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## Pain, fatigue and health-related quality of life in children and adolescents with chronic pain

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### Abstract

**OBJECTIVES**—Chronic pain and fatigue are common physical complaints among children and adolescents. Both symptoms can interfere considerably with daily life by affecting sleep and eating habits, engagement in physical and social activities, and school participation. The aim of this study was to examine the potential mediational role of fatigue in the relationship between pain and children’s school functioning and overall health-related quality of life (HRQOL). **METHODS:** Children seeking outpatient pain management services at two urban children’s hospitals were recruited for this study. The combined sample includes 80 children and adolescents between the ages of 8 and 18 ( $M = 13.89$ ,  $SD = 2.57$ ), 72.5% female, and their caregivers. The Pediatric Quality of Life Inventory (PedsQL™ 4.0) was used to assess HRQOL and the related PedsQL™ Multidimensional Fatigue Scale provided a comprehensive measure of fatigue.

**RESULTS**—Based on Preacher and Hayes’ mediation model (2004), fatigue functioned as a mediator between pain and overall HRQOL based on both self and proxy reports. Fatigue functioned as a mediator between pain and school functioning based on the caregiver proxy report only. Additionally, moderate relationships were found between self and caregiver proxy reports of HRQOL and fatigue, although children self-reported less fatigue, better school functioning, and greater quality of life than did their caregivers via proxy report.

**DISCUSSION**—Findings demonstrated that fatigue is a significant problem for many youth with chronic pain and may be an important target for clinical intervention.

## Keywords

fatigue; chronic pain; health-related quality of life; school functioning; children

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## INTRODUCTION

Chronic or recurrent pain is a common occurrence among children and adolescents, affecting as much as 25% of the pediatric population.<sup>1, 2</sup> Frequent complaints include abdominal pain, headache, and musculoskeletal pain.<sup>3</sup> Children and adolescents with chronic pain frequently report disturbances in sleep and eating habits, reduced participation in social activities or hobbies, and school absence,<sup>4, 5</sup> which affects their overall sense of well-being.

One method of assessing the impact of a chronic condition on the daily lives of children is to measure health-related quality of life (HRQOL). A comprehensive and multidimensional construct, HRQOL addresses an individual's subjective perception of his or her functioning across multiple domains, including physical, emotional, social, and school functioning. Children with chronic pain report significantly lower HRQOL than healthy peers<sup>6–8</sup> and children with other chronic conditions.<sup>9,10</sup> For example, a recent study conducted by Varni et al. found that children with fibromyalgia self-reported severely impaired physical and psychosocial functioning, and their HRQOL was more impaired than HRQOL in pediatric patients with cancer and other rheumatologic diseases.<sup>9</sup> Among adolescents with chronic pain, the greater the intensity and frequency of pain, the lower the self-reported quality of life.<sup>7</sup> Studies examining children with the specific conditions of spina bifida and juvenile arthritis have also found that pain is an important predictor of quality of life.<sup>11, 12</sup>

Fatigue is another physical symptom affecting a large portion of the pediatric population. Fatigue has been defined as an overwhelming sense of tiredness, lack of energy, and feeling of exhaustion.<sup>13</sup> Approximately one third of adolescents experience substantial fatigue four or more times a week.<sup>14</sup> In pediatric pain populations, there has been limited description of fatigue with the exception of studies of children with cancer and rheumatologic conditions.<sup>19, 20</sup>

Like pain, fatigue is a critical contributor to the impact of chronic illness on multiple domains of functioning. Among survivors of childhood cancer, for example, an inverse relationship exists between symptoms of fatigue and a patient's positive perception of HRQOL.<sup>15</sup> Notably, survivors who did not report fatigue were comparable to healthy controls on measures of functioning. Another study found that children with chronic idiopathic musculoskeletal pain, though similar on measures of pain intensity and disability, reported greater fatigue and lower levels of psychosocial functioning than children with juvenile chronic arthritis.<sup>16</sup>

