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Longitudinal evaluation of Patient Reported Outcomes Measurement Information Systems (PROMIS) measures in pediatric chronic pain

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Abstract

The Patient Reported Outcomes Measurement Information System (PROMIS) initiative is a comprehensive strategy by the National Institutes of Health to support the development and validation of precise instruments to assess self-reported health domains across healthy and disease-specific populations. Much progress has been made in instrument development but there remains a gap in the validation of PROMIS measures for pediatric chronic pain. The purpose of this study was to investigate the construct validity and responsiveness to change of seven PROMIS domains for the assessment of children (ages 8-18) with chronic pain – Pain Interference, Fatigue, Anxiety, Depression, Mobility, Upper Extremity Function and Peer Relationships. PROMIS measures were administered at the initial visit and two follow-up visits at an outpatient chronic pain clinic (CPC; N=82) and at an intensive amplified pain day-treatment program (AMP; N= 63). Aim 1 examined construct validity of PROMIS measures by comparing them with corresponding "legacy" measures administered as part of usual care in the CPC sample. Aim 2 examined sensitivity to change in both CPC and AMP samples. Longitudinal growth

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models showed that PROMIS Pain Interference, Anxiety, Depression, Mobility, Upper Extremity and Peer Relationship measures and legacy instruments generally performed similarly with slightly steeper slopes of improvement in legacy measures. All seven PROMIS domains showed responsiveness to change. Results offered initial support for the validity of PROMIS measures in pediatric chronic pain. Further validation with larger and more diverse pediatric pain samples and additional legacy measures would broaden the scope of use of PROMIS in clinical research.

Keywords

patient-reported outcomes; PROMIS; pediatric pain; quality of life; pain interference

Introduction

The Patient Reported Outcomes Measurement Information System (PROMIS) was initiated by the National Institutes of Health to develop and validate patient-reported outcomes (PROs) for use in clinical research and patient care. Traditionally, PROs have not been standardized to allow for meaningful comparison across clinical trials or patient populations, impose high respondent burden, may show lack of sensitivity to change, and demonstrate floor/ceiling effects. PROMIS aims to address these shortcomings by using a rigorous mixed methods approach, including item response theory (IRT) in scale development. IRT rests on the assumption (and careful testing) of invariance which enables comparison of results across studies. Calibration is at the level of individual items - which allows for computerized adaptive testing or use of parsimonious “short forms” of informative items, thereby reducing respondent burden. IRT yields a smaller standard error of measurement resulting in measures that have increased precision and are more sensitive to change - thus requiring fewer subjects to detect differences between treatment groups [2, 21]. The PROMIS Network has successfully applied this rigorous item development process to create several item banks for use across adult and pediatric chronic health conditions [1, 3, 21]. However, PROMIS measures have not been validated nor has their sensitivity to change been evaluated in pediatric chronic pain.

Chronic pain in children is highly prevalent and often associated with pain-related disability and reduced quality of life [7,12, 22, 24]. Pain can be widespread (multiple body areas) or regional (limited to a single body location) and can encompass a number of different pain syndromes (e.g., juvenile fibromyalgia, low back pain). Irrespective of the distinct entity, children with chronic pain often report impairments in physical, school, social, and emotional functioning [5, 7-10, 15, 20] and treatment is generally focused on functional rehabilitation consisting of physical therapy and cognitive-behavioral approaches. The etiologies of chronic pain are often uncertain and there are no objective disease markers, therefore assessment of clinical status requires heavy reliance on self-report of internal symptoms. Because the assessment is so highly dependent upon self-reports of pain and function, it is of great importance that PROs used be well-validated and responsive to change. Yet the field lacks consistency in which measurement scales are being used, making comparisons across studies very challenging.

The primary aim of this study was to evaluate the construct validity of PROMIS pediatric measures in children presenting for outpatient treatment of chronic pain by examining the congruence between PROMIS measures and corresponding legacy scales (i.e., validated measures currently administered in the clinic) over the course of outpatient treatment. It was hypothesized that there would be good congruence between the longitudinal trajectories of PROMIS measures and corresponding legacy scales measured at baseline and 2 follow-up assessments. The second aim was to examine the responsiveness to change of pediatric PROMIS measures in patients seen at two different chronic pain treatment settings: an outpatient clinic and an intensive day program. Differential rates of change in PROMIS scores were anticipated, with the more intensive day-treatment program yielding faster improvement.

Methods

Participants

Children and adolescents with chronic pain were recruited for this study from an outpatient multi-disciplinary pediatric Chronic Pain Clinic (CPC) (Aims 1 and 2) at a Midwestern children's hospital and an intensive day program, the Amplified Musculoskeletal Pain Program (AMP) (Aim 2) at a Northeastern children's hospital between October 2010 and January 2012. Patients were eligible if they were between the ages of 8 and 18 years, fluent in English and had been diagnosed by a pediatric pain physician or board certified pediatric rheumatologist to have a chronic pain condition (e.g., low back pain, widespread pain or fibromyalgia, complex regional pain or amplified regional pain). Children with a documented developmental delay or severe psychopathology (e.g., untreated bipolar disorder, psychosis) that would interfere with comprehension or accurate completion of self-report measures were excluded.

Procedure

Eligible patients were identified for the study through review of hospital electronic medical records or by referral from the physicians in each of the pain clinics. A research coordinator approached the family at a clinic visit and if they were interested in participating, the study was explained to them and any questions or concerns were addressed. Patients were assured that their clinical care would not in any way be affected regardless of their participation in the study. Written assent and consent were obtained from the participant and parent/legal guardian for this study which had Institutional Review Board approval at each of the sites.

