I, Jordan T. Jones, hereby submit this original work as part of the requirements for the degree of Master of Science in Clinical and Translational Research.

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

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

A thesis submitted to the
Graduate School
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Master of Science
in Clinical & Translational Research

In the Department of Environmental Health
Division of Epidemiology & Biostatistics
of the College of Medicine
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by

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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 consecutive 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 measures were obtained.

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 28% of the patients, respectively; 22% had high catastrophizing (PCS ≥ 26). On average, the PedsQL-GC/RM for cSLE were lower than in healthy norms. Presence of fatigue, anxiety, and decreased mood correlated highly with PedsQL-GC/RM scores (Pearson’s r > 0.65), but were unrelated with disease activity (r< 0.25). Regression analysis demonstrated HRQoL (PedsQL-GC/RM) was most impacted by fatigue, pain, depressed mood, and anxiety when evaluating all factors concurrently (p <0.01).

Conclusion: cSLE is associated with decreased HRQoL, and psychological aspects of health contribute substantially to diminish HRQoL, whereas, measures of cSLE activity seemed less relevant for HRQoL outcomes. Fatigue, pain, mood, and anxiety
symptoms are present in a large subgroup of patients and needs to be addressed to achieve optimal health outcomes.
ACKNOWLEDGEMENTS

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# TABLE OF CONTENTS

Abstract ............................................................................................................. 2

Acknowledgments ............................................................................................. 5

Introduction ........................................................................................................ 8

Methods and Materials
  Patient reported measures ................................................................. 9
  Physician completed measures ...................................................... 12
  Statistical Analysis ............................................................................... 13

Results
  Demographics ....................................................................................... 14
  HRQoL and pain, fatigue, and psychological variables 14
  Correlation analysis ............................................................................... 15
  Regression analysis ............................................................................... 15

Discussion ................................................................................................. 16

References ................................................................................................. 21

Tables and Figures .................................................................................. 24
LIST OF TABLES AND FIGURES

Table 1: Demographics and SLE features
Table 2: Health-related quality of life (HRQoL) and psychological variables
Table 3: Pearson Correlation Coefficients
Figure 1: Relationship of Modifiable Factors and HRQoL
INTRODUCTION

Research in both children and adults suggests that systemic lupus erythematosus 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 have shown that even with well controlled disease, HRQoL with lupus remains below that of comparative 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 factors (pain, sleep, fatigue, pain coping and catastrophizing, mood, anxiety) 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 report fatigue in cSLE.

The objectives of this study were to assess the presence of pain, fatigue and psychological functioning of patients with cSLE and assess the impact of these factors on HRQoL.

METHODS AND MATERIALS

As part of a population based, cross-sectional study, 60 children and adolescents with cSLE were 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
Systemic Lupus Erythematosus 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 questionnaires that measure 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 and assent were obtained from all legal guardians for all participants. Written assent was also obtained from participants 11 years of age or younger. This study was approved by the institutional review board at CCHMC and is 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 validated questionnaires to measure pain, sleep, fatigue, pain coping, pain catastrophizing, mood, anxiety, and HRQoL.

*Pain.* The Brief Pain Inventory (BPI) is a 10-item inventory, which inquires about pain duration, location, severity, interference and frequency (8, 9), and also includes a pain visual analog scale (Pain VAS; 1 – 10; 0= no pain) to indicate average pain severity 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 scale (1 = always, 2 = frequently, if not always, 3 = quite often, 4 = sometimes, 5 = once in awhile, 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 (α) for the ASWS subscales ranges from 0.60 to 0.81, while the full scale has a reliability of α = 0.80 (12).

**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 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 α = 0.95 (13). In addition, fatigue was obtained (as a dichotomized variable - “yes” or “no”) as part of standard medical review of systems.

**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 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 (14). The internal reliability for the eight subscales ranges from 0.78 to 0.86 and that of the three higher-order scales ranges from 0.85 to 0.89 (14).

*Pain* Catastrophizing. The Pain Catastrophizing Scale (PCS) consists of 13 items all rated on a 5-point 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 \( \alpha = 0.93 \) (15). PCS summary scores can be interpreted as follows: low (0 to 14), moderate (15 to 25), and high (≥ 26) pain catastrophizing (16).

*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 (17). The internal reliability of the CDI-I is \( \alpha = 0.88 \) (18).

*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 (\( \alpha \)) for the SCARED total sum score ranges from 0.89 to 0.92 (19).
HRQoL. The Pediatric Quality Of Life Inventory Generic Core scale 4.0 (PedsQL-GC) (20) and Rheumatology Module 3.0 (PedsQL-RM) (21), patient global assessment of health (Pt global; 10-point scale with higher score representative of better health), and functional disability inventory (FDI) (22) were used to assess HRQoL.