While it is increasingly recognized that some children and adolescents with chronic conditions report considerable disruptions to daily life and marked declines in quality of life, the complex relationships between chronic pain, fatigue, and HRQOL are less well understood. Berrin and colleagues conducted a recent study of children with cerebral palsy (CP) specifically examining this complex relationship between chronic pain, fatigue and HRQOL. The study examined the roles of pain and fatigue as mediators between diagnostic subtypes of CP and school functioning.<sup>17</sup> The study also examined fatigue as a potential mediator between pain and school functioning. Results revealed an indirect relationship between diagnosis and school functioning that was mediated by pain and fatigue. Fatigue partially mediated the relationship between pain and school functioning. This study highlights the importance of pain and fatigue as potential points of intervention to possibly improve HRQOL in youth with CP. Although Berrin and colleagues focused on youth with CP, the relationships among fatigue, pain, and aspects of HRQOL are relevant to all youth with persistent pain. Building on the limited work that has

been done in this area, we sought to test a similar mediation model in a broader sample of youth with chronic pain.

The present study examined fatigue and its relationships with chronic pain, and HRQOL among a heterogeneous sample of children and adolescents with chronic pain conditions seeking outpatient pain management services at two urban children's hospitals. Based on findings of Berrin, et al., 2007<sup>17</sup>, a similar mediation model was proposed where fatigue was hypothesized to mediate the effects of pain on children's HRQOL, specifically their school functioning. In addition, similar to previous research on proxy reports of HRQOL<sup>18</sup>, we hypothesized a low to moderate correlation between child self report and parent proxy report of HRQOL and fatigue.

## MATERIALS AND METHODS

### Participants

Eighty participants were recruited from The Childrens Hospital of Los Angeles and Oregon Health and Science University as part of larger studies at each institution. The combined sample included 80 children and adolescents between the ages of 8 and 18 ( $M = 13.89$ ,  $SD = 2.57$ ) 72.5% female, and their caregivers (see Table 1). The majority of caregiver respondents were mothers (71%). Racial backgrounds included Caucasian (67.5%) and Hispanic/Latino (21.3%). On average, participants reported moderate to severe pain intensity ( $M = 6.6$ ,  $SD = 1.6$  on 10 cm visual analog scale). Primary pain complaints were headaches ( $n = 32$ ), arm/leg pain ( $n = 26$ ), abdominal pain ( $n = 15$ ), and back pain ( $n = 7$ ). Fifty percent of participants reported pain in more than one location. Twenty percent of participants had diagnoses of a comorbid medical condition (e.g., juvenile rheumatoid arthritis, pancreatitis). Participants from OHSU were older than participants recruited from CHLA ( $t = -2.21$ ,  $p < .05$ ). There were no differences in gender, ethnicity, pain intensity or pain location between participants at the two pain centers.

### Procedures

IRB approval was obtained to conduct this study at both sites. Participants at both sites included patients currently receiving treatment at an outpatient pediatric chronic pain clinic. Participants at CHLA were approached during their initial pain management appointment with the clinical psychologist and the physician. Consenting participants were asked to fill out questionnaires at this initial appointment. Medical charts were later reviewed to obtain pain diagnoses.

Eligible participants were English speaking children and adolescents between the ages of 8 and 18 who had a caregiver present. If more than one caregiver was present, the primary caregiver (parent who spent the most time with the child) was asked to complete the measures. Participants were excluded if they had a developmental disability, cognitive, or neurological deficit that would prevent them from comprehending and completing the self-report assessment questionnaires (e.g., mental retardation, organic brain dysfunction). Seventy-eight children and their caregivers were approached to participate before obtaining the 54 completed protocols. Twenty participants returned incomplete protocols, two withdrew from the study, and one participant refused. This resulted in a CHLA participation rate of 69%. At OHSU, participants were recruited during pain clinic appointments using the same exclusion criteria. Thirty children were approached for participation and 26 children and parents agreed to participate (87% participation rate).

### Measures

**Sociodemographics**—Caregivers completed a background questionnaire to assess for patient age, sex, race, and ethnicity.

