Health-Related Quality of Life, Physical Function, Fatigue, and Disease Activity in Children with Established Polyarticular Juvenile Idiopathic Arthritis

SARAH RINGOLD, CAROL A. WALLACE, and FREDERICK P. RIVARA

ABSTRACT. ***Objective.*** To compare child self-report and parent/proxy report of health-related quality of life (HRQOL), disability, and fatigue in children with active polyarticular juvenile idiopathic arthritis (JIA) to that of children with inactive polyarticular JIA and to previous data from healthy controls.

Methods. Cross-sectional survey of children with polyarticular JIA diagnosed and treated between 2000 to 2006 and their parent/proxy. The Childhood Health Assessment Questionnaire, Pediatric Quality of Life Inventory (PedsQL) Generic Core Scales, PedsQL Rheumatology Module, and PedsQL Multidimensional Fatigue Scale were administered. Disease activity data were collected from the physician clinic notes. Comparisons were performed with t tests. Correlations between patient and parent/proxy reports were measured with Pearson correlation coefficients.

Results. Sixty children and/or their parents/proxies participated (79% response rate). Disease activity status was available for 52, and 32 met criteria for inactive disease (62%). Participants reported lower scores on the PedsQL Generic Core Scales (range 2.54–9.13 points lower) and the PedsQL Rheumatology Module (range 2.46–6.96 points lower) than those with inactive disease. Participants also reported lower scores on the PedsQL Multidimensional Fatigue Scale than did healthy controls, regardless of disease activity status (range 0.06–9.2 points lower).

Conclusion. Although children in this cohort with polyarticular JIA and inactive disease reported HRQOL scores similar to those of healthy controls, children with polyarticular JIA and their parents/proxies tended to report more fatigue than controls, regardless of disease activity. Application of these measures prospectively to larger cohorts of children with JIA is needed to assess these differences. (J Rheumatol First Release May 1 2009; doi:10.3899/jrheum.081028)

Key Indexing Terms:
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Juvenile idiopathic arthritis (JIA) is the most common of the pediatric rheumatic illnesses, with an estimated annual incidence of 3.2 to 6.1 in 100,000, depending on the population studied and the case definition applied[1-4]. Polyarticular JIA, defined as arthritis involving 5 or more joints during the first 6 months of illness, accounts for about 40% of children with JIA and has been the focus of the majority of clinical trials in JIA. Observational reports indicate that children with polyarticular JIA have disease that is particularly difficult to control and spend the majority of their course with active disease, as compared to children with other forms of JIA, and have a lower probability of achieving disease remission within 10 years than the other JIA subtypes[5].

From the Department of Pediatrics, Division of Rheumatology, Seattle Children's Hospital, Seattle, Washington, USA.

S. Ringold, MD, MS, Acting Instructor; C.A. Wallace, MD, Professor; F.P. Rivara, MD, MPH, Professor, Seattle Children's Hospital.

Address reprint requests to Dr. S. Ringold, Pediatrics, Seattle Children's Hospital, MS R-5420, 4800 Sandpoint Way NE, Seattle, WA 98105. E-mail: Sarah.Ringold@seattlechildrens.org

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Further, it has also been established that children with rheumatic diseases report lower health-related quality life (HRQOL) as compared to their healthy peers, and that children with polyarticular, extended oligoarticular, and systemic onset JIA report lower HRQOL than children with oligoarticular JIA[6,7]. Fatigue, an additional component of quality of life, is considered an important patient-reported outcome in adult rheumatoid arthritis (RA), and reports indicate that children with JIA may be affected by it as well[8-10]. While HRQOL is acknowledged to be an important outcome for children with polyarticular JIA, there is not a consensus on reporting of this outcome and a wide variety of measures have been used, including both generic and disease-specific measures, which has limited the scope of the published data[11].

Similarly, although the ultimate goal of treatment for polyarticular JIA is achievement and maintenance of inactive disease, standard definitions for inactive disease and remission in JIA did not exist until 2004, when consensus-derived, preliminary criteria for these disease states were published by Wallace and colleagues[11]. While it is hypothe-

sized that the achievement of the complete absence of disease activity (inactive disease) and sustained inactive disease (remission) will lead to improved HRQOL, decreased disability, and decreased fatigue in children with polyarticular JIA, it is not known if these outcomes actually differ between children with active versus inactive disease. Data regarding HRQOL status and inactive disease are therefore needed to support inactive disease as an important measure of health status. The goal of this investigation was to compare these domains among children with active disease, inactive disease, and healthy controls, using a series of well validated measures.