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 was α = 0.89. The PedsQL-RM is similar to the PedsQL-GC, but is relevant for children with rheumatic diseases, and has 22 items across five domains which include: pain and hurt, daily activities, treatment, worry and communication. Internal validity for the PedsQL-RM ranged from 0.75-0.86. 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(23). The internal reliability of the FDI ranges from 0.86 to 0.91 (24).

Physician completed measures

Measures of disease activity and damage. The Systemic Lupus Erythematosus Disease Activity index 2000 (SLEDAI, range 0 to 105; 0 = inactive disease) (25), 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) (26), 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 (27). Disease damage was evaluated with Systemic Lupus international Collaborating Clinics/ACR Damage Index (SDI, range 0 to 47; 0 = absence of damage) (28, 29).

**Statistical Analysis.** Numerical variables were summarized by mean and standard deviation; binary and categorical variables were summarized by frequency and percentage. HRQoL summary scores (PedsQL-GC and PedsQL-RM) and psychological variable means (PedsQL-FS) of patients were compared to published population norms (13, 21, 30) using a 2-sided unpaired t-test under consideration of population variances where appropriate. Other HRQoL (FDI) and psychological variable means (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 relationship between pain, fatigue, psychological variables, HRQoL summary scores and cSLE features. A Pearson correlation coefficient (r) between 0.2 and 0.39 is weak, 0.4 and 0.59 is moderate, 0.6 and 0.79 is strong, and 0.8 to 1.00 is a very strong correlation. Predictive factors were analyzed using a stepwise multiple linear regression analysis with HRQoL (PedsQL-GC and -RM) as the dependent factor and
pain, sleep, fatigue, pain coping and catastrophizing, mood and anxiety as the independent factors.

RESULTS

**Demographics.** A total of 60 patients were included in the analysis, and their demographics and disease features are summarized in Table 1. The cohort was 80% (49/60) female with a mean age of 16.1 years (SD 2.5), consisted of 50% (30/60) Caucasian, 41% (25/60) African American and 9% (5/60) other with 7% (4/60) of Hispanic ethnicity. The mean SLEDAI score was 5.9 (SD 5.8) and BILAG score was 10.1 (9.2), respectively, with SDI of 0.6 (1.1).

Of note, the included patients (n = 60) in this study were similar, to 31 patients at the center who met eligibility criteria but did not have a clinic visit within the study period and therefore were not approached for participation. Patients not included in 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). Of note, 17% (10/60) of enrolled patients were on antidepressants and 3% (2/60) were on anti-anxiety medications, which was also similar and not statistically significant compared with the unenrolled population.

**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 score), are summarized in Table 2.

The PedsQL-GC summary scores were significantly lower in the cSLE than in reference populations of healthy children, and the PedsQL-RM summary scores were
significantly lower in cSLE compared to children with arthritis. The majority of the cSLE patients reported no or only minimal functional disability, but 18% (11/60) of the cSLE patients reported moderate to high functional disability (FDI ≥13). On average, the cSLE patients reported significantly higher fatigue than healthy norms (indicated by lower PedsQL-FS scores), and 65% (39/60) of cSLE patients in the study sample reported fatigue. Although average scores for pain, pain coping, mood, anxiety, and sleep were within the normal range overall, subgroups of patients reported increased amounts of pain, depressed mood, and anxiety. Specifically, clinically relevant pain (Pain VAS > 3) was reported by 40% (24/60) of patients, while depressive symptoms (CDI-I > 12) were present in 28% (17/60), and clinically relevant anxiety (SCARED ≥ 25) in 37% (22/60) of the cSLE patients. Average pain catastrophizing (PCS) scores were in the moderately high range (15 to 25), and 22% (13/60) of the cSLE patients had high levels of (≥ 26) catastrophizing.

Correlation analysis. As summarized in Table 3, fatigue, anxiety, and decreased mood were highly and significantly correlated (r > 0.65) with HRQoL (PedsQL-GC and PedsQL-RM). Whereas none of the HRQoL measures or psychological variables correlated (r < 0.25) with disease activity measures (SLEDAI, BILAG, or MD global). Pain intensity ratings showed, a weak to moderate correlation with the disease activity measures (0.33, 0.55, and 0.42 respectively).