**Pain**—A pain questionnaire was completed by the children to assess their pain over the past month. The questionnaire included assessment of pain intensity and location. Pain intensity was measured using a 10 cm Visual Analog Scale ranging from 0 indicating “no pain” to 10 indicating “worst pain imaginable”. Location of pain was recorded by markings on a validated body outline displaying an anterior and posterior view of the body. Comorbid medical diagnoses were obtained from children’s medical records.

**Fatigue**—Children’s level of fatigue was assessed by self-report and caregiver proxy report using the PedsQL™ Multidimensional Fatigue scale.<sup>19</sup> Previous research has demonstrated excellent reliability and validity of the measure, and individual comparisons have distinguished between healthy children and children with fatigue secondary to rheumatologic disease.<sup>20</sup> The PedsQL™ Multidimensional Fatigue scale includes assessment of general fatigue (6 items; e.g., “I feel too tired to do things that I like to do”), sleep/rest fatigue (6 items; e.g., “I rest a lot”), and cognitive fatigue (6 items; “It is hard for me to remember what people tell me”). Questions are asked about the prior month. Higher scores indicate fewer difficulties related to fatigue.

**Health Related Quality of Life**—Children’s health related quality of life was assessed by self report and caregiver-proxy report using the PedsQL™ 4.0 Generic Core Scale, which has well established reliability and validity in children with both acute and chronic health conditions.<sup>6, 17, 21</sup> The PedsQL™ 4.0 Generic Core Scale has four subscales: physical functioning, emotional functioning, social functioning, and school functioning. All scales demonstrate high reliability.<sup>22</sup> Each scale uses a Likert 5-point scale to ask the child or caregiver how much of a problem each item has been over the past month (0 = never a problem, 1 = almost never a problem, 2 = sometimes a problem, 3 = often a problem, 4 = almost always a problem).<sup>23</sup> Raw scores are then transformed into standard scores ranging from 0 to 100. Higher HRQOL scores indicate better health-related quality of life. Varni and colleagues have established at-risk cutoff scores indicating poor HRQOL for the PedsQL™ 4.0 Core Scales. These scores were determined by approximating one standard deviation below mean scores for a normative sample of 5,972 healthy children aged 5–18 and 10,070 caregivers of children aged 2–18.<sup>21, 24</sup> For the purposes of this study, the authors used two scales, the school functioning subscale and the total HRQOL summary score.

## Data Analyses

Data analyses were conducted using SPSS v15.0.<sup>25</sup> Descriptive statistics were computed to examine mean scores for child self-report and caregiver proxy-report for the fatigue and HRQOL measures. Bivariate correlations among pain, fatigue, and HRQOL scores were examined with Pearson and Spearman Rho correlations. Due to the multiple comparisons, a Bonferroni correction was applied reducing the significant p value to  $p < .001$ . Agreement between child self-report and caregiver-proxy measures were assessed using intraclass correlations. A series of independent sample t-tests were conducted to examine differences in fatigue and HRQOL scores by gender, age, and ethnicity. Multiple regression analyses were used to test a model that fatigue would mediate the relationship between pain and HRQOL in children, specifically school functioning and total HRQOL scores. Analyses for estimating indirect effects in mediation models described by Preacher and Hayes<sup>26</sup> were followed.

## RESULTS

### Caregiver-child comparisons

Descriptive statistics on the PedsQL and Multidimensional Fatigue Module for the sample are summarized in Table 2. On the child-reported PedsQL, children were at risk for impaired total HRQOL ( $M = 59.04$ ), physical ( $M = 51.51$ ), emotional ( $M = 56.98$ ), and school functioning ( $M = 55.89$ ). Mean scores on these HRQOL subscales were lower than mean scores of children

with disease-related chronic illness from previous studies<sup>27</sup> and lower than children with other chronic pain conditions.<sup>9</sup> Of particular note, children were 2 standard deviations below the population sample mean on total HRQOL and 3 below the population mean on physical functioning. In addition, the study sample scored in the at-risk range on all measures of fatigue including general fatigue, sleep/rest fatigue, cognitive fatigue, and total fatigue. Children reported less fatigue, better school functioning, and greater quality of life than did their caregivers via caregiver proxy-reports. There were significant differences between child and caregiver proxy-reports on measures of emotional functioning, social functioning, school functioning, and general fatigue (Table 2). As hypothesized, however, there were moderate levels of agreement between child and caregiver reports on all measures (Table 2).