MATERIALS AND METHODS

Patients. Eligible families were identified through a search of the billing database of patients at Seattle Children's Hospital (SCH), Seattle, Washington, associated with the ICD-9 diagnosis codes for polyarticular juvenile RA (acute and chronic) and juvenile RA not otherwise specified (714.30, 714.31). Children identified by this search who were diagnosed and treated in the SCH rheumatology clinic between January 1, 2000, and December 31, 2006, and who had a minimum of 2 visits to the rheumatology clinic during that period were included in the cohort if they also met the Edmonton International League of Associations for Rheumatology criteria (2nd revision) for a diagnosis of polyarticular JIA [rheumatoid factor (RF) positive or negative][12], and if they had a visit to the SCH rheumatology clinic during the year prior to the start of this survey.

Families who were unable to complete the English language versions of the measures were excluded from the study. Children who were in foster care placements were excluded, as were children who were not accompanied to clinic by a legal guardian.

Approval for this study was obtained from the SCH institutional review board.

Measures. The following measures were administered to the parent or proxy and child: Childhood Health Assessment Questionnaire (CHAQ); PedsQL Generic Core Scales (version 4.0); PedsQL Rheumatology Module (version 3.0); and PedsQL Multidimensional Fatigue Scale (standard version). The CHAQ was completed by the parent or proxy unless the patient was ≥ 18 years of age. A pain visual analog score (VAS) assessed with a 100-mm line was also completed by the parent/proxy. Both patient self-report and parent or proxy report were obtained for each of the PedsQL measures unless the child was < 5 years of age, in which case only parent or proxy report was obtained, or if the child was ≥ 18 years of age, in which case only patient self-report was obtained. The details of the questionnaires' content, their administration, and scoring have been published[13].

The CHAQ was developed specifically as a measure of function for children with juvenile RA[14]. The questionnaire asks the parent or child to rate the child's ability to perform tasks of daily living over the 7 days prior to the administration of the instrument, and it has been found to be a valid measure of both disability and physical function in children with JIA. The score includes 30 items, divided into the domains of Dressing and Grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, and Activities. The child or parent/proxy grades each of these activities on a 0–3 score based on how difficult each task is to perform and the measure takes ≤ 10 minutes to complete. The score provides a number between 0 (no disability) and 3 (maximum disability).

The PedsQL has been widely validated in healthy cohorts and in cohorts of children with chronic diseases, including rheumatologic diseases[13,15,16]. These scores therefore have the advantage of being understood across specialties, and data from large cohorts of healthy children are available in the literature for comparison[15]. Each measure has 2 sections, one for patient/proxy report and one for child self-report. Child self-report for these measures has been validated for children ≥ 5 years of age[15]. Each measure provides a score between 0 (poorest quality of life) and 100 (highest quality of life). The PedsQL Generic Core Scales measure patient self-report and parent or proxy perception of the child's HRQOL in the domains of physical function, emotional function, social function, and school function during the month prior to completion of the questionnaire. In addition to scores for each specific domain, total scores are calculated for overall HRQOL, physical function, and psychosocial function[13]. The PedsQL Rheumatology Module assesses domains specifically related to rheumatologic disease, including pain and hurt associated with the illness, the effect of disease on daily activities, feelings about treatment, worry about the illness and/or medications, and communication about illness with providers and others. In addition to distinguishing children with rheumatologic diseases from healthy controls, the PedsQL Rheumatology Module has been found to be responsive to change in health status over time[6]. The PedsQL Multidimensional Fatigue Scale incorporates assessment of general fatigue, sleep/rest fatigue, cognitive fatigue, and a total fatigue score[17].

Procedures. Eligible families received initial notification of the study by mail and were given the opportunity to refuse to be contacted about the study. The clinic appointment schedule was reviewed daily for eligible families and enrollment occurred between October 2007 and March 2008. Eligible parents/proxies and children were approached by a trained research assistant after being checked in for their clinic visit and before their physician visit. Written consent for participation was obtained from one parent or proxy, if the child was < 18 years old, and from the child, if he/she was ≥ 14 years of age. Written assent was obtained from children who were 7–13 years of age.

