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Construct validity of Patient-Reported Outcomes Measurement Information System Paediatric measures in juvenile idiopathic arthritis and systemic lupus erythematosus: cross-sectional evaluation

Elissa R Weitzman ,[1,2,3] Amy Gaultney,[4] Emily von Scheven,[5] Sarah Ringold,[6] Courtney M Mann,[7] Kara M Magane,[1] Li Lin,[7] Renee Leverty,[8] Anne Dennos,[8] Alexy Hernandez,[7] Steven J Lippmann,[7] Fatma Dedeoglu,[9] Alexandra C Marin,[1,2] Rachele Cox,[1] Bryce B Reeve,[7,8,10] Laura E Schanberg [8,10]

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For numbered affiliations see end of article.

Correspondence to
Dr Elissa R Weitzman; elissa.weitzman@childrens.harvard.edu

ABSTRACT

Objectives Evaluate construct validity of Patient-Reported Outcomes Measurement Information System (PROMIS) Paediatric measures of symptoms and functioning against measures of disease activity among youth with juvenile idiopathic arthritis (JIA) or systemic lupus erythematosus (SLE).

Design Cross-sectional associations among PROMIS measures and clinical metrics of disease activity were estimated.

Setting Seven clinical sites of the Childhood Arthritis and Rheumatology Alliance (CARRA) in the USA.

Participants Youth aged 8–17 years enrolled in the CARRA Registry.

Intervention PROMIS measures were collected and associations with clinical measures of disease activity estimated, by condition, in bivariate and multivariable analyses with adjustment for sociodemographics, insurance status, medications and disease duration.

Main outcome measures PROMIS Paediatric measures of mobility, physical activity, fatigue, pain interference, family relationships, peer relationships, depressive symptoms, psychological stress, anxiety, and meaning and purpose, and clinical metrics of disease.

Results Among 451 youth (average age 13.8 years, 71% female), most (n=393, 87%) had a JIA diagnosis and the remainder (n=58, 13%) had SLE. Among participants with JIA, those with moderate/high compared with low/inactive disease had, on average, worse mobility (multivariable regression coefficient and 95% CIs) (–7.40; –9.30 to –5.50), fatigue (3.22; 1.02 to 5.42), pain interference (4.76; 3.04 to 6.48), peer relationships (–2.58; –4.52 to –1.64), depressive symptoms (3.00; 0.96 to 5.04), anxiety (2.48; 0.40 to 4.56) and psychological stress (2.52; 0.68 to 4.36). For SLE, youth with active versus inactive disease had on average worse mobility (–5.07; –10.15 to 0.01) but PROMIS Paediatric measures did not discriminate participants with active and inactive disease in adjusted analyses.

Conclusions Seven PROMIS Paediatric measures discriminated between active and inactive disease in youth with JIA. Results advance the usefulness of PROMIS for understanding well-being and improving interventions for youth with JIA, but larger studies are needed to determine utility in SLE cohorts.

Trial registration number National Institute of Arthritis and Musculoskeletal and Skin Diseases (U19AR069522).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study sample includes youth with juvenile idiopathic arthritis (JIA) and systemic lupus erythematosus (SLE) whose disease and treatment status were well characterised.
⇒ The study sample was drawn from seven different paediatric rheumatology clinical sites throughout the USA.
⇒ Patient-reported outcomes included in the validation study reflect a range of symptom and functional status domains of concern to patients, families and healthcare providers.
⇒ Construct validation was assessed against multiple measures of JIA and SLE disease activity including one that did not include a parent-reported measure of child well-being, affording insight into construct validity for youth who may not have an engaged parent/guardian.
⇒ The sample was opt-in and had a large percentage of youth from non-minoritised racial and ethnic groups, limiting generalisability for the population with JIA.

INTRODUCTION

Clinical measures do not fully capture the ways that paediatric-onset chronic rheumatic diseases (RDs) and their treatments impact

the lives of children and adolescents. Youth living with RD report poor health-related quality of life (HRQOL).[1 2] Even with treatment, youth may continue to experience disease-related symptoms.[3] Treatment side effects can adversely impact HRQOL even when treatment lessens disease activity (DA).[4] Moreover, depression, anxiety and stress are common among youth living with RD[5] and may worsen with, and exacerbate, DA.[6–8] The interconnected biopsychosocial factors that influence symptoms for a young person with RD complicate clinical decision-making and impact the ability of clinicians to select optimal interventions. For example, fatigue is a debilitating daily complaint of many youth with RD that adversely affects quality of life, school participation, family relationships and social life, imposing added burdens on youth and caregivers.[9] Despite its prevalence and salience, it is unclear whether fatigue reflects the discrete or combined effects of biophysiological disease processes, treatments, mental health distress or environmental stressors including family/household issues. Greater understanding of the drivers of symptoms such as fatigue and their association with DA is vital for ameliorating the impact of disease and treatment experiences on patients.

