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# Reciprocal Longitudinal Associations between Pain and Depressive Symptoms in Adolescents

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## Abstract

**Background—**Elevated depressive symptoms are common in youth with chronic pain, and pain symptoms are frequent in adolescents with depressive disorders. While studies have identified concurrent associations between pain and depression over time in youth, it is unclear how change in one symptom impacts change in the other symptom.

**Methods—**This three time point12-month longitudinal study examined reciprocal associations among pain and depression in a clinical samples of adolescents (12-18) diagnosed with chronic pain (n=55) or a depressive disorder (n=40). Mixed-effects multivariate models were used to test if changes over a preceding time interval predicted symptom severity at subsequent time points. Study group, age, sex, race, baseline pain intensity, and baseline depressive symptoms were included as covariates.

**Results—**Generalized estimating equations revealed pain and depressive symptoms were significantly associated over time ($\beta = 1.54$, $p<.001$). As hypothesized, changes in pain were associated with subsequent depressive symptoms ($B=1.16$, $p<.001$). Conversely, changes in depressive symptoms predicted subsequent pain ($B=.026$, $p<.05$), but with a weaker association. In the model predicting pain, an interaction between depressive symptoms and study group emerged ($\beta=-0.02$, $p<0.05$) with change in depressive symptoms having the greatest impact on pain in the depressed sample.

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**Conflict of interest:** None declared.

**Author Contributions**

Authors discussed the results and commented on the manuscript. Specific contributions are outlined below:

- A. Lewandowski Holley: Conceptualization/design, data analysis/interpretation, manuscript preparation
- E.F. Law: Conceptualization/design, data analysis/interpretation, manuscript preparation
- C. Zhou: Conceptualization/design, data analysis/interpretation, manuscript preparation
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**Conclusions—**Findings extend previous adult research to an adolescent sample showing changes in pain intensity are predictive of subsequent depressive symptoms. In comparison to adult data, changes in depressive symptoms had less impact on subsequent pain in youth. Future research can examine how targeting persistent pain may also aid the treatment of depressive symptoms in adolescents.

## Introduction

Elevated depressive symptoms are common in youth with chronic pain (Campo et al., 2004; Kashikar-Zuck et al., 2008) and have been associated with functional impairment (Gauntlett-Gilbert et al., 2007) and problems with school functioning (Logan et al., 2009). Risk for depression increases with pain frequency (Youssef et al., 2008), and depressive symptoms have been identified as a risk factor for pain frequency, pain persistence, and the development of new pain problems over time (Dunn et al., 2011; Larsson & Sund, 2005; Stanford et al., 2008). Similarly, research has documented that youth with depressive disorders commonly report painful symptoms. Youth diagnosed with depression endorse more frequent and severe pain than non-depressed youth (Egger et al., 1999; Murray et al., 2012), and are at higher risk for developing pain problems over time (Pine et al., 1996).

Several conceptual models and theories of chronic pain describe associations among pain and depression in children and adults. Von Baeyer and Champion (2011) suggest common vulnerabilities to pain and psychological symptoms theorizing both share genetic influences and antecedents (e.g., stress, behavioral modeling). Furthermore, Von Korff and Simon (1996) describe a reciprocal relationship proposing that pain stresses both physical and psychological systems, such that negative moods can amplify pain and impact one's ability to cope and tolerate unpleasant sensations.

Within these frameworks, it is important to examine how symptom-level changes in pain and depression influence each other over time in clinical populations. Longitudinal associations among pain and depression have been well described in adults (Fishbain et al., 1997), however the majority of research is cross-sectional or focused on group-level associations. Two recent adult studies extended this research using mixed modeling to examine longitudinal associations between pain and depression (Husted et al., 2012; Kroenke et al., 2011). Findings from both studies revealed changes in pain over preceding time periods predicted subsequent depressive symptoms, and similarly changes in depressive symptoms predicted subsequent pain. This mixed modeling approach showed change over time at the individual level rather than focusing on group-level associations.

