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Pain, Fatigue and Psychological Impact on Health-related Quality of Life in Childhood-onset Lupus

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Abstract

Objectives—To evaluate pain, fatigue and psychological functioning of childhood-onset lupus (cSLE) patients and examine how these factors impact health-related quality of life (HRQoL).

Methods—At a tertiary rheumatology clinic, 60 cSLE patients completed: a Visual Analog Scale of pain intensity (0-10; Pain-VAS), the Pediatric Quality of Life (PedsQL) multidimensional Fatigue Scale (FS), Pain Coping Questionnaire (PCQ), Pain Catastrophizing Scale (PCS), Children's Depression Inventory I (CDI-I), the Screen for Child Anxiety Related Emotional Disorders (SCARED) questionnaire and the PedsQL-generic core scale (PedsQL-GC) and rheumatology module (PedsQL-RM). Sociodemographics and multiple disease activity indicators were recorded.

Results—Fatigue was present in 65% of the patients; clinically relevant pain (Pain-VAS > 3), anxiety (SCARED ≥ 25) and depressive symptoms (CDI-I > 12) were observed in 40%, 37% and 30% of the patients, respectively; 22% had high catastrophizing (PCS ≥ 26). On average, the PedsQL-GC/RM for cSLE were lower than in healthy norms. Reduced PedsQL-GC/RM scores were highly correlated with greater levels of fatigue, anxiety, and depressive symptoms (Pearson r > 0.65), but had weak correlation with disease activity (Pearson r < 0.25). Regression analysis demonstrated HRQoL was most impacted by fatigue, pain, and anxiety when evaluating all factors concurrently ($p < 0.001$).

Conclusion—cSLE is associated with decreased HRQoL, and psychological aspects of health contribute substantially to low HRQoL, whereas measures of cSLE activity seem less relevant.

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Study conception and design. Jones, Cunningham, Kashikar-Zuck, Brunner

Acquisition of data. Jones

Analysis and interpretation of data. Jones, Cunningham, Kashikar-Zuck, Brunner

Fatigue, pain, mood, and anxiety symptoms are present in a large subgroup of patients and need medical attention to achieve optimal health outcomes.

Introduction

Research in both children and adults suggests that systemic lupus erythematosus (SLE) has an important negative impact on health-related quality of life (HRQoL), especially when permanent disease damage, increased disease activity, and fatigue are present (1-3). Further, studies in adults demonstrated that even with well controlled disease, HRQoL with SLE can remain below that of normative populations and is impacted by potentially modifiable factors such as depression, anxiety, and fatigue (4).

We have shown that children and adolescents with childhood onset SLE (cSLE) have impaired participation in developmentally appropriate activities, leading to chronically poor HRQoL (5, 6). However, the impact of potentially modifiable psychological and lifestyle factors and their relationship to HRQoL in cSLE is largely unknown. Despite the substantial impact of fatigue in adults with SLE, there are few studies that examine the role of fatigue in cSLE.

The primary objectives of this study were 1) to assess the presence of pain and fatigue in patients with cSLE and 2) to assess psychological functioning (anxiety, depressive symptoms, coping) and HRQoL of patients with cSLE. The second objective was to examine relationships between pain, fatigue, psychological factors, and HRQoL. The third objective was to examine the impact of pain, fatigue, and psychological factors on HRQoL in cSLE. We hypothesized that cSLE patients would show reduced HRQoL compared to reference populations of healthy children and those with arthritis, and that poorer HRQoL would be associated with higher levels of pain, fatigue, and psychological symptoms. Given the lack of prior research in the area, no specific hypotheses were made about predictors of HRQoL.

Methods and Materials

As part of a cross-sectional study, a convenience sample, of 60 children and adolescents with cSLE, was recruited at the Cincinnati Children's Hospital Medical Center (CCHMC) rheumatology clinic in sequential order over a six month period, provided eligibility criteria were met. Patients between the ages of 8-20 years were included, only if they fulfilled the revised American College of Rheumatology Classification Criteria for SLE by age 18 years (7). Patients with cSLE were excluded from participation if they had history of a comorbid chronic disease besides cSLE that might impact HRQoL.