The instructions for completion of the different measures were reviewed with the parent or proxy and child by the research assistant. The research assistant remained available to answer questions and to assist younger children with completion of the questions, if requested. Parents or proxies and children were asked to complete the measures separately but were not physically separated for completion of the measures. Families who felt they had inadequate time to complete the questions during their visit were given prepaid envelopes and allowed to complete the measures at home and return them by mail.

Additional data collection. Patient charts were reviewed to obtain each patient's sex, age at first SCH rheumatology clinic visit, and serology results. Each patient's disease status (active vs inactive disease) was determined by review of their clinical and laboratory data from their study visit. Patients were classified as having inactive disease if they met the following criteria: physician global assessment of disease activity of 0 on a 10-point VAS; no active arthritis; no active uveitis; no fever; no rash, serositis, splenomegaly, or lymphadenopathy attributable to JIA; normal erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP)[11]. Because laboratory testing was not carried out at every clinic visit, a normal ESR and/or CRP were not required for inactive disease classification if the patient otherwise met criteria for inactive disease. If the disease state could not be classified due to missing data or unclear documentation, it was recorded as "not classifiable."

Statistical analyses. Responses were pooled across the age ranges for parent/proxy reports and patient self-report. Unpaired t tests were used for comparisons of responses between groups. Comparisons are reported as a difference and 95% confidence interval, to illustrate the magnitude of difference. Pearson correlations were calculated to measure the associations between child self-report and parent or proxy report. Comparison data from healthy children for the PedsQL Generic Core Scales and Multidimensional Fatigue Scales (Table 2, Table 4) were obtained from published reports[15,17]. Data from healthy controls for the PedsQL Rheumatology Module have not been published and were therefore not available for comparison. Data were analyzed using Stata version 10.0 statistical software (Stata, College Station, TX, USA).

RESULTS

One hundred four eligible patients were identified. Four

patients were excluded for the following reasons: legal guardian not present (n = 1); non-English speaking (n = 1); or recent foster care placement (n = 2). An additional 24 patients were excluded because they had not had a rheumatology clinic visit in at least 1 year. Of the remaining 76 patients, 5 refused participation and 11 were not enrolled due to clinic appointment cancellations or lack of available research staff for their enrollment. A total of 60 patients and their parent or proxy were enrolled and completed the measures, for a response rate of 79% (Table 1). Disease status (active vs inactive disease) was available for 52 of the 60 patients (87%).

The mean CHAQ score for this cohort was 0.321 and CHAQ scores did not significantly differ between children with and without active disease (mean CHAQ scores 0.325 and 0.309, respectively; p = 0.9). The correlation between CHAQ scores and physician global assessment of disease activity was extremely low (–0.0039), indicating that the CHAQ may reflect disability due to joint damage from past disease as well as active disease at the time of completion. Children who were RF-positive in this cohort tended to have higher CHAQ scores than the children who were RF-negative (0.530 and 0.258, respectively; p = 0.05); however, there was no significant difference in mean physician global assessment of disease activity or in percentage of children with inactive disease between these 2 groups. Mean pain VAS score for the cohort was low (mean 9.3 mm, range 0–70 mm). Children with active disease tended to report higher mean levels of pain than children with inactive disease (15 mm vs 9 mm; p = 0.24).

Table 1. Patient characteristics (n = 60).

Characteristic	No. (%)	
Sex		
Female	50 (83)	
Male	10 (17)	
Antinuclear antibody		
Positive	24 (40)	
Negative	36 (60)	
Rheumatoid factor		
Positive	14 (27)	
Negative	38 (73)	
Anti-citric citrullinated peptide antibody		
Positive	7 (32)	
Negative	15 (68)	
Disease status at study visit		
Inactive	32 (62)	
Active	20 (38)	
	Mean (median)	Range
Age at first visit, yrs	8.4 (9.4)	1.3, 15
Age at study visit, yrs	11.73 (12)	3, 21
CHAQ	0.321 (0.125)	0, 2
Physician global assessment of disease activity*	0.72 (0)	0, 6

* 0–10 integer visual analog scale, 0 indicating no active disease. CHAQ: Childhood Health Assessment Questionnaire.