Measuring patient-reported outcomes (PROs) affords an opportunity to more fully characterise disease and treatment experiences of youth with RD, enabling clinicians to understand aspects of well-being relevant to treatment decision-making, as expressed from the perspective of affected youth.[10–16] While traditional clinical methods of taking a patient's history can be effective for generating useful information to guide care, these activities may be inconsistently performed, yielding information of inconsistent value. Capturing brief, structured, clinically validated PROs that show clear association patterns with established measures of DA may be especially useful as an adjunct for guiding treatment; research that builds understanding of the clinical validity of PROs is likely to have high clinical impact.[17 18] This study focuses on the National Institute of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) Paediatric measures that are used in research and practice settings around the world.[19–23]

Associations between DA and PROMIS Paediatric patient-reported and parent-proxy measures of anger, fatigue, mobility and pain interference have been demonstrated, although only parent-proxy-reported measures of psychological and social health distinguished youth with active versus inactive disease.[24] We sought to extend existing studies undertaken with single-site US[24] and European samples,[10 25] to understand how well the PROMIS Paediatric measures differentiate youth with active/inactive disease, a test of construct validity across 'known groups'. We included US youth with juvenile idiopathic arthritis (JIA) and systemic lupus erythematosus (SLE).[26] In addition, we sought to test whether measures of psychological and social well-being differentiate youth with active/inactive disease. Poor psychological and social health may exacerbate disease,[27] and these issues may worsen in the setting of greater DA. Quantifying associations among clinical metrics of DA and subjective measures of social, psychological and physical well-being may advance our ability to identify meaningful targets for psychosocial interventions as part of a comprehensive care model to improve outcomes and ameliorate suffering among youth with RD.

METHODS

Study design

We undertook a cross-sectional study of a convenience sample of children with JIA and SLE enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry,[28 29] a clinical database of children and adolescents diagnosed with paediatric-onset rheumatic conditions. The database includes information about diagnoses, treatment, disease status and clinical outcomes. Study participants were recruited from seven CARRA sites in the USA, and were aged 8–17 years, able to complete PROs on a tablet computer, and met Registry criteria for JIA or SLE according to the International League for Associations of Rheumatology and the American College of Rheumatology,[8 30] respectively. For the JIA group, study eligibility included patients with a new diagnosis of JIA (diagnosed within 6 months prior to enrolment), patients with an existing diagnosis newly starting a disease-modifying antirheumatic drug (DMARD) or biological therapy, and patients with an existing diagnosis and inactive disease. For the SLE group, study inclusion was based on SLE diagnosis. Exclusion criteria for both JIA and SLE were a concomitant condition that was likely to impact HRQOL, a significant developmental delay or cognitive impairment that would impede completing PRO measures per the parent or treating physician and being a non-English speaker.

Data sources and measures

Clinical data were obtained from the CARRA Registry.[28] Participants completed PROs electronically, via a tablet computer, using the PRO Core platform (https://pro.unc.edu/about.php), except in 29 participants whose data were collected using a paper form. Clinical and PROMIS measures captured the same reference period (past 7 days). Clinical measures included participants' age, sex, race, ethnicity, body mass index (BMI), primary RD diagnosis, current medications (reduced to four categories: DMARD, biological, glucocorticoid or a non-steroidal anti-inflammatory drug), date of onset of disease symptoms, date first seen by a paediatric rheumatologist and date of primary rheumatological disease diagnosis by a physician. Date of onset of disease symptoms and date of diagnosis were used to calculate disease duration.

We used two clinical measures of DA for participants with JIA, a continuous measure that required three inputs (active joint count, physician global assessment and parent global assessment), and a dichotomised measure