To date, longitudinal pediatric research using clinical pain populations is limited. The vast majority of information about depressive symptoms in youth with pain has been obtained from cross-sectional data and non-clinical samples (e.g., Mikkelsson et al., 1999; Larsson & Sund, 2005). To fill this gap, we obtained serial reports of pain and depressive symptoms over one-year and examined bidirectional associations among pain and depressive symptoms in adolescents with chronic pain and primary depression. Using a similar approach as Kroenke et al. (2011), models tested how changes in one symptom (pain or depression) influenced outcomes in the other domain (depression or pain) at a later time point. We hypothesized that across groups, changes in pain and depressive symptoms would be concurrent over the study period, with adolescents experiencing an increase/decrease in one symptom showing a simultaneous increase/decrease in the other. Furthermore, we hypothesized reciprocal associations in both groups such that: 1) changes in depressive symptoms over preceding time points would predict subsequent pain, and 2) changes in pain over preceding time points would predict subsequent depressive symptoms.

## Methods

Participants included 95 adolescents (ages 12-18 years) from 2 groups, adolescents with chronic pain (n=55) and adolescents diagnosed with depressive disorders (n=40), and their parents. All participants were recruited from the Northwest region of the United States, and were taking part in a larger longitudinal observational cohort study examining pain, mood, and sleep during adolescence. Previous publications from this dataset have reported on only cross-sectional data at study enrollment and focused on: daytime and nighttime sleep patterns (Law et al., in press), associations among depression, sleep and pain in youth with depression (Murray et al., 2012), psychosocial correlates of insomnia symptoms (Palermo et al., 2011), and temporal daily associations between pain and sleep (Lewandowski et al., 2010).

This study was approved by the hospital's Institutional Review Board. All participants who met eligibility criteria and were enrolled in the study completed informed consent. Parents and adolescents age 18 provided written informed consent, and adolescents age 12-17 provided written assent.

### Participant Recruitment

Adolescents with chronic pain were recruited from a multi-disciplinary pediatric pain clinic. All patients aged 12-18 years that were undergoing an initial evaluation at the pain clinic were approached in clinic or invited to participate in the study via a letter sent to their home immediately following their clinic visit. Participants then underwent additional screening to determine study eligibility. Inclusion criteria for adolescents with chronic pain specified participants: 1) were between ages 12-18 years and currently undergoing an initial evaluation at the pain clinic, 2) had pain present for 3 months or more that occurred at least 3 days per week, 3) pain was not related to a chronic disease (e.g., sickle cell disease, arthritis, cancer), 4) did not have evidence of a developmental disability, and 5) the parent and child could read and speak English.

The sample of adolescents diagnosed with depression were youth from two sources: 1) adolescents participating in a randomized controlled trial of depression in young people (brief cognitive behavioral therapy (CBT) versus usual care), or 2) adolescents identified from an HMO pharmacy database as being diagnosed with a depressive disorder. Participants recruited from the depression study consisted solely of youth randomized to the usual care condition (e.g., evaluation and/or medication management) and did not receive the brief CBT intervention. Further inclusion criteria for depressed participants were: 1) between ages 12-18 years, 2) met criteria for a diagnosis of major depressive disorder, dysthymic disorder, or depression not otherwise specified based on psychiatric interview using the Schedule for Affective Disorders for School-Age Children (K-SADS) (Kaufman et al., 1997), 3) had a minimum score of 16 for males and 20 for females on the Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977), and 4) both the parent and adolescent could read and speak English. Adolescents were excluded from the depressed group if any of the following were met: 1) history of schizophrenia, psychosis, or bipolar disorder, 2) any serious chronic medical condition (e.g., cancer, diabetes), or 3) any evidence of a developmental disability.

The current study utilized an observational cohort design, so adolescents from both groups were able to seek a variety of treatments for pain or mood symptoms during the course of the year. All treatments received were "usual care" as participants were not taking part in a treatment study. Adolescents with chronic pain had access to treatment services in the multidisciplinary pain clinic through which they were recruited and in their community including: medical management, psychological treatment, physical therapy, acupuncture,

massage, and chiropractic treatments. Similarly youth with primary depression were able to access psychiatry, psychology or other mental health treatment services during the 12 month period.