Patients completed self-report questionnaires of pain, sleep, fatigue, pain coping, pain catastrophizing, mood, anxiety, and HRQoL. Information collected as part of standard of clinical care of cSLE (medications, disease activity, duration and damage) was also obtained from the medical record. Prior to participation, the study was explained to each study participant and legal guardian. Written informed consent was obtained from patients > 18 years of age. Written informed consent and assent were obtained from all patients and parents/legal guardians if patients were minors. This study was approved by the institutional

review board at CCHMC and was conducted in accordance with the ethical standards established in the 1964 Declaration of Helsinki.

Patient reported measures

Patients were provided instructions to independently complete self-report questionnaires to measure pain, sleep, fatigue, pain coping, pain catastrophizing, mood, anxiety, and HRQoL. All measures have been validated for use in youth, school-age, and older, and were selected if they had been previously used in studies of pediatric pain or rheumatic disease.

Pain—The Brief Pain Inventory is a 10-item inventory, which inquires about pain duration, location, intensity, interference and frequency, currently and over the previous 24 hours (8, 9). A pain visual analog scale (Pain-VAS; 1 – 10; 0 = no pain, 10 = very severe pain) inquires about how much pain intensity has been experienced in the previous week with higher number representative of higher pain, and clinically relevant pain indicated by Pain-VAS > 3 (10, 11).

Sleep—The Adolescent Sleep Wake Scale (ASWS) is a 33-item questionnaire to assess overall sleep quality over the preceding one month. The items are grouped into five behavioral domains: going to bed, falling asleep, maintaining sleep, reinitiating sleep, and returning to wakefulness. Each item is rated on a 6-point Likert scale (1 = always, 2 = frequently, if not always, 3 = quite often, 4 = sometimes, 5 = once in a while, 6 = never). An ASWS summary score can be calculated from the unweighted average of the 33 item scores, with higher summary scores reflecting better sleep quality. The internal reliability (Cronbach α) for the ASWS subscales ranges from 0.60 to 0.81, while the full scale has a reliability of $\alpha = 0.80$ (12, 13). The ASWS in the current study had a Cronbach α of 0.71.

Fatigue—The Pediatric Quality of Life Inventory Multidimensional Fatigue Scale (PedsQL-FS) is an 18-item inventory that was designed to measure fatigue in pediatric patients over the previous month. It is comprised of three domains: general fatigue, sleep/rest fatigue and cognitive fatigue, with six items for each subscale. Items are rated on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always), and from the raw scores a summary score of 0 to 100 can be calculated with higher score representative of less fatigue. Internal reliability for child report was $\alpha = 0.95$ (14), and in this study the Cronbach α was 0.94. In addition, patient-reported, generalized fatigue was part of a checklist (yes, no) of multiple symptoms in a review of symptoms with a question stating, “Have you had (generalized) fatigue present in the last 7 days?” The question has “Yes” or “No” answer choices. All patients in the clinic complete the patient-reported review of systems checklist at each visit.

Pain coping—The Pain Coping Questionnaire (PCQ) is 39 items used to assess how children and adolescents cope with pain. The PCQ yields eight subscales: information seeking, problem solving, seeking social support, positive self-statements, behavioral distraction, cognitive distraction, externalizing, and internalizing catastrophizing and three higher-order scales: approach, distraction and emotion-focused avoidance. Items are rated on a 5-point Likert scale (1 = never, 2 = hardly ever, 3 = sometimes, 4 = often, 5 = very

often), and the PCQ summary score is calculated from the unweighted items scores, with higher score reflecting greater use of the coping strategy (15). The internal reliability (α) for the eight subscales is strong and ranges from 0.78 to 0.86 and that of the three higher-order scales ranges from 0.85 to 0.89 (15). When used in this study population the Cronbach α was 0.92.