that required two inputs (active joint count and physician global assessment). The clinical Juvenile Arthritis Disease Activity Score 10 (cJADAS10) continuous score variable[31–34] was calculated as the sum of values for: active joint count (joint count ≥10=10), physician global assessment (10-point Visual Analogue Scale) and parent global assessment (10-point Visual Analogue Scale), with a possible overall summed range of 0–30 with higher values representing more active disease. A novel dichotomised DA measure for JIA did not use the parent global assessment, making it more tolerant of parental absenteeism, an important consideration given not all youth have a present/involved parent. Participants were coded as having inactive disease if the physician global assessment value was less than or equal to 0.5 and the active joint count was 0; participants were coded as having active disease if the physician global assessment was greater than or equal to 1, or active joint count was greater than 0. Participants missing either physician global assessment or active joint count were excluded from all analyses (n=27), given that both were required for the calculation of each DA variable. Of 366 participants with JIA, n=72 (19.7%) lacked a parent global assessment measure and were not included in analyses that used the cJADAS10 continuous score variable. Differences in the requirement for a parent global measure resulted in two slightly different JIA analytical cohorts. Comparisons of participants with and without a parent global assessment measure indicated that a larger proportion of those without were older (14.6 vs 13.3 years; p=0.044), from homes where parents were not college educated (17.9% vs 66.1%; p<0.001) and had longer median disease duration (80.6 vs 59.5 months) (p=0.039) (data not shown).

For participants with SLE, the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[35–37] was calculated as a total sum score (continuous variable), with a SLEDAI score equal or greater than 4 representing active disease, and a score of less than 4 representing inactive disease.[38] A sensitivity analysis was undertaken using a modified SLEDAI (ie, the clinical or cSLEDAI) that excludes serologies and reducing the potential for categorising participants as having active disease in the absence of signs or symptoms of active disease related to inflammation.[39]

Ten PROMIS Paediatric measures were administered via computerised adaptive testing technology[40] using a reference period of the past 7 days. Participants were administered a battery of PROMIS scales to assess symptom domains (Fatigue V.2.0, Pain Interference V.2.0, Depressive Symptoms, Psychological Stress and Anxiety V.2.0), as well as functional domains (Mobility V.2.0, Physical Activity V.1.0, Family Relationships V.1.0, Peer Relationships V.2.0, and Meaning and Purpose V.1.0 (only administered to youth aged 13 years and older)). Higher PROMIS symptom T-scores reflect worse symptom levels and higher functioning scores reflect better functioning. PROMIS measures are designed such that the mean score of the relevant reference population (ie, healthy youth) is 50, with an SD of 10.[41] A 3-point difference on the PROMIS Paediatric T-score metric is considered a minimally important difference (MID).[42]

Statistical analysis

Differences in demographic characteristics between JIA and SLE cohorts and between inactive and active disease status for continuous variables were tested using Wilcoxon rank-sum tests, and for categorical variables by χ^2 tests. The two-sample Wilcoxon rank-sum tests along with general linear regression models were used to determine if disease activity was associated with each PROMIS Paediatric measure, in analyses that were undertaken separately for the JIA and SLE groups given disease heterogeneity. For each PROMIS Paediatric domain, we first examined differences in individual PROMIS domain measures between DA groups, after which we conducted a multivariable regression analysis to estimate associations between the PROMIS domain measure (the dependent variable) and DA adjusting for age, sex, race, ethnicity, parent education, insurance status, medications and disease duration. The sequence of estimating bivariate and multivariate associations was repeated separately for each PROMIS domain. For the JIA group, we followed this modelling approach for analyses using the cJADAS10 continuous and the dichotomised DA measures, with the latter a larger group that included participants lacking a parent global measure. We used a two-tailed significance level of α=0.05 for all assessments. Data analyses were done using SAS V.9.4.[43] For simplicity, we provide descriptive statistics for the JIA sample for which we could estimate a dichotomous measure of DA; we report multivariate regression analysis results for the sample for which we could estimate a dichotomous and separately a continuous measure of DA.

Patient and public involvement

We included a patient (parent) research partner in protocol design, measure selection and review of research findings. The CARRA Registry served as the study research platform, and plans and measures were reviewed by registry stakeholders and findings shared at annual registry meetings.

RESULTS

Participant characteristics

Of 451 enrolled participants, n=393 (87%) had JIA and n=58 (13%) had SLE (table 1). After excluding participants (n=27) who were missing both physician global assessment and active joint count, the average age was 13.9 years, a majority were female (71.7%), white (75.0%), reported parents with at least a college degree (55.7%) and a large majority were privately insured (82.5%). On average, the JIA group had a larger proportion of participants who were younger, male, white and non-Hispanic, privately insured and had parents who had not completed college (p<0.05) compared with the SLE group. The

Table 1 Sociodemographic and health characteristics of participants by disease group