Treatment Settings—Both the CPC and AMP programs followed an approach geared towards improving function and reducing pain using a multidisciplinary plan including medical assessment and monitoring (pain medications are included in the CPC program but not in the AMP program), physical/occupational therapy and cognitive behavioral therapy [4, 11, 16, 19, 23, 29]. The programs varied in intensity and duration. The outpatient CPC program is structured such that new patients undergo evaluation by a multidisciplinary team including a pain physician, nurse, physical therapist, and pain psychologist. A multidisciplinary plan is made with the patients and families based on information derived from history, physical exam, and relevant testing and radiographic data. Patients are

typically referred for physical therapy 1-3 times a week and the duration tailored to the patients' progress and tapered over time as the patient gains independent functioning. The cognitive behavioral therapy protocol recommended for most patients involves a series of approximately 4-6 weekly individual coping skills training sessions with the patient, supplemented with parental involvement (as clinically indicated) to enhance use of coping skills at home and to address school and social issues. Medication treatment is tailored to the patients' needs and ranged from none to muscle relaxants, anti-inflammatory agents, neuropathic medications, and opioids.

The AMP program is an intensive multidisciplinary day-treatment program for patients with musculoskeletal pain with a strong focus on physical and occupational therapy (2-3 hours of each therapy, five days a week). Additionally, patients participate in a minimum of 2 hours of music and art therapy each week, as well as 2-3 hours of cognitive behavioral therapy and family therapy as indicated. Both CPC and AMP programs address not only the patient's physical symptoms, but also psychosocial and school issues, with long-term goals being reintegration into school, functioning at an age-appropriate level of motor skills, improvement in activities of daily living and social situations, and referrals for continued psychosocial support as needed.

Assessment Protocols—All patients completed initial study assessments at their first outpatient CPC clinic visit or upon admission into the AMP program. Two additional assessments were completed at follow-up, the timeframes for which varied by site to reflect the differing courses of treatment. Specifically, follow-up assessments for the outpatient CPC program were conducted at clinic visits approximately 3-5 months and 6-12 months following the initial assessment. For the intensive AMP day-treatment program, the second assessment was completed at the time of discharge from the program, usually 3-4 weeks after the first assessment, and the third assessment was completed at a follow-up clinic visit approximately 6 months after completion of the program.

At initial assessment, basic demographic and clinical information was obtained which included age, sex, race, ethnicity, and diagnosis. Study questionnaires were administered via computer (PROMIS measures) and on paper (legacy measures). At both study sites, PROMIS pediatric short forms of the Pain Interference, Mobility, Upper Extremity, Anxiety, Depressive Symptoms, Fatigue, and Peer Relationships domains were administered on the computer. Legacy measures were administered only at the outpatient CPC and based on the standard clinical assessment battery which consisted of - the Functional Disability Inventory (FDI), Pain Intensity 0-10 Numeric Rating Scale, Pediatric Quality of Life Inventory Generic Core Scales (PedsQL™) and the Children's Depression Inventory (CDI). Short-form PROMIS measures and their corresponding legacy measures are listed in Table 1. At follow-up visits, patients completed the identical PROMIS short form measures (CPC and AMP program) and legacy measures (CPC clinic). Each assessment took approximately 20-30 minutes and the patients were allowed to take breaks as needed. For each assessment, the child or adolescent was given a cash incentive ($10) for time and effort in the study.

Measures

PROMIS Pediatric Short Forms—PROMIS Short Form measures included the Version 1.0 pediatric self-report versions of physical, mental, and social health that were potentially relevant for use in pediatric chronic pain populations, i.e. Pain Interference (8 items), Mobility (8 items), Upper Extremity Function (8 items), Anxiety (8 items), Depressive Symptoms (8 items), Fatigue (10 items), and Peer Relationships (8 items). Even though impairment in upper extremity function is relatively infrequent in chronic pain clinics, this measure was included because it was used as part of a larger investigation comparing the performance of PROMIS instruments in various painful pediatric conditions including those where upper extremities may be affected, e.g., juvenile arthritis. Each measure was developed to be a unidimensional assessment of the construct using only the most informative items. Response format is consistent across measures and is based on a 5-point Likert scale with the anchors “Never” (0) and “Almost always” (4). Raw score totals on each measure can be converted to a T-score using look-up tables. More information on these measures can be found at www.nihpromis.org.

Legacy Scales

Functional Disability Inventory – Child Version: The FDI is a 15-item self-report inventory developed to assess perceived difficulty in the performance of daily activities in home, school, recreational, and social domains [28]. The FDI is one of the most widely available questionnaires to assess disability in school-age children with chronic pain. Scores range from 0-60 with higher scores indicating greater disability. Healthy controls report a mean score of 3 on the FDI, whereas patients with chronic pain typically report total scores between 12-25, depending on the population [6, 22, 28].

PedsQL™ Version 4.0 Generic Core Scales, Child or Teen Report (PedsQL™): The PedsQL™ is a widely used 23-item, self-report questionnaire assessing children’s (5-7, 8-12 years) and adolescents’ (13-18 years) perceptions of health-related quality of life across four domains: physical, emotional, social, and school functioning. Responses are made on a 5-point Likert scale, from 0 (Never a problem) to 4 (Almost always a problem). The measure yields subscale scores on the four domains and a total summary score (0-100) [25-27]. The PedsQL has been shown to differentiate healthy from chronically ill children and adolescents [26].

Children’s Depression Inventory (CDI): The CDI is a 27-item scale assessing symptoms of depression in children and has been used extensively in the assessment of mood in children with chronic pain [13, 14, 17]. It yields a total score and subscale scores on negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem. Separate norms are available for boys and girls ages 7-12 and 13-17.