## Enrollment Statistics

Ninety-five potential participants with chronic pain were contacted and invited to participate. Twenty were excluded due to not meeting eligibility criteria, 16 declined, and 59 were enrolled. Of the 214 potential depressed participants who were screened, 134 were excluded due to not meeting eligibility criteria, 34 declined, and 46 were enrolled.

The most common reason for ineligibility for adolescents with chronic pain was pain related to presence of a comorbid chronic disease (e.g., arthritis); the most common reason for ineligibility for the depressed sample was not meeting KSADS criteria for a current diagnosis of a depressive disorder. An additional 6 participants with depression and 4 participants with chronic pain were excluded due to large amount of incomplete data, making data from 40 youth with depression and 55 youth with chronic pain available for analyses.

In the sample of youth with chronic pain, the most frequent primary pain locations identified were headache (n = 18, 32.7%), abdominal pain (n = 14, 25.5%) and limb pain (n = 9, 16.3%), with the majority (n = 45, 81.8%) of youth reporting daily pain. Average usual pain intensity was in the moderate range at 6.56 (SD=1.68, NRS 0-10). Average CES-D scores were 14.89 (SD = 10.08) for youth with chronic pain, with 4 males and 11 females meeting the clinical cut-off (16 for males and 20 for females) for depressive symptoms. Four youth (7.3%) were diagnosed with comorbid major depressive disorder (MDD) based on the K-SADS interview.

The majority of youth with primary depression endorsed pain symptoms (95%), with the most frequent primary pain locations being: headache (n = 11, 27.5%), limb pain (n = 9, 22.5%), and back pain (n = 8, 20.0%). Pain occurred an average of two to three times per week with average usual pain intensity in the low-moderate range at 4.78 (SD = 2.04) (0-10 NRS). Mental health diagnoses (as determined by KSADS evaluation) were major depressive disorder (MDD; n=31) and mood disorder not otherwise specified (mood disorder NOS; n=9). Mean CES-D scores were 29.18 (SD=6.85) reflecting high levels of depressive symptoms.

## Procedure

All adolescents and their parents participating in the study completed study questionnaires and separate K-SADS interviews at three time points: immediately after providing informed consent (study enrollment), 6-month follow-up, and 12-month follow-up. At enrollment, adolescents and their parents participated in a study visit in participants' homes or another agreed-upon public location (e.g., recreation center). Individual K-SADS interviews were conducted in-person and participants completed questionnaires during the study visit. At 6-month and 12-month follow-ups adolescents and their parents completed the K-SADS interviews via phone, with the written questionnaires sent and returned to research staff via mail. Adolescents and parents were instructed to complete all measures independently. Participants received gift cards to local stores after completion of interviews/questionnaires at each study wave.

## Measures

**Demographics—**Parents completed a questionnaire assessing their adolescent's age, gender, race/ethnicity, parental occupation, and family income.

**Pain intensity—**Adolescents rated their usual pain intensity in the past month using an 11-point Numerical Rating Scale with anchors of 0 = no pain and 10 = worst pain possible. Specifically adolescents responded to the following prompt: "How much pain do you usually have from aches and pains". The Numerical Rating Scale is widely used to assess pain intensity in children and adolescents and has demonstrated acceptable reliability and validity (von Baeyer et al., 2009).

**Depression—**Adolescents and their parents were administered the K-SADS (Kaufman et al., 1997) at enrollment and at each follow-up time point to determine whether the adolescents met diagnostic criteria for major depressive disorder, dysthymia, or depression not otherwise specified. Meeting criteria for a depressive disorder was a requirement at enrollment for inclusion in the depressed sample. The K-SADS is a semi-structured interview that is widely used to evaluate psychiatric disorders in children and adolescents, and has demonstrated excellent reliability and validity (Kaufman et al., 1997).