	Total	JIA	SLE	
	N (%)	N (%)	N (%)	P value
Total	442	366	58	
Sociodemographic and health characteristics				
Age (mean, SD)	13.9 (2.7)	13.6 (2.7)	15.5 (2.1)	<0.001
Sex, female	304 (71.7)	253 (69.1)	51 (87.9)	0.003
Race				<0.001
White	318 (75.0)	297 (81.1)	21 (36.2)	
Asian	19 (4.5)	6 (1.6)	13 (22.4)	
African American	18 (4.2)	9 (2.5)	9 (15.5)	
More than one race	19 (4.5)	15 (4.1)	4 (6.9)	
Other race	15 (3.5)	10 (2.7)	5 (8.6)	
Unknown	35 (8.3)	29 (7.9)	6 (10.3)	
Ethnicity				0.01
Non-Hispanic	383 (90.3)	336 (91.8)	47 (81.0)	
Hispanic	41 (9.7)	30 (8.2)	11 (19.0)	
Parent education				0.002
Less than college degree	43 (10.1)	31 (8.5)	12 (20.7)	
College degree or higher	236 (55.7)	201 (54.9)	35 (60.3)	
Prefer not to answer or missing	145 (34.2)	134 (36.6)	11 (19.0)	
Insurance				0.003
Private health insurance	350 (82.5)	311 (85.0)	39 (67.2)	
Government insurance	49 (11.6)	35 (9.6)	14 (24.1)	
Other	25 (5.9)	20 (5.5)	5 (8.6)	
BMI (mean, SD)	21.2 (4.8)	21.0 (4.6)	22.6 (5.5)	0.03
Disease duration in months (Q1, Q3)	58.8 (29.4, 100.8)	66.2 (33.8, 105.8)	33.1 (8.1, 57.4)	<0.001
Medication				
DMARDs/Cytoxan	373 (88.0)	316 (86.3)	57 (98.3)	0.01
Biologics	264 (62.3)	263 (71.9)	1 (1.7)	<0.001
NSAIDs	226 (53.3)	218 (59.6)	8 (13.8)	<0.001
Corticosteroids	48 (11.3)	13 (3.6)	35 (60.3)	<0.001
PROMIS measure scores (mean, SD)				
Mobility	50.4 (9.6)	50.6 (9.7)	48.9 (8.9)	0.2
Physical activity	48.1 (8.7)	48.9 (8.4)	43.1 (8.9)	<0.001
Fatigue	45.0 (10.9)	44.3 (10.6)	49.6 (11.6)	0.001
Pain interference	44.1 (8.6)	43.9 (8.5)	45.6 (9.6)	0.25
Peer relationships	51.9 (9.0)	52.2 (8.8)	49.9 (9.6)	0.08
Family relationships	51.3 (10.2)	51.5 (10.0)	50.5 (11.4)	0.64
Depressive symptoms	48.3 (9.8)	47.8 (9.4)	51.4 (11.4)	0.02
Anxiety	45.4 (9.6)	44.9 (9.4)	48.0 (10.7)	0.04
Psychological stress	52.5 (9.1)	52.1 (8.9)	55.2 (10.1)	0.049
Meaning and purpose*	46.5 (9.5)	46.5 (9.1)	46.5 (11.1)	0.8
Clinical measures of disease activity				
cJADAS10 continuous score (mean, SD)†		3.7 (4.8)	—	
Dichotomous measure of active and inactive disease‡		133 (36.3)	—	
SLEDAI score (mean, SD)		—	4.0 (6.3)	

*n=272 for meaning and purpose which was only asked of respondents aged 13 years and older.
†n=294 for cJADAS10 continuous score sample.
‡n=366 for dichotomous measure of disease activity sample.
BMI, body mass index; cJADAS10, clinical Juvenile Arthritis Disease Activity Score 10; DMARDs, disease-modifying antirheumatic drugs; JIA, juvenile idiopathic arthritis; NSAIDs, non-steroidal anti-inflammatory drugs; PROMIS, Patient-Reported Outcomes Measurement Information System; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

Table 2 Sociodemographic and health characteristics of youth with JIA by disease activity status, measured using the dichotomous measure of disease activity