Statistical Analyses

Aim 1: To determine construct validity of pediatric PROMIS measures—Parallel process longitudinal growth models (LGM) were employed to examine congruence between PROMIS measures and corresponding legacy scales over the course of treatment. This statistical approach was selected for several reasons. Similar to other approaches (e.g.,

within-subjects ANOVA), LGMs can estimate the average level at which children start the study (the intercept) and the average change in PROMIS and legacy measures' scores over time (the slope). LGMs also offer several other advantages: 1) they can empirically describe the amount of variance in scores (across children) at baseline (intercept variance) and the amount of variance in change across time (slope variance). In this way, LGMs properly account for dependence in the data (multiple observations on the same children), estimate change, and describe variance. 2) Parallel process LGMs can simultaneously estimate change in two (or more) measures across time and allow one to directly compare the amount of change across time. 3) They also provide an estimate of the size of the correlation between two processes' slopes. 4) LGM's utilize all available data (individuals can have missing data for one or more time points) and unequal amounts of time between observations across individuals is easily accommodated. Thus, these models provide a powerful method to examine congruence between PROMIS measures and corresponding legacy measures over time.

In this study, parallel process LGMs were estimated for 6 domains assessed by PROMIS (Pain Interference, Mobility, Upper Extremity Function, Depressive Symptoms, Anxiety, and Peer Relationships) and related legacy measures administered at the CPC clinic. There was no legacy measure for the Fatigue domain; hence the validity of this construct was not tested in this Aim. For all other measures, we examined the average amount of change in each construct across time, the amount of variance in each construct at the study's start, the amount of variance in each construct's trajectory, the extent to which a child's initial value on a PROMIS measure predicted a child's initial value on the corresponding legacy measure, and the extent to which a child's change on a PROMIS measure predicted a child's change on the corresponding legacy measure. In the models, we coded "time" as the number of months from an individual's initial visit. Mplus 7.1 [18] was used to estimate the LGM models. For all models, we ensured that the assumptions associated with LGM parallel process models (e.g., heteroscedasticity, influence, leverage, etc.) were met. Effects of child age were tested for all models and found not to be statistically significant. Therefore, age was not used a covariate in the final models.

Aim 2: Responsiveness/sensitivity of pediatric PROMIS measures to change —To examine the responsiveness to change of the pediatric PROMIS measures, single process LGMs were employed. In these models, we examined change across time and whether differential treatment setting (outpatient CPC vs. AMP intensive day program) was associated with different initial levels and different rates of change (as hypothesized). We first fit unconditional growth models (no predictors other than time) to assess the average trajectory over time and the inter-individual variability. We then fit two conditional models: the first included site (CPC, AMP) as predictor and the second conditional model included the site by time interaction.

Results

A total of 145 participants were enrolled and completed baseline assessments (CPC N=82, AMP N=63). The majority of the patients (83.3%) were female and White/Caucasian (93.8%). The mean age of the patients was 14.56 years (SD = 2.38). The sample consisted of

a mixed group of primarily musculoskeletal pain conditions with patients reporting pain in the following body locations: generalized musculoskeletal pain (45.5%), back pain (24.8%), lower extremity pain (22.1%), upper extremity pain (4.1%), neck pain (2.1%) and upper and lower extremity pain (1.4%). Due to differences in nomenclature in the CPC and AMP programs, diagnostic groupings such as fibromyalgia or complex regional pain were not used. Retention of CPC participants at first follow-up was 70.7% and 52.4% for the second follow-up, which is typical for a CPC outpatient clinic. Retention of AMP participants at first follow-up was 100% and 87.1% for the second follow-up, which is reflective of higher retention for the shorter, more intensive course of treatment in the AMP program.

Construct validity of PROMIS measures (fixed effect models)

The fixed effects (slopes and intercepts) for each PROMIS domain and their corresponding legacy measure over time in each parallel process model were examined in the CPC group where both PROMIS and legacy measures were administered (Table 2). The slopes represent change in scores over time where a negative slope indicates a decrease in the construct being measured, and a positive slope indicates an increase in the construct being measured. For example, a negative slope for pain interference indicates a reduction (improvement) in pain interference scores over time, whereas a positive slope for mobility represents an improvement in physical function scores over time. In each of the six models examined, PROMIS and legacy measures performed similarly over the course of outpatient treatment.

For the models simultaneously estimating change across time, three domains showed statistically significant improvement over time. For PROMIS Pain Interference and the FDI, statistically significant slopes for both measures were observed (Pain Interference slope = −0.06, $p < 0.01$; FDI slope = −0.72, $p < 0.01$). The standardized slopes showed that Pain Interference decreased more slowly than the FDI (−0.86 vs. −1.12). The models for comparing PROMIS Mobility versus PedsQL Physical Function, and PROMIS Anxiety versus PedsQL™ Emotional Function showed a similar pattern of results (Table 2), with scores showing significantly improved functioning across time and the PROMIS measures (using the standardized metric) showing slightly slower rates of improvement.

The parallel-process models examining PROMIS Depressive Symptoms versus CDI Total scores, and PROMIS Peer Relationships versus PedsQL™ Social Function scores again showed that the PROMIS and legacy measures performed similarly, with both showing no statistically significant change. In the PROMIS Upper Extremity and PedsQL™ Physical Function parallel process model, no significant improvement was found in PROMIS Upper Extremity scores but statistically significant improvement across time for the PedsQL™ Physical Function scores was observed.

Construct validity of PROMIS measures (random effect models)

The random effect parallel process models examined variances in the intercepts and slopes, as well as the covariances among the slopes and intercepts. Across all parallel process LGMs, we saw statistically significantly correlated intercepts (Table 3) with the majority of these correlations being larger than 0.9. These findings indicated that a child's score on the

legacy measure strongly predicts a child's score on the related PROMIS measure. Also, rank orderings across measures were markedly consistent. Both these findings support the construct validity of PROMIS measures. For all the parallel process LGM (with the exception of the PROMIS Peer Relationship versus PedsQL™ Social Function and PROMIS Depressive Symptoms versus CDI Total Score models), statistically significantly correlated slopes were also observed. Again, all correlations were high, with the majority being larger than 0.9. These results indicate that - a child's rate of change on the legacy measure strongly predicted a child's rate of change on the related PROMIS measure, and that a rank order of children's rates of change on the legacy measure corresponded closely to a rank order of the children's rates of change on the related PROMIS measure. Table 3 summarizes the random effects for all models. Finally, Figure 1 uses a side-by-side panel approach to graphically illustrate the results of the parallel process LGMs for the Pain Interference – FDI model as an example. The remaining models showed very similar results showing that PROMIS and legacy measures performed comparably.

