table 1

Socio-demographics and pain characteristics of the sample at T1

(N=88)		
Child's age (years, M, range 10–17)	13.76	
Child's sex (n, %)		
Female	53	60.2
Male	35	39.8
Body mass index (M, SD)	23.1	5.15
Child's Race (n, %)		
White	48	54.6
Black or African-American	6	6.8
Asian	1	1.1
American Indian/Alaskan Native	1	1.1
More than one race	25	28.4
Not reported	6	6.8
Ethnicity (n, %)		
Hispanic	16	18.2
Non-Hispanic	64	72.7
Not reported	8	9.1
Household income (n, %)		
Less than \$29,999	15	17.4
\$30,000 – \$39,999	10	11.4
\$40,000 – \$69,999	14	15.9
\$70,000 – \$89,999	6	6.8
More than \$90,000	41	46.6
Not reported	2	2.3
Referral Source		
Emergency Department	47	53.4
Orthopedics	41	46.6
Primary pain location		
Leg or foot	48	54.5
Hand/arm	21	23.9
Back or Spine	9	10.2
Shoulder	4	4.5
Hip	4	4.5
Neck	1	1.1
Sustained Fracture		
Yes	27	30.7
No	61	69.3

Table 2

T1 biopsychosocial characteristics for total sample and by T2 persistent pain status (persistent versus recovered)

	Total M(SD)	Persistent Pain M(SD)	Recovered M(SD)	t*	p
Pain Intensity	4.81 (2.20)	4.74 (1.91)	4.55 (2.35)	-.37	.713
Pain Frequency	2.47 (1.26)	2.71 (1.24)	2.26 (1.33)	-1.46	.150
Pain-Related Disability	15.80 (11.56)	17.01 (10.68)	13.85 (11.83)	-1.16	.249
Depressive Symptoms	14.73 (11.77)	15.06 (11.22)	12.58 (11.40)	-.91	.367
Fear of Pain	23.20 (16.93)	24.04 (14.49)	21.86 (19.05)	-.50	.621
Pain Catastrophizing	9.68 (7.91)	9.61 (6.47)	8.67 (8.28)	-.52	.605
Sleep Quality	3.99 (.68)	3.90 (.70)	4.10 (.70)	.99	.326
Quality of Life	70.73 (15.42)	68.45 (16.27)	75.22 (13.15)	1.87	.066
CPM Index Score	100.63 (6.55)	98.04 (6.70)	102.38 (6.24)	-.52	.010

* t = results of independent samples t-tests comparing groups on T2 "persistent pain", versus "recovered" status

Table 3

Logistic regression model estimating effects of T1 biopsychosocial factors on persistent pain status

Persistent Pain	B	SE	Wald	p	Exp(B)
Sex	3.49	1.19	8.55	.003	32.67
Pain Intensity	-.13	.19	.44	.504	.88
Sleep Quality	.53	.81	.43	.514	1.70
Depressive Symptoms	.03	.04	.49	.485	1.03
Pain Catastrophizing	.07	.08	.86	.354	1.03
Fear of Pain	-.02	.03	.35	.556	.98
CPM Index	-.15	.08	3.99	.046	.86
(Constant)	6.63	8.39	.62	.430	757.83

Model $\chi^2 = 23.49$, $df = 7$, $p < .001$

Hierarchical linear regression analyses of T1 biopsychosocial factors predicting pain-related functioning at 4 months

Table 4

Variable (T1 values) (1)	T2 Pain-related disability				T2 Quality of life			
	B	SE B	β	p	B	SE B	β	p
Step 1 (constant)	−5.07	5.40		.352	31.53	10.45		.004
Sex	5.72	2.85	.26	.050	−4.66	3.52	−.14	.193
T1 variable *	.21	.11	.25	.065	.78	.11	.71	.000
Step 2 (constant)	54.09	27.02		.051	47.10	32.4		.155
Sex	3.05	2.93	.14	.305	−1.92	3.24	−.06	.557
T1 variable *	.14	.14	.17	.308	.52	.12	.47	.000
Pain Intensity	.47	.71	.09	.514	−.59	.79	−.07	.461
Sleep Quality	1.21	2.71	.08	.658	−1.11	3.22	−.04	.731
Depressive Symptoms	.35	.14	.39	.018	−.65	.18	−.44	.001
Pain Catastrophizing	.03	.28	.02	.928	−.59	.32	−.29	.066
Fear of Pain	−.02	.14	−.03	.911	.17	.14	.18	.236
CPM Index Score	−.65	.22	−.37	.005	.16	.27	.06	.549

* T1 variable: T1 pain-related disability in model predicting T2 pain-related disability; T1 quality of life in model predicting T2 quality of life