Pain Catastrophizing—The Pain Catastrophizing Scale (PCS) consists of 13 items all rated on a 5-point Likert scale (0 = not at all, 1= mildly, 2 = moderately, 3 = severely, 4 = extremely) that can be grouped in three subscales: rumination (four items), magnification (three items), and helplessness (six items). A PCS summary score (range 0 to 52) can be calculated from the sum of the item scores, with higher summary scores representative of increased catastrophizing. The internal reliability of the PCS is excellent: α= 0.93 (16), and in this study Cronbach α was 0.94. PCS summary scores can be interpreted as follows: low (0 to 14), moderate (15 to 25), and high (≥ 26) pain catastrophizing (17).

Mood—The Children's Depression Inventory Version I (CDI-I) is a 27-item measure that assesses mood and depressive symptoms. Each item has three responses to choose from that quantifies a range of depressive symptoms, and is scored 0, 1, or 2. A higher total score indicates higher level of depressive symptoms with a cut-off CDI-I value of 12 reflecting the presence of clinically relevant depression (18). The internal reliability of the CDI-I is very high: α = 0.88 (19). The current study had a Cronbach α of 0.93.

Anxiety—The Screen for Child Anxiety Related Emotional Disorders (SCARED) consists of 41 items grouped into five subscales: panic/somatic symptoms, generalized anxiety, separation anxiety, social anxiety, and school phobia and a total sum score (≥ 25) that represents presence of anxiety disorder. Items are rated on a 3-point scale (0 = not true or hardly ever true, 1= somewhat true or sometimes true, 2 = very true or often true), with higher score representative of more anxiety. The internal reliability (α) for the SCARED total sum score is excellent and ranges from 0.89 to 0.92 (20), and in this study the Cronbach α was 0.96.

HRQoL and Disability—The Pediatric Quality Of Life Inventory Generic Core scale 4.0 (PedsQL-GC) (21) and Rheumatology Module 3.0 (PedsQL-RM) (22), patient global assessment of health (10-point numerical scale with higher score representative of better health), and functional disability inventory (FDI) (23) were completed.

The PedsQL-GC is a self-report tool comprised of 23 items divided among four domains which include: physical, emotional, social and school function. Internal consistency reliability is excellent: was α = 0.89, and in this study the Cronbach α was 0.94. The PedsQL-RM is administered along with the PedsQL-GC and probes HRQoL domains relevant to children with rheumatic diseases. The PedsQL-RM consists of 22 items grouped into five domains which include: pain and hurt, daily activities, treatment, worry and communication. The Internal validity for the PedsQL-RM range from 0.75-0.86, and for this study the Cronbach α was 0.92. For both the PedsQL-GC and -RM, items are rated on a 5-point scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always), and

from the raw scores a summary score of 0 to 100 can be calculated with higher score representative of better HRQoL.

The Functional Disability Inventory (FDI) is a 15-item measure that assesses difficulty in physical and psychological function, and perceived activity limitations. The FDI has a 5-point scale (0 = no trouble, 1 = a little trouble, 2 = some trouble, 3 = a lot of trouble, 4 = impossible), and the total score is comprised of the sum of the item scores. FDI total scores of less than 12 are considered to reflect no or minimal disability, 13 to 29 moderate disability and greater than 30 severe disability, respectively (24). The internal reliability of the FDI ranges from 0.86 to 0.91 (25), and in this study the Cronbach α was 0.90.

Physician completed measures

Measures of disease activity and damage—The Systemic Lupus Erythematosus Disease Activity index (SLEDAI, range 0 to 105; 0 = inactive disease) (26), British Isles Lupus Activity Group index (BILAG, disease activity in eight domains – general, mucocutaneous, neurological, musculoskeletal, cardiovascular and respiratory, vasculitis, hematology and renal with alphabetical value that is transformed to numerical score (A = 12, B = 8, C = 1, D = 0, E = 0); 0 = inactive disease) (27), and physician global assessment of disease activity (MD global) were used to assess disease activity. Both have been validated in cSLE and the BILAG was added because it contains items that address subjective symptoms that cannot be objectively measured which include, but are not limited to, fatigue, arthralgias and myalgias (28). Disease damage was evaluated with Systemic Lupus international Collaborating Clinics/ACR Damage Index (SDI, range 0 to 47; 0 = absence of damage) (29, 30).