Sensitivity of PROMIS measures to change (unconditional models examining change over time only)

Results of the unconditional growth models showed that all PROMIS measures showed sensitivity to change (CPC and AMP samples combined). As such, significant improvements were observed on PROMIS measures of Pain Interference, Mobility, Upper Extremity Function, Fatigue, Depressive Symptoms, Anxiety and Peer Relationships. Tables 4 through 6 present the results for all PROMIS measures.

Sensitivity of PROMIS measures to change (conditional models examining change over time by site)

In the first conditional model, site by time effects were observed in several domains showing a faster rate of improvement in the AMP program compared to the CPC. For Pain Interference, site significantly predicted the average growth trajectory as expected, such that AMP patients had a larger change (improvement) in Pain Interference scores than CPC patients. In the second conditional model, the site by time interaction was significant (see Figure 2, upper left panel), suggesting that the trajectories for each site are not parallel. The AMP program had a steeper overall trajectory, indicating that the patients in the AMP program experienced a more rapid rate of improvement in their Pain Interference scores over time. The same pattern of result was observed for the PROMIS Mobility (see Figure 2, lower left panel) measure, which showed a faster rate of improvement in Mobility in the AMP program.

For PROMIS Depressive Symptoms, the first conditional model indicated that the change in Depression over time did not differ between sites. In the second conditional model, the time by site interaction was statistically significant, indicating that the trajectories for each site were not parallel (see Figure 2, lower right panel). The results of the two conditional models suggest that the patients in the AMP program showed a more rapid improvement in PROMIS Depression scores over time than the CPC, but that the difference between the trajectories was not as large as it was for PROMIS Pain Interference, Mobility, and Upper Extremity Function measures. The same pattern of results was observed for the PROMIS

Fatigue measure (see Figure 2, upper right panel). For the PROMIS Anxiety measure, there were no significant site differences, or significant site by time interaction observed. This suggests that the change over time in Anxiety was similar and parallel for the two sites. For the PROMIS Peer Relationships measure, the first conditional growth model indicated that CPC patients had overall higher average Peer Relationship scores (across time points) than AMP patients. In the second conditional growth model, the site by time interaction was also significant, indicating that the trajectories for the two sites were not parallel. Scores of AMP patients (who scored lower than CPC patients at the initial time point) had a steeper overall trajectory, indicating more rapid improvement in Peer Relationship scores over time whereas the CPC group showed a less steep trajectory but maintained higher Peer Relationship scores overall.

Discussion

Results of this study provided preliminary support for the validity and responsiveness of PROMIS measures in a clinical pediatric pain population. Participants in this study were school-age children primarily with chronic musculoskeletal pain undergoing multidisciplinary treatment in one of two tertiary care pediatric settings (outpatient CPC and intensive AMP programs). The construct validity of 6 PROMIS pediatric short-form scales (Pain Interference, Mobility, Upper Extremity Function, Anxiety, Depressive Symptoms and Peer Relationships) were examined in the CPC sample by comparing them with legacy instruments routinely administered in the clinic. Evidence of convergent validity was found for 5 of the 6 PROMIS scales (Pain Interference, Mobility, Anxiety, Depressive Symptoms and Peer Relationships) which corresponded well with legacy measures in all analyses performed. For each of these scales, patients' scores on legacy measures were strongly correlated with PROMIS measures, consistency in rank-order was seen and PROMIS and legacy measures performed similarly over the course of outpatient treatment. Only one PROMIS scale - Upper Extremity Function did not perform similarly to the legacy measure (PedsQL Physical Function). This is not unexpected because items in the PROMIS Upper Extremity scale are unidimensional and specifically relevant to activities using upper limbs and fine motor dexterity which are often not impaired in a chronic pediatric pain population. Hence, the lack of consistency in the PROMIS Upper Extremity scale and PedsQL Physical Function subscale may be an indication that this scale is not likely to be particularly useful in many chronic pain clinic patients.

The second aim of this study was to determine if PROMIS measures were sensitive to change in pediatric patients receiving usual care at multidisciplinary chronic pain programs and again, strong evidence was found indicating that PROMIS measures demonstrated the anticipated response across both CPC and AMP programs. Specifically, significant reductions in PROMIS Pain Interference, Fatigue, Anxiety and Depressive symptom scores were found over the course of time, along with significant increases in Mobility, Upper Extremity Function and Peer Relationship scores. Furthermore, as expected, the rate of change as demonstrated by the trajectories of change in PROMIS measures showed differential rates – with faster improvement in the intensive AMP program compared to the less intensive outpatient treatment approach. It should be noted that a limitation of this study was that it was not a comparative trial of the two clinical approaches. To test differential

efficacy and rigorously test responsiveness to treatment effects, a different study design would be needed with standardized treatment and uniform assessments over a longer time period since these varied considerably between programs, systematic measurement of adherence to treatment recommendations, and potentially a third, no-treatment control condition to estimate change purely as a function of time. However, these types of study designs are challenging to implement in a real-world clinical setting. Nevertheless, it is reassuring that given the varied formats and timeframes of treatment, the PROMIS measures showed improvements as expected indicating that findings may be generalizable to similar clinical settings.