	Total	Low/inactive disease activity*	Active (moderate/high) disease activity†	
	N (%)	N (%)	N (%)	P value
Total	366	233	133	
Sociodemographic and health characteristics				
Age (mean, SD)	13.6 (2.7)	13.4 (2.6)	14.0 (2.8)	0.01
Sex, female	253 (69.1)	155 (66.5)	98 (73.7)	0.15
Race				0.65
White	297 (81.1)	190 (81.5)	107 (80.5)	
Asian	6 (1.6)	3 (1.3)	3 (2.3)	
African American	9 (2.5)	5 (2.1)	4 (3.0)	
More than one race	15 (4.1)	12 (5.2)	3 (2.3)	
Other race	10 (2.7)	5 (2.1)	5 (3.8)	
Unknown	29 (7.9)	18 (7.7)	11 (8.3)	
Ethnicity				0.10
Non-Hispanic	336 (91.8)	218 (93.6)	118 (88.7)	
Hispanic	30 (8.2)	15 (6.4)	15 (11.3)	
Parent education				0.04
Less than college degree	31 (8.5)	22 (9.4)	9 (6.8)	
College degree or higher	201 (54.9)	137 (58.8)	64 (48.1)	
Prefer not to answer or missing	134 (36.6)	74 (31.8)	60 (45.1)	
Insurance type				0.80
Private health insurance	311 (85.0)	196 (84.1)	115 (86.5)	
Government insurance	35 (9.6)	24 (10.3)	11 (8.3)	
Other	20 (5.5)	13 (5.6)	7 (5.3)	
BMI (mean, SD)	21.0 (4.6)	20.9 (4.8)	21.1 (4.3)	0.29
Disease duration in months (Q1, Q3)	69.5 (33.8, 105.8)	77.4 (42.5, 111.0)	55.6 (23.8, 92.8)	<0.001
Medication				
DMARDs/Cytoxan	316 (86.3)	194 (83.3)	122 (91.7)	0.02
Biologics	263 (71.9)	160 (68.7)	103 (77.4)	0.07
NSAID	218 (59.6)	143 (61.4)	75 (56.4)	0.35
Corticosteroids	13 (3.6)	3 (1.3)	10 (7.5)	0.002
PROMIS measure scores (mean, SD)				
Mobility	50.6 (9.7)	53.7 (8.1)	45.2 (9.9)	<0.001
Physical activity	48.9 (8.4)	49.4 (8.4)	48.1 (8.5)	0.13
Fatigue	44.3 (10.6)	42.5 (10.0)	47.4 (10.9)	<0.001
Pain interference	43.9 (8.5)	41.7 (7.6)	47.7 (8.6)	<0.001
Peer relationships	52.2 (8.8)	53.0 (8.6)	50.9 (9.1)	0.046
Family relationships	51.4 (10.0)	52.1 (10.3)	50.3 (9.5)	0.04
Depressive symptoms	47.9 (9.4)	46.4 (9.1)	50.4 (9.4)	<0.001
Anxiety	45.0 (9.4)	43.9 (9.2)	46.8 (9.5)	0.004
Psychological stress	52.1 (8.9)	50.7 (8.8)	54.5 (8.4)	<0.001
Meaning and purpose‡	46.5 (9.1)	46.9 (9.5)	45.9 (8.6)	0.36

*Low/inactive disease activity: physician global value ≤0.5 and active joint count=0.
†Active (moderate/high) disease activity: physician global value ≥1 and active joint count >0.
‡n=212 for meaning and purpose which was only asked of respondents aged 13 years and older.
BMI, body mass index; DMARDs, disease-modifying antirheumatic drugs; JIA, juvenile idiopathic arthritis; NSAIDs, non-steroidal anti-inflammatory drugs; PROMIS, Patient-Reported Outcomes Measurement Information System.

Table 3 Adjusted associations among PROMIS measures of symptoms and functioning by disease activity assessed using the cJADAS10 continuous or dichotomous measure of disease activity, or the SLEDAI dichotomous measure*

	JIA		SLE
	cJADAS10 continuous score measure (N=294)	Dichotomous disease activity measure (based on PGA and joint count) (N=366)	SLEDAI dichotomous (N=58)
	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
Mobility	−1.23 (−1.43 to −1.03)	−7.40 (−9.30 to −5.50)	−5.07 (−10.15 to 0.01)
Physical activity	0.04 (−0.18 to 0.26)	−1.04 (−2.92 to 0.84)	−0.74 (−6.35 to 4.87)
Fatigue	0.90 (0.66 to 1.14)	3.22 (1.02 to 5.42)	−0.21 (−7.66 to 7.24)
Pain interference	0.97 (0.79 to 1.15)	4.76 (3.04 to 6.48)	4.02 (−2.00 to 10.04)
Depressive symptoms	0.58 (0.34 to 0.82)	3.00 (0.96 to 5.04)	2.98 (−3.66 to 9.62)
Anxiety	0.50 (0.26 to 0.74)	2.48 (0.40 to 4.56)	−1.24 (−8.08 to 5.60)
Psychological stress	0.51 (0.29 to 0.73)	2.52 (0.68 to 4.36)	−0.35 (−6.52 to 5.82)
Meaning and purpose†	−0.17 (−0.48 to 0.14)	−1.10 (−3.77 to 1.57)	3.09 (−5.40 to 11.58)
Family relationships	−0.24 (−0.49 to 0.01)	−1.50 (−3.68 to 0.68)	6.12 (−1.15 to 13.39)
Peer relationships	−0.44 (−0.66 to −0.22)	−2.58 (−4.52 to −0.64)	−1.54 (−7.71 to 4.63)