Statistical Analysis

Numerical variables were summarized by mean and standard deviation (SD); binary and categorical variables were summarized by frequency and percentage. The means of PedsQL-GC, PedsQL-RM, PedsQL-FS of patients were compared to published population norms (14, 22, 31) using a 2-sided unpaired t-test under consideration of population variances where appropriate. Scored FDI, SCARED, CDI-I, Pain-VAS, PCS were compared to normative cutoff values with a 2-sided, one- sample t-test. Pearson correlation analysis was done with cross-sectional data to assess the relationships between pain (Pain-VAS), fatigue (PedsQL-FS), psychological variables (SCARED, CDI-I, ASWS, PCQ, PCS), HRQoL summary scores (PedsQL-GC, PedsQL-RM) and cSLE measures (SLEDAI, BILAG, SDI, MD global). A Pearson correlation coefficient (r) between 0.2 and 0.39 is considered to be weak, 0.4 and 0.59 is considered moderate, 0.6 and 0.79 is strong, and 0.8 to 1.00 is a very strong correlation (32). Two separate stepwise multiple linear regression analyses were done with HRQoL (PedsQL-GC and -RM) as the dependent variable and pain, sleep, fatigue, pain coping and catastrophizing, mood and anxiety as the independent variable.

Results

Population & Demographics

Of the 91 eligible cSLE patients who obtain care at CCHMC, a convenience sample of 64 were consecutively approached for study participation and 60 (94%) agreed to participate. Demographics and disease features of these 60 participants included in the statistical analysis are summarized in Table 1. The cohort was 80% female, had a mean age of 16.1 years and 50% were Caucasian. The mean SLEDAI score was 5.9 (5.8) and BILAG score was 10.1 (9.2), respectively, with SDI of 0.6 (1.1). Of note, 17% (10/60) of enrolled patients were prescribed medication for depression, which is higher than an average of 11% in the general population (12 years of age and older)(33).

Study participants (n = 60) were similar to 31 patients at the center who met eligibility criteria but declined to participate (n = 4) or were not approached for participation because they did not come to a clinic visit within the study period (n = 27). Patients excluded from this report were 71% (22/31) female with mean age of 16.6 years (SD 2.8), 39% (12/31) Caucasian, 42% (13/31) African American, 19% (6/31) other and 3% (1/31) Hispanic ethnicity with a mean SLEDAI score of 3.7 (SD 8.0) and mean SDI of 0.4 (SD 0.6).

HRQoL and pain, fatigue, and psychological variables

The mean summary scores for all HRQoL measures and psychological variables, with comparison to healthy normative population (or cutoff scores) are summarized in Table 2.

The PedsQL-GC, PedsQL-RM and PedsQL-FS summary scores were significantly lower in the cSLE than in reference populations of healthy children, and those with arthritis. Although the majority of cSLE patients reported no more than minimal functional disability, 18% (11/60) of them reported moderate to high functional disability (FDI ≥13). Of the cSLE patients in the study sample, 65% (39/60) reported to have fatigue on the clinician administered checklist, with 40% (24/60) reporting clinically relevant pain (Pain-VAS > 3). Further, 30% (18/60) of the study participants reported clinically important depressive symptoms (CDI-I > 12), 37% (22/60) reported clinically relevant anxiety (SCARED ≥ 25), and 22% (13/60) reported a high level of pain catastrophizing (PCS ≥ 26). On average, fatigue, anxiety and depression were not found to be significantly greater among patients on steroid therapy compared to those not requiring steroid therapy (fatigue/PedsQL-FS score: 55.0 vs. 60.5; anxiety/SCARED score: 24.1 vs. 20.7; depression/CDI-I score: 9.6 vs. 9.8; all p-values were not significant).