An interesting finding that emerged from this study was that although the PROMIS measures of Pain Interference, Mobility, Anxiety, Depressive Symptoms and Peer Relationships performed similarly to legacy measures administered in the CPC clinic, they did not show as steep a change in improvement trajectories over time as their corresponding legacy measures. Close examination and comparison of individual items comprising the measures reveals that this most likely relates to the unidimensionality and precision of the PROMIS measures with respect to a particular construct, whereas the legacy scales tend to be more multidimensional and capture various aspects or a construct. For example, items on the PROMIS Depressive symptoms scale focus primarily on feelings on sadness, lack of enjoyment and being unhappy. The CDI, on the other hand is known to encompass 5 factors which include negative mood, interpersonal difficulties, ineffectiveness, anhedonia and negative self-esteem. A clinician might indeed want information about each of these dimensions to make a clinical diagnosis of depression for which the CDI may be a better choice than the PROMIS measure of depressive symptoms Alternatively, pain clinics might want a brief “screener” for depressed mood that can be quickly administered as part of a screening battery of measures than can identify areas for further assessment or an easily administered tool that can be incorporated into a larger patient registry tracking specific outcomes over time, for which the PROMIS short-form may be a better choice. Therefore, the selection of PRO measures, whether for clinical care or for clinical research, requires careful consideration of what construct/s exactly the investigator is interested in measuring and the specificity of the PRO “assay” that is required for the study. In this regard, PROMIS measures through rigorous IRT methods have distilled brief, specific, but highly informative measurement tools for each domain. Several of these are highly applicable and relevant to pediatric chronic pain conditions as demonstrated in this study.

Although this study provided good support for the use of PROMIS measures in chronic musculoskeletal pain, results may not be generalizable to other common pediatric recurrent pain conditions (e.g., functional abdominal pain or pediatric migraine) or disease-related pain (juvenile arthritis, sickle cell disease) which requires further study. Of note, juvenile arthritis and sickle cell disease are being studied separately as disease-specific sub groups in other studies by the PROMIS network.

In addition, further examination of the construct validity of the PROMIS Fatigue scale (for which a legacy measure was not available in this study) and the PROMIS Anxiety scale (for which a closely corresponding anxiety legacy measure was not available) is needed. Other limitations of this study were the length of some legacy measures, the relatively small

sample sizes for the overall sample, and the lower retention rate in the CPC sample - which although typical of real-world clinical settings, may have over-represented treatment compliers in the sample. Therefore, testing the stability of the LGM models in more rigorous clinical trials or longitudinal research studies with more time points and larger sample sizes and assessment of treatment compliance would allow stronger testing of responsiveness to treatment effects more specifically. Larger samples would also allow comparison of responses to PROMIS measures in different pediatric pain subgroups. Despite these limitations, this is the first investigation that offers support for several rigorously developed and easily accessible PROMIS Short-Form measures that are currently available. These measures have the potential to greatly strengthen PRO measurement and consistency in pediatric pain conditions which, due to the need for subjective report, by definition rely heavily on patient report for symptom monitoring and determination of treatment outcomes. Further study of minimally important differences and clinically-relevant cut-offs of PROMIS short-forms for pediatric chronic pain will likely facilitate greater adoption of PROMIS measures in pediatric chronic pain research and clinical care.

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References

[1]. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, Ader D, Fries JF, Bruce B, Rose M. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. Medical care. 2007; 45(5 Suppl 1):S3. [PubMed: 17443116]

[2]. Chang C-H, Reeve BB. Item response theory and its applications to patient-reported outcomes measurement. Evaluation & the health professions. 2005; 28(3):264–282. [PubMed: 16123257]

[3]. DeWalt DA, Rothrock N, Yount S, Stone AA. Evaluation of item candidates: the PROMIS qualitative item review. Medical care. 2007; 45(5 Suppl 1):S12. [PubMed: 17443114]

[4]. Eccleston C, Palermo TM, Williams AC, Lewandowski Holley A, Morley S, Fisher E, Law E. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev. 2014; 5:CD003968. [PubMed: 24796681]

[5]. Guite JW, Logan DE, Sherry DD, Rose JB. Adolescent self-perception: associations with chronic musculoskeletal pain and functional disability. Journal of Pain. 2007; 8(5):379–386. [PubMed: 17275417]

[6]. 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):1600–1607. [PubMed: 21458162]

[7]. 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):341–349. [PubMed: 11783815]

[8]. Kashikar-Zuck S, Johnston M, Ting TV, Graham BT, Lynch-Jordan AM, Verkamp E, Passo M, Schikler KN, Hashkes PJ, Spalding S, Banez G, Richards MM, Powers SW, Arnold LM, Lovell D. Relationship between school absenteeism and depressive symptoms among adolescents with juvenile fibromyalgia. J Pediatr Psychol. 2010; 35(9):996–1004. [PubMed: 20360017]

[9]. Kashikar-Zuck S, Lynch AM, Graham TB, Swain NF, Mullen SM, Noll RB. Social functioning and peer relationships of adolescents with juvenile fibromyalgia syndrome. Arthritis and Rheumatism. 2007; 57(3):474–480. [PubMed: 17394218]

[10]. Kashikar-Zuck S, Parkins IS, Graham TB, Lynch AM, Passo M, Johnston M, Schikler KN, Hashkes PJ, Banez G, Richards MM. Anxiety, mood, and behavioral disorders among pediatric patients with juvenile fibromyalgia syndrome. Clinical Journal of Pain. 2008; 24(7):620–626. [PubMed: 18716501]

[11]. Kashikar-Zuck S, Ting TV, Arnold LM, Bean J, Powers SW, Graham TB, Passo MH, Schikler KN, Hashkes PJ, Spalding S, Lynch-Jordan AM, Banez G, Richards MM, Lovell DJ. Cognitive behavioral therapy for the treatment of juvenile fibromyalgia: A multisite, single-blind, randomized, controlled clinical trial. Arthritis Rheum. 2012; 64(1):297–305. [PubMed: 22108765]