Adolescents also completed the Center for Epidemiological Studies Depression Scale (CES-D (Radloff, 1977)) to assess depressive symptoms. Items on the CES-D 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 in males and 20 or greater in females indicates clinically significant depressive symptoms. The CES-D is widely used to assess depressive symptoms in children and adolescents, and has demonstrated acceptable 1-week test-retest reliability (Radloff, 1977). Validity of the CES-D is supported by documented relationships with other measures of internalizing symptoms (Radloff, 1977). Internal consistency in the current sample was good ($\alpha = .82$).

## Statistical Analyses

Summary statistics were used to describe the demographic characteristics of the sample. Means and standard deviations were used for continuous data, and categorical items were summarized using frequencies and proportions. Analyses of variance and chi-square analyses were conducted to compare various characteristics (age, gender, race/ethnicity and income levels) between groups (chronic pain versus depression). Generalized estimating equations (GEE) (Zeger et al., 1986) were used to examine concurrent associations among pain and depression over time. Participants' responses were treated as continuous, and GEE was fitted with the Gaussian family identity link function and an exchangeable working correlation structure. Pearson's correlation coefficients were used to assess associations among changes in pain and changes in depressive over time for the total sample. Paired t-tests were then used to examine within-subject changes in pain and depressive symptomsfrom enrollment to 6-months, 6 to 12 months, and enrollment to12-months.

Finally, multivariate mixed effects models (Pinheiro et al., 2009) were applied to 1) assess the associations between changes in pain and changes in depressive symptoms over time (12 months), and 2) to test prospective associations between changes in symptoms in one domain with subsequent change in the other domain over time. Specifically, subject-specific random intercepts were used to account for within-subject correlation in the outcomes due to repeated assessments. To test prospective reciprocal associations between pain and depression two models were used: Model 1 examined how changes in pain severity across the 12 month period predicted depression at subsequent time points, and Model 2 examined how changes in depression severity across the 12 month period predicted pain at subsequent time points. Each model was analyzed using both unadjusted analyses and adjusted analyses. In the unadjusted analyses, each model was run with solely the predictor (changes in pain or changes in depressive symptoms) and outcome variable (level of pain or depressive symptoms) at the subsequent follow-up time point. In the adjusted analyses, age, sex,

ethnicity, study group, and baseline pain and depressive symptoms were included as covariates to account for their potential confounding effects. We further tested whether the effect of changes in pain (or depressive symptoms) on subsequent depressive symptoms (or pain) differed across study groups by including their interaction terms in the models. Analyses within pain and primary depression groups were conducted as part of sensitivity analysis.

The mixed-effects models accounts for the correlation among outcomes within individuals due to repeated assessments. Failure to adjust for such correlation may lead to a biased estimate of standard errors and therefore inaccurate inference. It is known there is no closed form formula for the test statistic without making unreasonable assumptions, therefore we tested the significance of parameter estimates using a Markov chain Monte Carlo (MCMC) approach after the mixed effects models had been fitted (Pinheiro et al., 2009). This approach samples parameter values (random effects b and fixed effects β) from their posterior distributions p (b, β | y, X) and the uncertainty on the parameters is then summarized using these posterior samples (e.g., highest posterior density interval or posterior means/medians). All analyses were conducted in R statistical software version 2.13.2 (R Developmnet Core, 2008).

## Results

### Descriptives at Enrollment

Descriptive characteristics of participants are presented in Table 1. Adolescents had a mean age of 15.24 years (SD = 1.73) and 69% of participants were female. Complete data were available for all participants at each assessment time point (enrollment, 6 month follow-up, and 12 month follow-up). Groups did not differ on age, gender, family income or racial background variables. Cross-sectional comparisons of pain and depression symptoms between the chronic pain and primary depression groups at each time point were conducted using t-tests. As expected, results revealed significant group differences on pain intensity and depressive symptoms at enrollment, 6 month, and 12 month follow ups (all p's <.001), with youth with chronic pain reporting higher pain and youth with primary depression reporting higher depressive symptoms at each time point (see Table 2).

### Longitudinal associations between pain intensity and depressive symptoms for the total sample

GEE models revealed that for the total sample, pain intensity and depressive symptoms were significantly associated over time (β = 1.54, p<.001). When analyzed by group, GEE models showing associations among pain and depressive symptoms over time remained significant for both participants with chronic pain (β = 1.67, p<.001) and primary depression (β = 1.06, p<.01).