Correlation analysis

As summarized in Table 3, the scores of the fatigue (PedsQL-FS), anxiety (SCARED), and decreased mood (CDI-I) were all highly and significantly correlated ($r > 0.65$; all p-values < 0.01) with HRQoL (PedsQL-GC and PedsQL-RM), whereas none of the HRQoL measures or psychological variables correlated ($r < 0.25$; all p-values not significant) with disease activity measures (SLEDAI, BILAG, or MD global). Pain intensity ratings (Pain-VAS) showed weak to moderate correlations with the disease activity measures (SLEDAI, BILAG, and MD global: $r = 0.33$, 0.55, and 0.42, respectively; all p-values < 0.05).

The Brief Pain Inventory and Pain-VAS were highly correlated and also featured similar correlations to the remaining variables. Therefore, the Brief Pain Inventory was dropped from further consideration in the regression analyses, and pain severity was represented by Pain-VAS rating only.

Regression analysis

We used hierarchical regression analysis to evaluate the relative importance of modifiable factors of HRQoL as measured by the PedsQL-GC and PedsQL-RM in cSLE, respectively. As summarized in Table 4, HRQoL measured by PedsQL-GC was significantly impacted by fatigue, and pain (R-square = 0.75; p-value < 0.001), with fatigue predicting 42% and pain predicting 33% of model variance, but pain coping, anxiety, pain catastrophizing and depression did not significantly predict PedsQL-GC scores. The PedsQL-RM was significantly impacted by pain, fatigue and anxiety (R-square = 0.71; p-value <0.001) with pain predicting 33%, fatigue predicting 25% and anxiety predicting 7% of model variance, but pain coping, pain catastrophizing, and depression did not significantly predict PedsQL-RM scores. Taken together HRQoL estimation using a generic measure (PedsQL-GC) and a specific measure for pediatric rheumatic diseases (PedsQL-RM) both support the notion that pain, fatigue, and to a lesser extent anxiety, account for significantly diminished HRQoL observed observed in cSLE patients.

Discussion

In this study, we studied HRQoL and modifiable factors that can impair HRQoL in a representative sample of cSLE patients treated at a tertiary medical center. We confirm previously published findings that, despite improved treatments and survival rates over the past decade, children with cSLE continue to have significantly lower HRQoL than their healthy peers. Further, our results indicate that even with well controlled disease activity and low disease damage (SDI score = 0 in 68% (41/60) of the patients), a sizable sub-group of cSLE patients continues to experience substantial pain, fatigue, and anxiety that all negatively impacted their HRQoL. These results strongly suggest that drug therapy to improve cSLE associated inflammation and damage alone is insufficient to normalize HRQoL outcomes.

Consistent with literature on adults with SLE (34) and a previous report in cSLE (35), fatigue was present in the majority of the youth with cSLE. Similar to fatigue, pain appears common in cSLE and adults with SLE. Based on limited data 71 to 89% of adults with SLE experience some degree of pain, indicating that pain may be very common (4). In our study, 40% of cSLE patients reported clinically significant pain, and we showed pain had a significant, negative impact on HRQoL. Undoubtedly, besides pain frequency, its intensity is important, and the latter had a weak to moderate association with cSLE activity. This association will need further investigation but is likely due to cSLE manifestations resulting in pain, such as joint and muscle involvement or serositis.

In this study, 30% of cSLE patients had clinically overt depression, which is similar to a previous report of about one-third of all cSLE patients with depression, however, in the previous study antidepressant use was not documented (36), and in our study 22% of those

with clinically overt depression were on therapeutic antidepressant medication. Almost half of our study participants reported clinically relevant levels of anxiety (43%), a proportion that is much higher than 22% prevalence reported in an earlier study of cSLE patients. The reason for this difference is due to unknown differences in the cohorts and not entirely clear (37).

Moderate pain catastrophizing was endorsed in the majority of cSLE patients, while high pain catastrophizing was present about 22%. This appears to have therapeutic relevance as pain catastrophizing is clearly a psychological factor that is potentially modifiable by means of cognitive behavioral therapy which has been successfully used to treat juvenile fibromyalgia patients with elevated levels of pain catastrophizing (38).