*Models controlled for sex, age (centred at 8 years of age), insurance type, parent education, disease duration in months (centred at 60 months) and medications (all categories).
†Meaning and purpose was only asked of respondents aged 13 years and older, respectively, n=161, n=212, and n=52 for cJADAS10 continuous sum, dichotomous disease activity measures and SLEDAI analyses.
cJADAS10, clinical Juvenile Arthritis Disease Activity Score 10; JIA, juvenile idiopathic arthritis; PGA, physician global assessment; PROMIS, Patient-Reported Outcomes Measurement Information System; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

average BMI was 21.2, with lower BMI among the JIA group; average disease duration was 58.8 months, with higher duration, on average, for the JIA group (p<0.001). Youth with JIA reported higher levels of physical activity and lower levels of fatigue, depressive symptoms, anxiety and psychological stress compared with those with SLE (p<0.05) (table 1).

Disease activity, sociodemographics and PROMIS scores for youth with JIA

Of 366 youth with JIA, 133 (36%) had active disease per the dichotomous DA measure. In bivariate analyses, active disease was associated with older age, lower levels of parental education, shorter disease duration, DMARD use and glucocorticoid use (p<0.05) (table 2). PROMIS scores differed between DA groups for all domains, except physical activity and meaning and purpose. In regression analyses adjusted for participant sociodemographic characteristics, including insurance status, medications and disease duration (table 3), youth with active disease reported less mobility, greater fatigue and pain interference, worse peer relationships, and higher levels of depressive symptoms, anxiety and psychological stress than those with inactive disease (all p<0.05). PROMIS measures of physical activity, family relationships, and sense of meaning and purpose did not discriminate between JIA youth with active versus inactive disease in adjusted analyses. Findings were mostly similar across analyses that used the cJADAS10 continuous and the dichotomised measures (table 3).

Disease activity, sociodemographics and PROMIS measures for youth with SLE

Of 58 youth with SLE, 16 (27.6%) had active disease, which was associated with younger age and shorter disease duration (p<0.05) (table 4). PROMIS measures of mobility and family relationships discriminated between youth with active versus inactive disease in bivariate analyses: youth with active disease had less mobility and better family relationships than those with inactive disease (all p≤0.01). In regression analyses that adjusted for sociodemographic characteristics, insurance status, medications and disease duration, these associations were not significant (table 3). Results from the sensitivity analysis that used the cSLEDAI categorised 21 (36.2%) participants with SLE as having active disease, and found that the PROMIS measure of mobility discriminated between youth with active versus inactive disease (regression coefficient −4.90, SE 2.35, p=0.04) in adjusted analyses.

DISCUSSION

This multisite study of youth living with JIA or SLE finds that PROMIS Paediatric measures distinguished between youth with active and inactive disease for most dimensions of symptoms and functioning among youth with JIA. Further, PROMIS Paediatric measures distinguished between youth with active and inactive disease with high but not perfect consistency for continuous and dichotomous DA measures, the latter a novel and abbreviated measure that does not include a parent global assessment. Associations among measures of DA and PROMIS

Table 4 Sociodemographic and health characteristics of youth with SLE by disease activity status, measured using the dichotomous measure of disease activity