There were no significant differences in fatigue or HRQOL scores with regard to age, gender, or ethnicity.

As expected, significant relationships were found between the majority of HRQOL and fatigue variables according to both child- and caregiver-report (Table 3).

### Fatigue as a mediator of the relationship between pain and HRQOL

**Total HRQOL**—Fatigue was tested as a mediator between pain intensity and total HRQOL assessed by child self-report (see Table 4). In step 1, pain was significantly associated with HRQOL reported by children ( $\beta = -.23, p = .03$ ). In step 2, pain was significantly associated with fatigue ( $\beta = -.27, p = .02$ ). In step 3, fatigue was significantly associated with HRQOL after controlling for pain intensity ( $\beta = .78, p < .001$ ). In step 4, the relationship between pain and total HRQOL assessed by self-report was not found to be significant after controlling for fatigue ( $\beta = -.01, p > .05$ ), suggesting a mediating effect of fatigue. The Sobel test found this mediated effect to be statistically significant,  $z = -2.49, p = .01$ .

Fatigue was also tested as a mediating variable between pain and HRQOL assessed by caregiver proxy-report. In Step 1 for the caregiver proxy report, pain was significantly associated with HRQOL reported by caregivers ( $\beta = -.30, p = .01$ ). In step 2, pain was significantly associated with fatigue ( $\beta = -.29, p = .01$ ). In step 3, fatigue was significantly associated with HRQOL after controlling for pain intensity ( $\beta = .49, p < .001$ ). In step 4, after controlling for fatigue, pain was not significantly associated with HRQOL ( $\beta = -.15, p > .05$ ), suggesting a mediating effect of fatigue. The Sobel test found this mediated effect to be statistically significant,  $z = -2.38, p = .02$ .

**School Functioning**—Fatigue was not found to be a mediator between pain intensity and school functioning for child self-report (see Table 5). No significant relationship between pain and self-reported school functioning was found.

Fatigue was tested as a mediating variable between pain and school functioning assessed by caregiver proxy-report. In Step 1 for the caregiver proxy report, pain was significantly associated with school functioning ( $\beta = -.22, p = .05$ ). In step 2, pain was significantly associated with fatigue ( $\beta = -.29, p = .01$ ). In step 3, fatigue was significantly associated with school functioning after controlling for pain intensity ( $\beta = .60, p < .001$ ). In step 4, the relationship between pain and school functioning was not found to be significant after controlling for fatigue ( $\beta = -.05, p > .05$ ), suggesting mediating effect of fatigue. The Sobel test found this mediated effect to be statistically significant,  $z = -2.35, p = .02$ .

## DISCUSSION

In this study, we examined the relationships among pain, fatigue, and HRQOL in a heterogeneous sample of children receiving treatment for chronic pain. Although previous



studies have emphasized associations between either pain or fatigue and HRQOL, the integration of these constructs has received limited attention. Similar to recent findings in a population of children with pain related to CP<sup>17</sup>, we also found fatigue to be a mediator of the relationship between pain and overall HRQOL in a mixed population of children with chronic pain. This effect was demonstrated in both self- and caregiver proxy-reports of HRQOL. However, unlike the Berrin model, fatigue did not demonstrate the same mediation effects for the relationship between pain and school functioning across all informants. Rather, an indirect relationship between pain and school functioning mediated by fatigue was found only for caregiver proxy-report. These findings suggest that fatigue may help to explain the association between chronic pain and overall quality of life.

In addition, the current findings document that many children with chronic pain have significant problems with comorbid fatigue, highlighting the importance of inquiries about this set of symptoms. Both caregiver- and child-reports demonstrate that children have moderate to severe impairments in total fatigue, general fatigue, cognitive fatigue, and sleep/rest fatigue compared to the population-based normative sample<sup>19</sup>, as well as children with cancer or rheumatologic conditions.<sup>20</sup> In general, children with these impairments feel that they need to rest during the day, that their attention and memory are impaired, and that they are too tired to participate in activities.