Sleep and pain coping (other than catastrophizing) were investigated in this study, but these appear to be less relevant for cSLE patients' HRQoL.

Previous studies have indicated increased cSLE disease activity and damage as risk factors for poor HRQoL (1). Conversely, we failed to recognize a strong relationship between disease activity and damage with patient HRQoL. This might have been due to the fact the cSLE was generally well controlled in the study population (62% [37/60] with SLEDAI ≤ 5), and disease damage was often absent (SDI score = 0 in 68% [41/60] of the patients).

Limitations to this study include that the majority of the patients were teenagers, small sample size and cross-sectional design which precludes more sophisticated data analysis including structural equation modeling and subgroup analysis of patients based on psychological variable domains. However, patients studied were well phenotyped and are representative for those followed at this and other tertiary pediatric rheumatology. Study findings are primarily relevant to teenage cSLE populations while they may not be applicable to younger children with cSLE. Future studies in a larger population will allow for a more detailed exploration of pain, fatigue, and psychological variables. While this study supports musculoskeletal pain accounts for a portion of pain, further studies are needed to determine the etiology and amount of non-musculoskeletal pain that cSLE patients report (e.g. headaches and abdominal pains not associated with underlying cSLE). There are also numerous confounders of HRQoL which includes socioeconomic status (SES), however, there is no widely accepted measure of SES and we cannot assume the adolescents SES is the same as their parent (40).

This study of children and adolescents with cSLE reinforces the notion of persistent detrimental effects of cSLE on HRQoL, even in the setting of well controlled disease and low disease damage. Our findings suggest that the presence of pain, fatigue and anxiety have a potential capacity to lower HRQoL in cSLE patients. Routine clinical surveillance for pain, fatigue, anxiety and depression, with simple questionnaires, would allow for a systematical way to identify patients that may require or benefit from additional resources (e.g. psychologist, psychiatrist, pain intervention) to improve HRQoL, and prevent detrimental impairment and chronically poor HRQoL.

Additional research is warranted to develop therapeutic interventions (e.g. cognitive behavioral therapy, which has shown good evidence for management of pain and improved

coping among children with chronic pain and fatiguing conditions, such as juvenile fibromyalgia (41, 42), or short-term use of antidepressants for those who have clinically elevated levels of depressive symptoms).

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Significance and Innovations

- Children and adolescents with childhood-onset lupus (cSLE) endorse poorer health-related quality of life (HRQoL), even with well controlled disease activity and low disease damage, compared to reference populations of healthy children and children with arthritis.
- Similar to adults with lupus, we found that a considerable proportion of children and adolescents with cSLE report substantial fatigue, pain, and anxiety; all these factors have a significant negative impact on HRQoL.
- This is the first report of pain catastrophizing in cSLE, which affected more than half the children and adolescents and has a significant relationship with fatigue and HRQoL.

Table 1

Demographics and SLE features

Measure		Frequency, n (%)	Mean (SD)
Age, years			16.1 (2.5)
Female		49 (80%)	
Race	African American	25 (41%)	
	Caucasian	30 (50%)	
	Other	5 (9%)	
Ethnicity (Hispanic)		4 (7%)	
Disease duration, years			2.6 (2.6)
Current Medications	Prednisone (mg/day)	31 (51%)	11.9 (9.8)
	Mycophenolate	24 (39%)	
	Azathioprine	3 (5%)	
	Methotrexate	2 (3%)	
	Cyclophosphamide	4 (7%)	
	Hydroxychloroquine	58 (95%)	
	NSAID	29 (57%)	
	Antihypertensive	15 (25%)	
	Antidepressants	10 (17%)	
SLEDAI score*			5.9 (5.8)
BILAG score**			10.1 (9.2)
SDI score†			0.6 (1.1)