[12]. Kashikar-Zuck S, Vaught MH, Goldschneider KR, Graham TB, Miller JC. Depression, coping and functional disability in juvenile primary fibromyalgia syndrome. Journal of Pain. 2002; 3(5): 412–419. [PubMed: 14622745]

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

[14]. 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. J Pain. 2013; 14(7):689–698. [PubMed: 23642409]

[15]. Logan DE, Simons LE, Stein MJ, Chastain L. School impairment in adolescents with chronic pain. J Pain. 2008; 9(5):407–416. [PubMed: 18255341]

[16]. Maillard SM, Davies K, Khubchandani R, Woo PM, Murray KJ. Reflex sympathetic dystrophy: a multidisciplinary approach. Arthritis Care & Research. 2004; 51(2):284–290. [PubMed: 15077274]

[17]. McGrath PJ, Walco GA, Turk DC, Dworkin RH, Brown MT, Davidson K, Eccleston C, Finley GA, Goldschneider K, Haverkos L, Hertz SH, Ljungman G, Palermo T, Rappaport BA, Rhodes T, Schechter N, Scott J, Sethna N, Svensson OK, Stinson J, von Baeyer CL, Walker L, Weisman S, White RE, Zajicek A, Zeltzer L. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. Journal of Pain. 2008; 9(9):771–783. [PubMed: 18562251]

[18]. Muthén, LK.; Muthén, BO. Mplus user's guide. 6th ed.. Muthén & Muthén; Los Angeles: 1998-2010.

[19]. Oerlemans HM, Oostendorp RA, de Boo T, Goris RJA. Pain and reduced mobility in complex regional pain syndrome I: outcome of a prospective randomised controlled clinical trial of adjuvant physical therapy versus occupational therapy. Pain. 1999; 83(1):77–83. [PubMed: 10506674]

[20]. Palermo TM, Fonareva I, Janosy NR. Sleep quality and efficiency in adolescents with chronic pain: relationship with activity limitations and health-related quality of life. Behav Sleep Med. 2008; 6(4):234–250. [PubMed: 18853307]

[21]. Reeve BB, Hays RD, Bjorner JB, Cook KF, Crane PK, Teresi JA, Thissen D, Revicki DA, Weiss DJ, Hambleton RK. Psychometric evaluation and calibration of health-related quality of life item banks: plans for the Patient-Reported Outcomes Measurement Information System (PROMIS). Medical care. 2007; 45(5):S22–S31. [PubMed: 17443115]

[22]. Reid GJ, Lang BA, McGrath PJ. Primary juvenile fibromyalgia: psychological adjustment, family functioning, coping, and functional disability. Arthritis and Rheumatism. 1997; 40(4): 752–760. [PubMed: 9125260]

[23]. Sherry DD, Wallace CA, Kelley C, Kidder M, Sapp L. Short- and long-term outcomes of children with complex regional pain syndrome type I treated with exercise therapy. Clin J Pain. 1999; 15(3):218–223. [PubMed: 10524475]

[24]. Varni JW, Burwinkle TM, Limbers CA, Szer IS. The PedsQL as a patient-reported outcome in children and adolescents with fibromyalgia: an analysis of OMERACT domains. Health Qual Life Outcomes. 2007; 5:9. [PubMed: 17295915]

[25]. Varni JW, Limbers CA, Burwinkle TM. Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL™ 4.0 Generic Core Scales. Health and quality of life outcomes. 2007; 5(1):43. [PubMed: 17634123]

[26]. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Med Care. 2001; 39(8):800–812. [PubMed: 11468499]

[27]. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the pediatric quality of life inventory. Med Care. 1999; 37(2):126–139. [PubMed: 10024117]

[28]. 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: 1826329]

[29]. White KP, Nielson WR. Cognitive behavioral treatment of fibromyalgia syndrome: A follow-up assessment. Journal of Rheumatology. 1995; 22(4):717–721. [PubMed: 7791170]

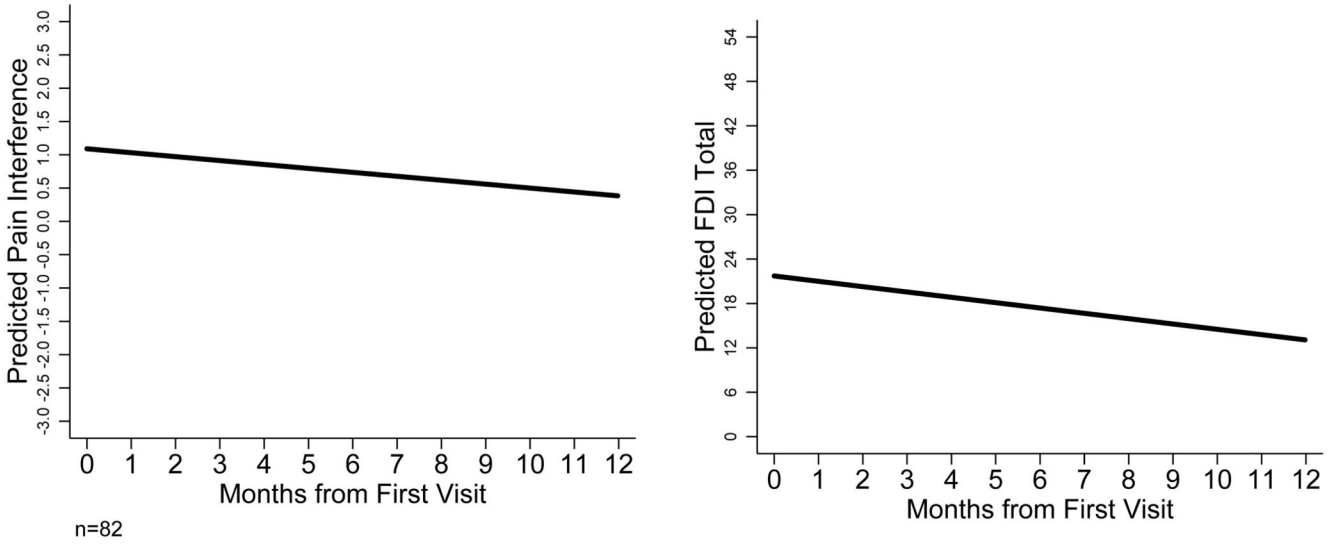

Figure 1.
Parallel process LGM for PROMIS Pain Interference and Functional Disability Inventory (FDI)