Consistent with previous studies of children with specific chronic pain conditions, this study also provides further evidence that children with a variety of chronic pain conditions are at-risk for poor overall quality of life.<sup>6-10</sup> Scores on the HRQOL scales were lower than those reported by Varni and colleagues<sup>20, 27</sup> in populations of children with other chronic health conditions and the scores were also well below the normative scores for healthy children.

In line with previous cross-informant findings on the PedsQL, caregivers in our sample reported lower functioning than their children.<sup>17, 28</sup> One reason for this discrepancy between self and caregiver-proxy reports of functioning may be that caregivers rely solely on behavioral and visual cues to assess the functioning of their child.<sup>28</sup> The child, however, also has access to internal emotional cues contributing to their assessment of how they feel they are functioning relative to others. Additionally, the children may have adapted to and accepted their chronic pain while their caregivers may have not.<sup>17</sup> However, despite caregivers reporting lower functioning than their children, the cross-informant correlations revealed moderate to high associations, suggesting that proxy-report methods are important measures of child functioning

Study findings should be interpreted in light of several limitations. We were limited to cross-sectional subjective data in analyzing the relationships among pain, fatigue, and HRQOL. There is some overlap present among different dimensions of HRQOL that were examined in the present study given that school functioning goes into the overall HRQOL score. Nonetheless we found different patterns of mediation among these outcomes suggesting some independence of these variables. Prospective studies are needed to more fully explore fatigue as a potential mechanism in the pain-HRQOL relationship and to identify the temporal sequence by which problems with pain, fatigue, and HRQOL develop over time. In addition, a variety of factors that may impact fatigue were not examined in the present study including sleep problems, depressive symptoms, and medication effects. For example, sleep patterns of the participants were not assessed and therefore, sleep restriction or sleep disturbance as potential causes of fatigue could not be determined. Effects of pain medications on fatigue also could not be assessed in our sample and remains an important area of inquiry. Another limitation is that the sample was limited to treatment-seeking patients at two chronic pain clinics. Although the combination of two study sites enhances generalizability, the sample size was too small to fully examine group differences on individual factors such as pain diagnosis. The addition of a control or comparison group of youth without chronic pain would have

strengthened the interpretation of findings. Additionally, though multiple raters were used to assess child functioning, teacher-report may enhance the understanding of school and social functioning in future studies. Also, recall bias could be a potential limitation associated with asking participants to recall their pain from the past month. More accurate pain ratings might be obtained by asking participants to prospectively record pain. Strengths associated with the current study include use of well standardized measures to examine comorbid fatigue and replication of the mediation model of fatigue in the relationship between chronic pain and HRQOL/school functioning, as previously noted in children with CP.<sup>17</sup>

The study findings have several clinical implications for the assessment and treatment of children with chronic pain. Because fatigue is a significant problem for many children, assessment and management of fatigue should be a standard part of care for children with chronic pain. Clinicians could benefit from the use of standard self-administered questionnaires to assess fatigue routinely in their clinics. Ultimately, practitioners could conduct comprehensive evaluations to determine best clinical practice for further treatment. Due to the variety of potential etiologies associated with fatigue, such as the direct effects of chronic daily pain, poor sleep hygiene, and medication effects, many clinical interventions could be offered. Clinical treatments may include cognitive-behavioral interventions, medications to help decrease fatigue, and exercise programs, all of which require evaluation in the pediatric population.

Further research is required to better understand the role of fatigue in children with chronic pain in order to identify strategies to reduce its impact. Because fatigue may have a large impact on children's physical function and their ability to participate in age appropriate activities, the methods used to cope with fatigue may be particularly salient to identify.