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

Regression analysis. HRQoL measured by PedsQL-GC was most impacted by pain, fatigue, and mood (R-square = 0.78; p-value < 0.01), and PedsQL-RM was most
impacted by pain, fatigue and anxiety (R-square = 0.70; p-value < 0.01); fatigue was most impacted by pain catastrophizing, mood and sleep (R-square = 0.67; p-value < 0.01), and pain was most impacted by disease activity based on BILAG and anxiety (R-square = 0.41; p-value < 0.01). Figure 1 provides details of the relationship of psychological variables and HRQoL.

**DISCUSSION**

With cSLE, preventing permanent disease damage, and increased disease activity are currently the main focus of medical interventions. While much progress has been made in modifying the inflammatory disease process and preventing damage due to cSLE, studies in adults have shown that even with well controlled disease, HRQoL with lupus remains below that of comparative normative populations and is impacted by potentially modifiable factors such as depression, anxiety, and fatigue (4). Based on this we understand that simply controlling disease outcomes does not equate to improved HRQoL, and further investigation is necessary to evaluate potentially modifiable factors that negatively impact HRQoL.

This study aimed to identify potentially modifiable factors that are associated with chronic disease (pain, sleep, fatigue, pain coping and catastrophizing, mood, and anxiety) and evaluate the impact of these factors on HRQoL in youth with cSLE.

Our study confirms previously published findings that despite improved survival over the past decade for children with cSLE, they 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), some cSLE patients continue to have substantial pain, fatigue, anxiety, and
depressed mood that negatively impacts HRQoL. These results strongly suggest that drug therapy alone to improve cSLE associated inflammation and prevent damage is insufficient to normalize HRQoL outcomes.

Consistent with literature on adults with lupus (31), fatigue was the most prevalent of the factors evaluated in this study of youth with cSLE. This finding is also in line with a previously reported estimate that showed approximately two-thirds of cSLE patients have fatigue (32). This indicates that fatigue is prevalent in cSLE and an important area to focus on to improve HRQoL as it has a significant, negative impact on HRQoL.

Fatigue is understudied in cSLE perhaps due to difficulty in classification of fatigue, use of many different measures of fatigue, and omission of fatigue from standard assessments. Fatigue is a complex construct, difficult to classify, and in this respect, often omitted from HRQoL measures (31). A multidimensional fatigue scale, as used in our study, is best suited to elucidate the intricacies of fatigue, and help delineate potential treatment strategies aimed at improving fatigue. In one study of adults with SLE, physical fatigue was found to be more related to disease activity, damage and sleep, and mental fatigue was more impacted by anxiety and psychosocial environment, and both were impacted by depressed mood and pain (33). In this study, fatigue was most impacted by pain catastrophizing, depressed mood, and sleep which illustrates the complexities of this overlap between physical and mental fatigue, and brings forth pain catastrophizing as another modifiable factor not previously described in cSLE. Further evaluation of pain catastrophizing in cSLE is needed, but also multidimensional aspects of fatigue are needed to target appropriate treatment strategies to improve fatigue.
Our study also shows that in addition to fatigue, pain, depressed mood, and anxiety, also have a significant, negative impact on HRQoL in cSLE patients. Similar to fatigue, pain is understudied in cSLE and adults with lupus with only a few studies in adults that show 71 to 89% experience some degree of pain (4). This is almost double the 40% we report, which argues for further investigation of pain in cSLE patients. Often pain is indirectly captured and evaluated in the SLEDAI and BILAG through arthritis, myositis, arthralgias, and myalgias, and often indirectly factored into the physician global assessment. Interestingly, the musculoskeletal domains of the SLEDAI were low in this study, but elevated on BILAG, which further supports arthralgias and myalgias more than arthritis and myositis as a portion of reported pain, and also explains the higher correlation of pain with the BILAG than the SLEDAI. While this study shows musculoskeletal pain accounting 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).

Our results for depression are similar to a previous report that one-third of cSLE patients have depressive symptoms (34) which indicates depression should be routinely screened for in cSLE patients. Our study also found more anxiety (43%) compared to a previous study that reported anxiety in 22% of cSLE patients. The difference is unclear, but may be attributable to the fact our study had a higher mean SLEDAI score and lower mean age (35). Additional research is warranted to ascertain a frequency of anxiety in cSLE and more studies are necessary to further support these results, however, a routine screen for anxiety may be necessary.

To the best of our knowledge, our study is the first to systematically study sleep, pain coping and pain catastrophizing in cSLE. Unexpectedly, moderate pain
catastrophizing appears to be present in the majority of cSLE patients with high pain catastrophizing in a significant number as well. This appears to have therapeutic relevance because pain catastrophizing is clearly a psychological trait 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 (36). In this study, sleep and pain coping seemed to be less relevant factors for cSLE and had little impact on 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 and disease damage was often absent (SDI score = 0 in 68% (41/60) of the patients).