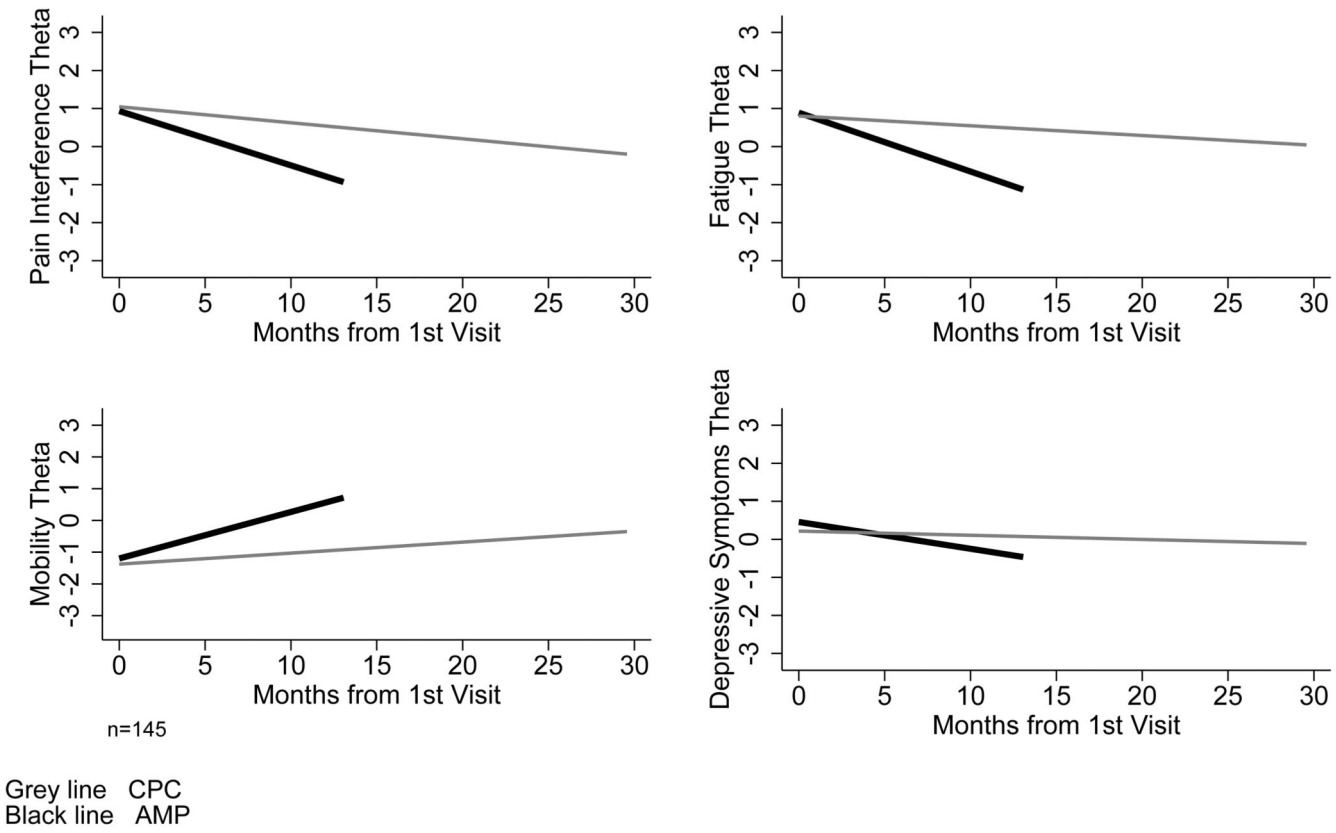

Figure 2.

Main Effects model of change in PROMIS Pain Interference, Fatigue, Mobility and Depressive Symptoms by Site

Note: For pain interference, fatigue, and depressive symptoms, a negative slope represents improvement. For Mobility, a postive slope indicates improvement.

Table 1

PROMIS Measures and corresponding legacy scales (Aim 1)

PROMIS Short Form	Legacy Scale
1. Pain Interference	Functional Disability Inventory (FDI)
2. Mobility	Peds QL 4.0™ Physical Functioning
3. Upper Extremity	Peds QL 4.0™ Physical Functioning
4. Fatigue †	*n/a*
5. Depressive Symptoms	Children's Depression Inventory (CDI)
6. Anxiety‡	Peds QL 4.0™ Emotional Functioning
7. Peer Relationships	Peds QL 4.0™ Social Functioning

† no legacy measure available for comparison

‡ no specific anxiety legacy measure was available for comparison but the PedsQL Emotional Functioning scale which broadly assesses psychological distress including anxiety and depressive symptoms was used.