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**Table 1**

## Characteristics of chronic pain sample

Variable	M	(SD)
Age	13.89	2.57
Average Pain	6.6	1.6

  

Variable	%	n
Gender		
Female	73	58
Male	27	22
Race		
Caucasian	68	54
Hispanic/Latino	21	17
Other	11	19
Pain Locations		
Headaches	45	36
Arm/Leg	41	33
Abdominal	41	33
Back	40	32
Chest	10	8
Widespread musculoskeletal	39	31
Comorbid Medical Conditions		
Yes	20	16
No	80	64

**Table 2**  
Scale descriptive statistics, cross-informant correlations, and differences for PedQL Generic score and Multidimensional Fatigue Module

	Child		Caregiver	Cross-informant		Difference
	N	Mean (SD)	Mean (SD)	r	t	
Pain	80	6.15 (1.88)	N/A	N/A	N/A	N/A
<b>Total HRQOL</b>	79	59.04 (20.19)	57.19 (18.74)	.59**		.94
Physical functioning	79	51.51 (26.77)	47.75 (25.57)	.56**		1.26
Emotional functioning	79	56.98 (23.29)	51.13 (22.38)	.56**		2.45*
Social functioning	79	75.97 (21.08)	65.95 (25.72)	.50**		3.89**
School functioning	76	55.89 (25.23)	49.34 (25.20)	.53**		2.17*
N = 80						
<b>Fatigue Total</b>	79	55.63 (22.80)	53.40 (20.55)	.66**		1.29
General Fatigue	79	53.44 (27.34)	48.52 (23.41)	.68**		2.18*
Cognitive Fatigue	79	61.38 (27.28)	62.53 (26.41)	.62**		-.40
Rest Fatigue	79	52.04 (23.22)	62.53 (26.41)	.70**		1.40
N = 79						

\* p &lt; .05;

\*\* p &lt; .01

**Table 3**  
 Bivariate Correlations among Pain, HRQOL, and Fatigue according to Child-and Caregiver-report.

Variables	CAREGIVER										
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Co-morbid Medical Condition	--	-.090	-.070	-.103	-.182	-.086	.097	-.212	-.036	-.262	-.195
2. Pain	-.090	--	-.111	-.336	.008	-.223	-.300	-.177	-.279	-.258	-.286
3. Physical	-.192	-.176	--	.326	.388*	.552*	.525*	.533*	.443*	.332	.518*
4. Emotional	-.091	-.280	.625*	--	.477*	.358*	.361*	.535*	.361*	.479*	.541*
5. Social	-.171	-.251	.579*	.487*	--	.308	.464*	.375*	.396*	.380*	.458*
6. School	-.055	-.107	.588*	.510*	.502*	--	.524*	.560*	.535*	.433*	.612*
7. Total HRQOL	-.168	-.234	.907*	.793*	.751*	.782*	--	.410*	.530*	.400*	.535*
8. General	-.274	-.238	.706*	.514*	.535*	.557*	.722*	--	.561*	.705*	.890*
9. Cognitive	-.219	-.226	.572*	.508*	.544*	.693*	.704*	.728*	--	.423*	.804*
10. Rest	-.235	-.251	.630*	.442*	.416*	.513*	.633*	.680*	.556*	--	.831*
11. Total Fatigue	-.276	-.271	.724*	.558*	.572*	.673*	.784*	.921*	.878*	.832*	--

\* Note: p < .001

**Table 4**

Mediation analyses for total HRQOL by child and caregiver report

Predictor	Outcome	Child Report		Caregiver Report	
		$\beta$	p	$\beta$	p
Pain Intensity	Total HRQOL	-.23	.03	-.30	.01
Pain Intensity	Fatigue	-.27	.02	-.29	.01
Pain Intensity	Total HRQOL	.78	.00	.49	.00
Fatigue	Total HRQOL	-.01	.85	-.15	.16
Sobel's Test		z = -2.49, p = .01		z = -2.38, p = .02	

**Table 5**

Mediation analyses for school HRQOL by child and caregiver report

Predictor	Outcome	Child Report		Caregiver Report	
		$\beta$	p	$\beta$	p
Pain Intensity	School HRQOL	-.11	.35	-.22	.05
Pain Intensity	Fatigue	-.27	.02	-.29	.01
Pain Intensity	School HRQOL	.70	.00	.60	.00
Fatigue Pain Intensity	School HRQOL	.09	.31	-.05	.61
Sobel's Test		z = -2.43, p = .02		z = -2.35, p = .02	