Correlations were used to examine associations among changes in pain intensity and changes in depressive symptoms across each time period (enrollment to 6 months; 6 to 12 months; enrollment to 12 months). Results revealed low to moderate relationships between changes in pain and depressive symptoms over time (enrollment to 6 months correlation r =. 19; 6 months to 12 months r = .36; enrollment to 12 months r =.32). These correlations between changes in pain and changes in depressive symptoms achieved statistical significance at 6 months to 12 months t(93) = 3.69, p<.001 and enrollment to 12 months t(93)=3.27, p<.001), indicating that pain and depression were changing in the same direction over time.

### Within-person changes in pain and depressive symptoms over time

Results of paired-tests that examined within-subject changes in pain intensity and depressive symptoms from: enrollment to 6 months, 6 months to 12 months, and enrollment to 12 months are presented in Table 3. For the pain group, pain intensity decreased from enrollment to 6 months [$t(54) = 2.1$, $p<.05$], however pain intensity at 12 months was not significantly different from enrollment. Depressive symptoms did not significantly change for adolescents with chronic pain over time. In the primary depression sample, depressive symptoms declined from both enrollment to 6 months [$t(39) = 4.08$, $p<.001$] and enrollment to 12 months [$t(39) = 3.67$, $p<.001$]. Changes in pain intensity (a decline in pain scores) for youth with primary depression were significant only from enrollment to 12 months [$t(39) = 2.28$, $p<.05$].

### Change in pain intensity as a predictor of subsequent depressive symptoms

In the unadjusted model for the total sample, change in pain predicted subsequent depression ($\beta=0.91$, $p<.001$). When adjusting for covariates (study group, age, sex, and race) and baseline pain and depressive symptoms, the association between change in pain intensity and subsequent depressive symptoms remained significant ($\beta = 1.16$, $p<.001$), such that a 1 point change in pain intensity over a 6 month time period (enrollment to 6 months, 6 months to 12 months) was associated with a 1.16 point change on the CES-D depression measure at the subsequent time point.

In the adjusted model, group status and baseline depressive symptoms also significantly predicted subsequent depressive symptoms ($\beta=5.74$, $p<.05$; $\beta =0.35$, $p<0.001$, respectively) (see Table 4). On average, as expected, adolescents with primary depression scored 5.74 points higher on the depression measure than participants with chronic pain ($p<.05$) (see Table 3). A final model was used to test whether associations between change in pain and subsequent depressive symptoms differed by group. The model was not significant, which suggests that the impact of change in pain on subsequent depressive symptoms was similar for adolescents with chronic pain and those with primary depression.

### Change in depressive symptoms as a predictor of subsequent pain

In the unadjusted model, change in depressive symptoms predicted subsequent pain intensity ($\beta=0.028$, $p<.05$). When adjusting for covariates (study group, age, sex, and race) and baseline pain and depressive symptoms, associations among change in depressive symptoms and subsequent pain intensity remained statistically significant ($\beta=.026$, $p<.05$) (see Table 4). Results of these analyses revealed that a 5 point change in depressive symptoms would correspond with a .13 (NRS 0-10) change in pain at the subsequent time point (e.g., enrollment to 6 months, 6 months to 12 months).

In the adjusted model, group status was a significant predictor of subsequent pain, with membership in the chronic pain group more strongly associated with subsequent pain intensity than membership in the depressed group ($\beta=-1.09$, $p<.05$). Baseline pain intensity was also significantly associated with subsequent pain intensity ($\beta=0.56$, $p<0.001$) (see Table 4). A final model was used to test whether the association between change in depressive symptoms and subsequent pain intensity differed by group. The interaction between depressive symptoms and study group was significant ($\beta=-0.02$, $p<0.05$) indicating that change in depressive symptoms had a greater impact on subsequent pain intensity for the participants in the primary depression sample.