Limitations to this study include the small sample size which prevents more sophisticated data analysis and evaluation of patients based on psychological variable domains. Demographic, disease activity and damage comparisons were made with those that refused and were unapproached for participation, which showed no significant differences, to ensure the study population was representative. Additionally, most patients were adolescents, and findings may therefore not be applicable to younger children with cSLE. We only used patient-reported questionnaires for this study so we are unable to compare the findings with proxy-reported results. There are multiple reports in the literature of discrepancy between self-report and parent-proxy reports, however these seem to be minor in the adolescent population (37), which was the majority of patients enrolled in the study. 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 (38).

This study of children and adolescents with cSLE reinforces the notion of 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 and fatigue as well as potentially modifiable psychological factors, such as elevated anxiety, and depressed mood have a significant negative impact on HRQoL in cSLE patients. These psychological and potentially lifestyle related factors must be evaluated and addressed on a regular basis as part of routine care of children and adolescents with cSLE to improve HRQoL, prevent impairment and chronically poor HRQoL. An ideal initial approach would be a nonpharmacologic approach, such as cognitive behavioral therapy which has shown good evidence for management of pain and improving coping among children with chronic pain and fatiguing conditions, such as juvenile fibromyalgia (39, 40) that could be developed to address and target the specific needs of cSLE patients, perhaps followed by pharmacologic or in combination with pharmacologic means (e.g., for more severe anxiety or mood difficulties) if necessary to maximize HRQoL. As a first step, future studies should evaluate the evidence for cognitive-behavioral interventions for youth with cSLE to address the unmet needs for improving HRQoL in this population.
REFERENCES

## TABLES AND FIGURES

### Table 1. Demographics and SLE features

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

* Systemic Lupus Erythematosus Disease Activity Index 2000
** 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

<table>
<thead>
<tr>
<th>Measures</th>
<th>Normative population mean (SD) or cutoff value</th>
<th>cSLE mean (SD)</th>
<th>p-value†</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>mean (SD) or cutoff value</td>
<td>mean (SD)</td>
<td></td>
</tr>
<tr>
<td><strong>HRQoL Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PedsQL Generic Core Scale</td>
<td>83.9 (12.5)</td>
<td>70.8 (18.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>PedsQL Rheumatology Module</td>
<td>84.4 (18.0)</td>
<td>73.1 (18.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Functional Disability Index (FDI)</td>
<td>≤ 12</td>
<td>7.2 (8.0)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Psychological Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue (PedsQL-FS)</td>
<td>80.5 (13.3)</td>
<td>57.7 (21.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Anxiety (SCARED)</td>
<td>≤ 25</td>
<td>22.1 (17.2)</td>
<td>0.201</td>
</tr>
<tr>
<td>Mood (CDI1)</td>
<td>&lt; 12</td>
<td>9.6 (8.6)</td>
<td>0.038</td>
</tr>
<tr>
<td>Sleep (ASWS)</td>
<td>*</td>
<td>4.1 (0.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain (Pain VAS)</td>
<td>≤ 3</td>
<td>2.9 (2.7)</td>
<td>0.698</td>
</tr>
<tr>
<td>Pain Coping (PCQ)</td>
<td>**</td>
<td>2.6 (0.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain Catastrophizing (PCS)</td>
<td>≤ 14</td>
<td>18.3 (12.0)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* Denotes no established normative or cutoff value; range 1-6, higher values = better sleep
** Denotes no established normative or cutoff value; range 1-5, higher values = worse coping
† Denotes use of Students T-test to determine p-values
### Table 3. Pearson Correlation Coefficients

<table>
<thead>
<tr>
<th>HRQoL Measures</th>
<th>Psychological Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>PedsQL-GC</td>
<td>PedsQL-RM</td>
</tr>
<tr>
<td>1</td>
<td>0.83**</td>
</tr>
<tr>
<td>1</td>
<td>0.70**</td>
</tr>
<tr>
<td>1</td>
<td>-0.63**</td>
</tr>
<tr>
<td>1</td>
<td>0.66**</td>
</tr>
<tr>
<td>1</td>
<td>-0.61**</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>0.39**</td>
</tr>
</tbody>
</table>

* Denotes p-value of 0.05
** Denotes p-value of 0.01
Figure 1. Relationship of Modifiable Factors and HRQoL

**PHYSICAL**
Disease Activity, Damage, Duration

**PSYCHOLOGICAL**
Mood & Anxiety
Pain Coping & Catastrophizing
Sleep

**MEDIATING FACTORS**

**Quality of life**
Physical Function

**Pain Fatigue**