*Systemic Lupus Erythematosus Disease Activity Index

**British Isles Lupus Activity Group index; alphabetical scores converted as follows: A=12, B=8, C=1, D=0, E=0.

†Systemic Lupus international Collaborating Clinics/ACR Damage Index

Table 2

Health-related quality of life (HRQoL) and psychological variables

Measures	Normative population mean (SD)	cSLE mean (SD)	Frequency, n (%) above cutoff value†	p-value
HRQoL Variables				
PedsQL Generic Core Scale	83.9 (12.5)	70.8 (18.7)		0.001
PedsQL Rheumatology Module	84.4 (18.0)	73.1 (18.8)		0.001
Functional Disability Index (FDI)		7.2 (8.0)		
FDI > 12			11 (18%)	
Psychological Variables				
Fatigue (PedsQL-FS)	80.5 (13.3)	57.7 (21.0)		0.001
Anxiety (SCARED)		22.1 (17.2)		
SCARED > 25			22 (37%)	
Mood (CDI-I)		9.6 (8.6)		
CDI-I > 12			18 (30%)	
Pain (Pain-VAS)		2.9 (2.7)		
Pain-VAS > 3			24 (40%)	
Pain Catastrophizing (PCS)		18.3 (12.0)		
PCS ≥ 15			35 (58%)	
Pain Coping (PCQ)		2.6 (0.6)	*	
Sleep (ASWS)		4.1 (0.5)	**	

† Denotes cutoff values for clinically important symptoms for each variable where applicable

* Denotes no established normative or cutoff value; range 1-5, higher values = worse coping

** Denotes no established normative or cutoff value; range 1-6, higher values = better sleep

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Table 3

Pearson Correlation Coefficients

	HRQoL Measures		Psychological Variables						
	PedsQL-GC	**PedsQL-RM**	**Fatigue**	**Anxiety**	**Mood**	**Sleep**	**Pain**	**Coping**	**Catastrophizing**
PedsQL-GC	1	0.83**	0.83**	-0.65**	-0.74**	0.65**	-0.57**	-0.27*	-0.59**
PedsQL-RM		1	0.70**	-0.70**	-0.66**	0.49**	-0.58**	-0.40**	-0.57**
Fatigue			1	-0.63**	-0.72**	0.67**	-0.42**	-0.32*	-0.65**
Anxiety				1	0.66**	-0.41**	0.26*	0.38*	0.52**
Mood					1	-0.61**	0.36**	0.18	0.58**
Sleep						1	-0.22	-0.24	-0.43**
Pain							1	0.23	0.35**
Coping								1	0.39**
Catastrophizing									1
SLEDAI	-0.07	-0.04	-0.19	-0.04	0.06	0.02	0.33*	0.09	0.13
BILAG	-0.18	-0.21	-0.23	-0.12	0.14	0.03	0.55**	0.06	0.10
MD global	-0.11	-0.15	-0.15	-0.08	0.01	0.01	0.42**	0.12	0.09
Patient overall well-being	0.57**	0.62**	0.43**	-0.29**	-0.45**	0.21	-0.59**	-0.24	-0.47**

*Denotes p-value of 0.05

**Denotes p-value of 0.01

Table 4

Hierarchical regression analyses predicting HRQoL (PedsQL-GC & PedsQL-RM)

Predictor Variable	Predicting PedsQL-GC				Predicting PedsQL-RM			
	β*	p-value	R^{2**}	R^2 change	β*	p-value	R^{2**}	R^2 change
Step 1			0.33	0.33			0.33	0.33
Pain	-0.57	<0.001			-0.58	<0.001		
Step 2			0.75	0.42			0.58	0.25
Fatigue	0.71	<0.001			0.55	<0.001		
Step 3			0.79	0.05			0.71	0.13
Anxiety	-0.17	0.06			-0.37	0.001		
Mood	-0.18	0.09			-0.12	0.32		
Coping	0.05	0.49			-0.08	0.36		
Catastrophizing	0.02	0.98			-0.03	0.77		

*Represents the standardized coefficients

**Coefficient of multiple determination (how much model variance is predicted by each step, and the change with each additional step added to the model)