## Discussion

To our knowledge, this is the first study to examine longitudinal bidirectional associations between pain and depressive symptoms in an adolescent sample. Results from the current study revealed important reciprocal associations between depression and pain, with the strongest association being the influence of change in pain on subsequent depressive symptoms. While a few previous studies have examined the longitudinal course of pain and depression in youth with chronic pain [e.g., (Hoff et al., 2006; Larsson & Sund 2005; Mikkelsson et al., 1999; Rhee 2000)], and epidemiologic research has examined concurrent associations between pain and depression in children (Youssef et al., 2008), these studies described only group level associations. Our findings extend this prior research by examining temporal reciprocal associations between pain and depressive symptoms at the individual rather than group level in adolescents.

Our primary findings demonstrating reciprocal associations among pain and depressive symptoms are consistent with recent studies in adult pain samples, which found similar associations in a primary care sample (Kroenke et al., 2011) and in adults with psoriatic arthritis (Husted et al., 2012). Given the developmental differences in psychological, social, and biological factors that influence adolescent chronic pain, it is critically important to conduct such studies directly in the adolescent population. The current work extends findings from the adult literature to clinical populations of youth with chronic pain and youth with primary depression. The inclusion of two samples, adolescents diagnosed with chronic pain and those with primary depression is a strength of this study as we were able to examine how group-level effects play a role in these associations. Von Korff & Simon's (1996) conceptual framework describing reciprocal associations among pain and depression can be used to understand findings that suggest changes in pain intensity over time influence subsequent depressive symptoms. For example, adolescents who experience an increase in pain symptoms may in turn decrease activity participation, have greater pain-related psychological distress, and fewer available resources to cope with mood symptoms, all factors that are implicated in depression.

In contrast to the two previous (Husted et al., 2012, Kroenke et al., 2011) studies conducted in adult samples which reported relatively equal reciprocal associations in mixed effects models, findings in our study revealed changes in adolescent depressive symptoms had less impact on subsequent pain than changes in pain on depression. One possible explanation for this finding is that other factors unique to adolescents with chronic pain that were not assessed in the current study (e.g., parental responses to pain behaviors, maladaptive thoughts about pain) may have contributed to maintenance of pain symptoms even if depression level changed. This hypothesis is supported by our finding that change in depressive symptoms had a greater impact on pain for youth with primary depression. It is possible that for many youth with chronic pain, changes in depressive symptoms alone were not sufficient to impact pain intensity.

Previous studies investigating the shared biological mechanisms underlying both pain and depression may also help explain these longitudinal, reciprocal associations. Shared brain regions process pain and regulate emotions and common neurotransmitters (e.g., serotonin, norepinephrine) are implicated in both depression and pain signaling (Ward et al., 1982). It will be important to extend this research on mechanisms of associations between pain and depression into the translational arena to examine how survey results showing differences in reports of pain and depression are linked to changes at the neurological level. For example, FMRI may be used to show activity in cortical areas that corroborate self-report.

The current study has several strengths, including longitudinal assessment, the inclusion of two study groups, and the use of a mixed effects repeated measures multivariable modeling approach. In particular, multivariable mixed modeling allows for the examination of change over time at the individual level rather that focusing solely on group-level data. The research design and corresponding statistical analyses advance the pediatric pain literature as the majority of previous studies utilized a cross-sectional single time point design or are limited to epidemiologic or community samples. There have been recent calls for additional longitudinal studies in pediatric pain (Jones, 2011) and the current work helps to fill this gap by providing preliminary data on the trajectory of pain and depressive symptoms in a clinical sample of treatment-seeking adolescents. An important next step will be to replicate these findings in adolescents from community samples, furthering previous work that has shown longitudinal associations among pain and depressive symptoms at the group level in these youth (e.g., Rhee, 2000; Larsson & Sund 2007).

Despite these strengths some limitations should be considered when interpreting the findings. Participants in this study represent samples of youth from one institution and who were predominately Caucasian and middle class. It will be important to conduct a similar study with a larger more diverse patient population to see if results are generalizable. Moreover, replicating these results separately in larger samples of youth with chronic pain and youth with primary depression will address potential concerns about small sample size. Future research could also examine how findings may differ among adolescents by type of chronic pain problem (e.g., headache, abdominal pain, musculoskeletal pain) and by type of depressive disorder (e.g., major depressive disorder, dysthymia) as it is possible that the association among pain and depressive symptoms may differ within each of these groups.