Table 2

Fixed Effects Models for PROMIS and Legacy Measures over time

	Unstandardized	Standardized
	Betas	
Pain Interference Intercept	1.09**	2.31**
Pain Interference Slope	−0.06**	−0.86*
FDI Total Intercept	21.72**	3.15**
FDI Total Slope	−0.72**	−1.12**
	Unstandardized	Standardized
	Betas	
PROMIS Mobility Intercept	−1.42**	−2.66**
PROMIS Mobility Slope	0.06**	0.69*
PedsQL Physical Intercept	38.33**	2.67**
PedsQL Physical Slope	1.65**	1.06*
	Unstandardized	Standardized
	Betas	
PROMIS Upper Extremity Intercept	−0.68**	−0.98**
PROMIS Upper Extremity Slope	0.03	0.62
PedsQL Physical Intercept	38.47**	2.96**
PedsQL Physical Slope	1.51**	1.21*
	Unstandardized	Standardized
	Betas	
PROMIS Depression Intercept	0.25	0.35
PROMIS Depression Slope	−0.03	−0.91
CDI Total Score Intercept	10.76**	−0.91
CDI Total Score Slope	−0.18	−0.50
	Unstandardized	Standardized
	Betas	
PROMIS Anxiety Intercept	0.11	0.13
PROMIS Anxiety Slope	−0.04*	−0.84
PedsQL Emotional Intercept	41.25**	2.35**
PedsQL Emotional Slope	−1.22**	−1.16*
	Unstandardized	Standardized
	Betas	
PROMIS Peer Intercept	0.03	0.04
PROMIS Peer Slope	0.01	0.63

PedsQ Social Intercept	71.90**	4.99**
PedsQ Social Slope	0.61	1.24

Unstandardized coefficients are interpretable in a measure's original metric. Standardized coefficients are comparable across measures.

* $p = 0.05$

** $p = 0.01$

Table 3

Random Effects Models for PROMIS and Legacy Measures over time

	Pain Interference		FDI Total	
	Intercept	Slope	Intercept	Slope
Pain Interference Intercept	*0.22*			
Pain Interference Slope	0.00	*0.01*		
FDI Total Intercept	**0.98****	0.07	*47.61***	
FDI Total Slope	−0.08	**0.99****	0.00	*0.42*
	PROMIS Mobility		PedsQL Physical	
	Intercept	Slope	Intercept	Slope
PROMIS Mobility Intercept	*0.29**			
PROMIS Mobility Slope	0.00	*0.01*		
PedsQL Physical Intercept	**0.99****	0.12	*206.89***	
PedsQL Physical Slope	−0.12	**0.99****	0.00	*2.41*
	PROMIS Upper Extremity		PedsQL Physical	
	Intercept	Slope	Intercept	Slope
PROMIS Upper Extremity Intercept	*0.49***			
PROMIS Upper Extremity Slope	0.00	*0.00*		
Peds QL Physical Intercept	**0.87****	−0.17	*168.44**	
Peds QL Physical Slope	0.09	**0.86****	0.00	*1.55*
	PROMIS Depression		CDI Total Score	
	Intercept	Slope	Intercept	Slope
PROMIS Depression Intercept	*0.51***			
PROMIS Depression Slope	0.00	*0.00*		
CDI Total Score Intercept	**0.93****	0.09	*35.53***	
CDI Total Score Slope	0.01	0.93	0.00	*0.14*
	PROMIS Anxiety		PedsQL EF	
	Intercept	Slope	Intercept	Slope
PROMIS Anxiety Intercept	*0.71***			
PROMIS Anxiety Slope	0.00	*0.00*		
PedsQL Emotional Intercept	**0.99****	0.08	*307.83***	
PedsQL Emotional Slope	−0.07	**0.98***	0.00	*1.10*
	PROMIS Peer		PedsQL Social	
	Intercept	Slope	Intercept	Slope

PROMIS Peer Intercept	*0.62***			
PROMIS Peer Slope	0.00	*0.00*		
PedsQL Social Intercept	**0.95****	−0.18	*207.79**	
PedsQL Social Slope	0.13	0.80	0.00	*0.24*

Variances constitute each matrix's diagonal elements *(in italics)*. Correlations constitute each matrix's off-diagonal elements. Significant correlations are in **bold** font.

* $p = 0.05$

** $p = 0.01$

Table 4

Parameters for the Unconditional Growth Models for PROMIS Measures

Measure	$\beta_{intercept}$	β_{slope}	$\sigma^2_{intercept}$	σ^2_{slope}
Pain Interference	0.97**	−.07**	.27**	.006*
Mobility	−1.26**	.07**	.20**	.006*
Upper Extremity	−.67**	.04**	.46**	.001*
Peer Relationships	−.009	.01**	.57**	.001*
Depression	.31**	−.03*	.53**	.001
Fatigue	.80**	−.06**	.82**	.002
Anxiety	.21*	−.04**	.64**	.002

* $p < .05$

** $p < .01$

Table 5

Parameters for Conditional Growth Model 1 for PROMIS Measures

Measure	$\beta_{intercept}$	β_{slope}	β_{site}	$\sigma^2_{intercept}$	σ^2_{slope}
Pain Interference	.83**	−.07**	.27*	.26**	.006
Mobility	−1.07**	.07**	−.38**	.17**	.004
Upper Extremity	−.60**	.04**	−.14*	.45**	.001
Peer Relationships	−.04**	.01**	.05*	.57**	.001
Depression	.37**	−.02*	−.12	.53**	.001
Fatigue	.71**	−.06**	.19	.82**	.001
Anxiety	.25*	−.04**	−.09	.64**	.002

* $p < .05$

** $p < .01$

Table 6

Parameters for Conditional Growth Model 2 for PROMIS Measures

Measure	$\beta_{intercept}$	β_{slope}	β_{site}	$\beta_{siteXtime}$	$\sigma^2_{intercept}$	σ^2_{slope}
Pain Interference	.94**	−.14**	.11	.10	.28**	.004
Mobility	−1.20**	.15**	−.18	−.12**	.21**	.003
Upper Extremity	−.75**	.11**	.08	−.10	.45**	.001
Peer Relationships	−.08**	.04**	.11	−.03**	.57**	.001
Depression	.46**	−.07**	−.24	.06*	.54**	.001
Fatigue	.89**	−.16**	−.09	.13**	.88**	.001
Anxiety	.33*	−.09**	−.20	.06	.64**	.001

* p <.05

** p<.01