	Total	Low/inactive disease activity*	Active (moderate/high) disease activity†	
	N (%)	N (%)	N (%)	P value
Total	58	42	16	
Sociodemographic and health characteristics				
Age (mean, SD)	15.5 (2.1)	15.8 (2.1)	14.7 (1.9)	0.02
Sex, female	51 (87.9)	38 (90.5)	13 (81.3)	0.34
Race				0.34
White	21 (36.2)	15 (35.7)	6 (37.5)	
Asian	13 (22.4)	11 (26.2)	2 (12.5)	
African American	9 (15.5)	5 (11.9)	4 (25.0)	
More than one race	4 (6.9)	3 (7.1)	1 (6.3)	
Other race	5 (8.6)	5 (11.9)	0 (0.0)	
Unknown	6 (10.3)	3 (7.1)	3 (18.8)	
Ethnicity				0.44
Non-Hispanic	47 (81.0)	33 (78.6)	14 (87.5)	
Hispanic	11 (19.0)	9 (21.4)	2 (12.5)	
Parent education				0.56
Less than college degree	12 (20.7)	10 (23.8)	2 (12.5)	
College degree or higher	35 (60.3)	25 (59.5)	10 (62.5)	
Prefer not to answer or missing	11 (19.0)	7 (16.7)	4 (25.0)	
Insurance type				0.79
Private health insurance	39 (67.2)	29 (69.0)	10 (62.5)	
Government insurance	14 (24.1)	10 (23.8)	4 (25.0)	
Other	5 (8.6)	3 (7.1)	2 (12.5)	
BMI (mean, SD)	22.6 (5.5)	23.3 (5.7)	20.6 (4.4)	0.10
Disease duration in months (Q1, Q3)	33.1 (8.1, 57.4)	39.8 (23.0, 68.6)	4.7 (2.1, 24.5)	<0.001
Medication				
DMARDs/Cytoxan	57 (98.3)	41 (97.6)	16 (100.0)	0.53
Biologics	1 (1.7)	0 (0.0)	1 (6.3)	0.10
NSAIDs	8 (13.8)	5 (11.9)	3 (18.8)	0.50
Corticosteroids	35 (60.3)	23 (54.8)	12 (75.0)	0.16
PROMIS measure scores (mean, SD)				
Mobility	48.9 (8.9)	50.8 (8.0)	43.8 (9.5)	0.01
Physical activity	43.1 (8.9)	43.6 (8.7)	41.8 (9.5)	0.55
Fatigue	49.6 (11.6)	49.6 (12.0)	49.4 (11.0)	0.81
Pain interference	45.6 (9.6)	44.8 (9.5)	47.6 (9.8)	0.29
Peer relationships	49.9 (9.6)	50.4 (9.1)	48.5 (10.9)	0.40
Family relationships	50.5 (11.4)	48.2 (11.9)	56.5 (7.2)	0.01
Depressive symptoms	51.4 (11.4)	51.0 (12.2)	52.2 (9.1)	0.72
Anxiety	48 (10.7)	48.4 (11.4)	47.2 (9.0)	0.83
Psychological stress	55.2 (10.1)	55.8 (11.0)	53.6 (7.5)	0.53
Meaning and purpose‡	46.5 (11.1)	45.2 (11.3)	50.4 (10.2)	0.18

*Low/inactive disease activity: physician global value ≤0.5 and active joint count=0.
†Active (moderate/high) disease activity: physician global value ≥1 and active joint count >0.
‡n=52 for meaning and purpose which was only asked of respondents aged 13 years and older.
BMI, body mass index; DMARDs, disease-modifying antirheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; PROMIS, Patient-Reported Outcomes Measurement Information System.

Paediatric measures for youth with SLE, a small exploratory subsample, were not found in adjusted analyses.

For youth with JIA, we found statistically significant and meaningful (ie, MIDs >3 points) differences in PROMIS Paediatric measures of physical well-being by DA status. Youth with active disease reported less mobility and greater pain interference and fatigue. Similarly, we found statistically significant and meaningful differences in psychological well-being measures by DA status—youth with active disease reported higher levels of depressive symptoms, anxiety and psychological stress. Notably, youth with active disease, as measured by the cJADAS10 continuous measure, reported lower levels of family involvement and peer relationships, compared with youth with inactive disease; however, this did not exceed the MID threshold. Findings were consistent across many of the analyses that considered DA as a continuous or dichotomous measure. However, the measure of family relationships discriminated between youth with active and inactive disease in analyses using the cJADAS10 continuous measure, but not in analyses using the dichotomous measure (calculated without a parent global assessment). Loss of discriminatory power may reflect information loss from reducing a continuous to a dichotomous measure. Some patients lacked the parent global score and were only classified using the dichotomous measure, creating sample composition differences for the two measurement approaches. Understanding differences in the discriminatory power of PROMIS Paediatric measures when using DA measures that do not include parent measures is important, since parent measures may not be available in clinical and registry data, and not all youth have a present or involved parent. Results support use of pragmatic and parsimonious measures,[44] and afford inclusion in analytical samples of who lack parent-reported data.

Exploratory analyses of youth with SLE found few indications of construct validity except for mobility and family relationship measures. In bivariate analyses, mobility was worse and family relationships were better for the active disease group. In adjusted analyses, effects for mobility approached significance, while effects were attenuated for the measure of family relationships. Using an alternate DA anchor (the cSLEDAI) increased the percentage of youth categorised as having active disease and found that mobility discriminated active from inactive disease groups. Overall, findings support the construct validity of mobility for youth with SLE; however, the SLE small sample size is an important constraint. Lack of differences in PROs by DA for other measures including fatigue, an extremely common symptom for lupus,[45 46] is surprising. Studies with larger samples of youth with SLE are needed.