The conclusions of the study are also limited by data collection at only three time points. Although three time points are the minimum for mixed modeling analyses, it is possible that symptoms of pain and depression may have fluctuated more over the course of the year or had differing associations at other time periods. Examination of pain and depressive symptoms at more frequent intervals may provide more information about reciprocal relationships over time.

Finally, this is an observational cohort study that examined naturalistic changes in pain and depressive symptoms over the course of the year. While the data show statistical significance, conclusions regarding clinical or social significance cannot be made. Future research examining the reciprocal association among pain and depression in the context of treatment would provide an important replication and direct test of these findings. Moreover, a similar multilevel modeling statistical approach could be used to compare treatment effects of multi-arm intervention studies. Such analyses can examine how order of intervention (e.g., pain treatment followed by depression treatment, versus depression treatment followed by pain treatment) impacts symptom change and reciprocal outcomes over time.

In summary, data from the present study provides preliminary support for the assertion that changes in pain and depressive symptoms exert influence on each other, extending previous adult research examining reciprocal associations between pain and depressive symptoms.

These findings may also generate additional studies that have more direct implications for the management of pain and depression in adolescents. Current cognitive behavioral interventions for adolescents with chronic pain have some overlap with cognitive behavioral interventions for depression, including teaching problem-solving, providing instruction in relaxation and cognitive strategies, and focusing on reintegration into physical and social activities (Kashikar-Zuck et al., 2012, Palermo et al., 2009). At present, there are not specific treatment recommendations for youth with chronic pain who have significant

comorbid depressive symptoms, and this remains an important population to consider in future intervention research.

Future work can also build on the findings from the current study by assessing how changes in pain and depressive symptoms are associated with important functional outcomes such as school attendance and family/peer relationships. Research has revealed that adults with comorbid depressive disorders and painful physical symptoms are less productive in the workplace and show less help-seeking behavior (Demyttenaere et al., 2006). Moreover, in a cross-sectional study of youth with chronic pain, higher depressive symptoms predicted more school impairment (e.g., absences, school adjustment, scholastic competence, grades) (Logan et al., 2009). In future prospective research it will be important to examine how reduction or remission of symptoms and dually focused treatments may lead to improvements in children's socio-emotional functioning and activity participation.

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**Bulleted Statements**

*What is already known about this topic?*

- Elevated depressive symptoms are common in children with chronic pain; pain is frequent in youth with depressive disorders.
- Research in adults with chronic pain has demonstrated reciprocal associations among pain and depressive symptoms over time.

*What does this study add?*

- Findings contribute to limited longitudinal pediatric pain research examining changes in symptoms over time.
- The mixed-modeling analytic approach examines reciprocal associations among pain and depressive symptoms in adolescents.

## Table 1

Demographic characteristics for the total sample and by group.

| Characteristic | Overall (N=95) | Pain group (N=55) | Depression group (N=40) |
|---|---|---|---|
| Age, mean (SD), year | 15.24 (1.73) | 15.10 (1.71) | 15.43 (1.76) |
| Gender, n (%) | | | |
| Male | 29 (31%) | 14 (25%) | 15 (37%) |
| Female | 66 (69%) | 41 (75%) | 25 (63%) |
| Race, n (%) | | | |
| Caucasian | 78 (82%) | 48 (87%) | 30 (75%) |
| African American | 1 (1%) | 0 (0%) | 1 (3%) |
| American Indian | 4 (4%) | 2 (4%) | 2 (5%) |
| Asian | 2 (2%) | 1 (2%) | 1 (3%) |
| Other | 10 (10%) | 4 (7%) | 6 (15%) |
| Ethnicity, n (%) | | | |
| Hispanic | 10 (11%) | 4 (7%) | 6 (15%) |
| Non-Hispanic | 80 (84%) | 49 (89%) | 31 (78%) |
| Not reported | 5 (5%) | 2 (4%) | 3 (7%) |
| Family Income | | | |
| < $29,000 | 6 (6%) | 5 (9%) | 1 (3%) |
| $30,000 – $49,000 | 15 (16%) | 10 (18%) | 5 (13%) |
| $50,000 – $69,000 | 20 (21%) | 8 (14%) | 12 (30%) |
| > $70,000 | 47 (50%) | 28 (51%) | 19 (48%) |
| Not reported | 7 (7%) | 4 (8%) | 3 (6%) |