Findings add to the growing body of work detailing the value of capturing dimensions of patient well-being using PROMIS Paediatric measures. A recent report[47] found higher levels of anxiety, pain and fatigue, and less mobility among youth with 1 of 10 chronic illness conditions primarily affecting physical health (eg, asthma, type 1 diabetes, SLE, JIA) in comparison with levels among youth in the general population. Less marked differences were found for measures of social health (ie, peer relationships). Variability in PROMIS Paediatric measures was greater within than between the paediatric disease cohorts, suggesting that something in the experience of chronic illness rather than the nature of a specific disease affects well-being. The current study extends findings about the construct validity of PROMIS Paediatric measures completed by youth with JIA in the area of psychological well-being, which had previously demonstrated construct validity for parent-proxy reports only.[24] This is significant given open questions about the correspondence of parent-proxy and youth reports[24] and goals of engaging youth in describing and managing their own health.[48–50] Results also confirm the relevance of assessing social engagement with family and peers as a potentially meaningful metric of well-being associated with DA for youth with JIA.[51] Findings are inconclusive for youth with SLE, and studies with larger samples are needed.

Surprisingly, we did not find that PROMIS Paediatric measures of physical activity discriminated between youth with active and inactive disease for either disease group. This is puzzling given the likelihood that youth with active disease experience more pain and mobility problems and social withdrawal, all factors that can inhibit physical activity.[46 51 52] Results may reflect the small percentage of patients with extremely active disease. Research using direct observation of physical activity via wearables may help explain this result. Additionally, in analyses with youth aged ≥13 years, we did not find that the meaning and purpose measure discriminated between youth with active and inactive disease. The small sample of this age group may preclude seeing a difference. Alternatively, youth sense of meaning and purpose may be relatively stable and resistant to short-term fluctuations in DA.[2] Consistent with studies of resilience and grit, a sense of meaning and purpose may be protective against the adverse effects of living with RD on many outcomes, including subjective evaluation of HRQOL and educational attainment.[2 53 54] Additional research is needed to replicate this finding and explore whether a sense of meaning and purpose is associated with long-term disease trajectories.

Limitations

Findings extend the literature demonstrating construct validity of PROMIS Paediatric measures for youth with RD. While strengths include the multisite sample and use of validated DA measures (ie, cJADAS10 and SLEDAI), we note limitations including the use of cross-sectional data that demonstrate association, not prediction. The dichotomous DA measure used for the JIA group has not been validated. Non-English speakers were excluded, and study samples were disproportionately female (JIA and SLE are known to disproportionately affect girls).[55] The convenience sample may reflect a more engaged population, limiting generalisability. The small sample of youth with SLE is a constraint.

Conclusion

PROMIS Paediatric measures distinguished youth with active and inactive disease for most youth with JIA, and there is suggestive exploratory evidence that the PROMIS Paediatric mobility measure may do so for youth with SLE. Results advance our ability to use PROMIS measures clinically and in research to identify meaningful intervention targets and assess treatment efficacy for improving outcomes among youth with RD.

Author affiliations
[1]Division of Adolescent/Young Adult Medicine, Boston Children's Hospital, Boston, Massachusetts, USA
[2]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA
[3]Computational Health Informatics Program, Boston Children's Hospital, Boston, Massachusetts, USA
[4]Pediatric Rheumatology, Children's Hospital of Orange County, Orange, California, USA
[5]Pediatric Rheumatology, University of California San Francisco, San Francisco, California, USA
[6]Pediatrics, Seattle Children's Hospital, Seattle, Washington, USA
[7]Population Health Sciences, Duke University School of Medicine, Durham, North Carolina, USA
[8]Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina, USA
[9]Division of Immunology, Boston Children's Hospital, Boston, Massachusetts, USA
[10]Department of Pediatrics, Duke University School of Medicine, Durham, North Carolina, USA

Twitter Elissa R Weitzman @elissa_weitzman

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Contributors All authors have participated in relevant study conception and design (ERW, EvS, SR, CMM, RL, BBR and LES), acquisition of data (ERW, EvS, SR, KMM, AD, FD, ACM and LES), and analysis and data interpretation activities (ERW, AG, EvS, CMM, LL, AD, AH, SJL, FD, ACM, RC, BBR and LES). All authors contributed to drafting or revising the manuscript and have approved the manuscript as submitted. ERW accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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ORCID iDs
Elissa R Weitzman http://orcid.org/0000-0003-1299-0008
Laura E Schanberg http://orcid.org/0000-0002-1913-6472

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