**Table 2**

Results of t-tests comparing group differences in pain and depressive symptoms at each time point.

| | Pain intensity, Mean (SD) | | | Depressive symptoms, Mean (SD) | | |
|---|---|---|---|---|---|---|
| **Time periods** | **Pain group** | **Depression group** | **P-value** | **Pain group** | **Depression group** | **P-value** |
| Baseline | 6.56 (1.68) | 4.78 (2.04) | <0.001 | 14.89 (10.08) | 29.18 (6.85) | <0.001 |
| 6 month | 6.05 (2.01) | 4.47 (2.04) | <0.001 | 13.93 (9.46) | 23.23 (8.07) | <0.001 |
| 12 month | 6.16 (2.18) | 4.05 (2.04) | <0.001 | 14.55 (10.19) | 23.30 (8.15) | <0.001 |

**Table 3**

Results of within-person analyses examining changes in pain intensity and depressive symptoms presented by group

| **Change in pain intensity** | | | | | | |
|---|---|---|---|---|---|---|
| | **Enrollment to 6 months** | | **6 months to 12 months** | | **Enrollment to 12 months** | |
| | **t** | **P-value** | **t** | **P-value** | **t** | **P-value** |
| Pain Group | 2.1 | 0.04 | −.37 | 0.72 | 1.4 | 0.17 |
| Depression Group | 1.04 | 0.31 | 1.65 | 0.11 | 2.28 | 0.03 |
| Change in depressive symptoms | | | | | | |
| | Enrollment to 6 months | | 6 months to 12 months | | Enrollment to 12 months | |
| | t | P-value | t | P-value | t | P-value |
| Pain Group | .71 | 0.48 | −0.51 | 0.62 | 0.23 | 0.82 |
| Depression Group | 4.08 | <0.001 | −.06 | 0.95 | 3.67 | <0.001 |

**Table 4**

Change in pain intensity as a predictor of subsequent depression and change in depressive symptoms as a predictor of subsequent pain intensity as reflected in mixed linear modeling analysis.

| | Depressive Symptoms | | | Pain Intensity | | |
|---|---|---|---|---|---|---|
| Predictors | Beta | 95% CI | P-value | Beta | 95% CI | P-value |
| Unadjusted model | | | | | | |
| Change Pain | 0.91 | (0.13, 1.57) | <0.001 | - | - | - |
| Change Depression | - | - | - | 0.028 | (0.01, 0.08) | 0.026 |
| Fully adjusted models | | | | | | |
| Change Pain | 1.16 | (0.75, 2.03) | <0.001 | - | - | - |
| Change Depression | - | - | - | 0.026 | (0.01, 0.07) | 0.04 |
| Depression Group | 5.74 | (2.24, 9.58) | 0.01 | −1.09 | (−1.95, -0.33) | 0.02 |
| Age | −0.43 | (−1.17, 0.26) | 0.32 | 0.06 | (−0.06, 0.25) | 0.49 |
| Female Gender | 1.79 | (−.91, 4.52) | 0.29 | 0.18 | (−0.41, 0.76) | 0.61 |
| Non-Hispanic | 1.05 | (−2.96, 4.91) | 0.67 | −0.08 | (−.95, 0.78) | 0.87 |
| Baseline Depression | 0.35 | (0.21, 0.49) | <0.001 | 0.01 | (−0.02, 0.05) | 0.49 |
| Baseline Pain | 0.65 | (0.01, 1.42) | 0.14 | 0.56 | (0.42, 0.72) | <0.001 |

Note: Both 95% confidence intervals and P-values are based on MCMC simulations for the parameters from the fitted mixed effects models.