PedsQL Generic Core Scales. Compared to a cohort of healthy controls, children with active disease and their parents/proxies tended to report lower scores in the majority of domains of the PedsQL Generic Core Set (Table 2). Children with inactive disease in this cohort and their parents/proxies reported scores that were similar to, or higher than, those of the healthy controls for the majority of domains of the PedsQL Generic Core Scales (Table 3). Both children and their parent/proxy reported higher social functioning than the healthy controls, regardless of disease activity status, reflecting the overall high mean score for social functioning in this cohort (90.55 for child self-report and 88.80 for parent/proxy report).

Children with active disease reported lower scores in all domains of the PedsQL Generic Core Scales than did the children with inactive disease (Table 3). The largest difference was for the emotional functioning domain (–9.13; 95% CI –20.33, 2.06). The parents/proxies of children with active disease also reported lower scores in all domains of this measure than did the parents/proxies of children with inactive disease, with the largest difference in the physical health domain (–6.58; 95% CI –17.80, 4.63).

PedsQL Rheumatology Module. Children with active disease reported lower scores on each of the domains of the PedsQL Rheumatology Module than the children with inactive disease, with the exception of the communication domain, on which they reported higher mean scores (5.53; 95% CI –6.61, 17.67; Table 4). Parents/proxies of children with active disease reported lower scores on each domain of this measure than did the parents/proxies of children with inactive disease (Table 4). The largest difference was in the domain of pain and hurt (–6.94; 95% CI –20.21, 6.32).

PedsQL Multidimensional Fatigue Scale. Children in this cohort and their parents/proxies reported lower scores on all domains of the Multidimensional Fatigue Scale than the healthy controls, regardless of disease activity status (Table 5). Similarly, children with active disease also reported lower scores on each domain of the PedsQL Multidimensional Fatigue Scale than children with inactive disease (Table 6). Parents/proxies of children with active disease tended to report lower scores on the general fatigue and sleep/rest fatigue domains as compared to the parents/proxies of children with inactive disease. The correlation between pain VAS score and total fatigue was lower for children with active disease (–0.51) than for children with inactive disease (–0.75).

Correlations between child self-report and parent or proxy report. The correlations between child self-report and parent/proxy report for the PedsQL measures were evenly distributed between moderate and good (0.41–0.6 and 0.61–0.8, respectively) for the cohort as a whole (Table 7). Correlations were less strong between children with inactive disease and their parent/proxy. There were 3 domains for which the correlations were poor to fair (≤ 0.4): emotional

Table 2. PedsQL Generic Core Scales in polyarticular JIA: comparison to a healthy control population[15]. Healthy control data derived from a mail survey of new enrollees in California's Children's Health Insurance Program.

	Polyarticular JIA		Healthy Controls		Comparison,
	N	Mean (SD)	N	Mean (SD)	Difference (95% CI)
Child self-report					
Total score	55	82.54 (12.34)	5079	83.91 (12.47)	–1.37 (–4.72, 1.98)
Physical health	55	82.27 (17.40)	5070	87.77 (13.21)	–5.50 (–10.22, –0.78)
Psychosocial health	55	82.77 (14.48)	5070	81.83 (13.97)	0.94 (–2.99, 4.87)
Emotional functioning	55	81.14 (16.85)	5068	79.21 (18.02)	1.93 (–2.65, 6.51)
Social functioning	55	90.55 (13.39)	5056	84.97 (16.71)	5.58 (1.93, 9.23)
School functioning	55	77.18 (19.76)	5026	81.31 (16.09)	–4.13 (–9.49, 1.23)
Parent/proxy report					
Total score	56	82.23 (16.74)	8713	82.29 (15.55)	–0.06 (–4.55, 4.34)
Physical health	55	82.06 (18.10)	8696	84.08 (19.70)	–2.02 (–6.93, 2.89)
Psychosocial health	55	82.13 (17.99)	8714	81.24 (15.34)	0.94 (–3.89, 5.77)
Emotional functioning	55	81.41 (20.18)	8692	81.20 (16.40)	0.21 (–5.26, 5.68)
Social functioning	55	88.80 (15.05)	8690	83.05 (19.66)	4.35 (–10.10, 1.40)
School functioning	54	78.70 (21.01)	7287	78.27 (19.64)	1.07 (–4.65, 6.79)

Table 3. PedsQL Generic Core Scales in polyarticular JIA: comparisons by disease activity status.

	Polyarticular JIA: Active Disease		Polyarticular JIA: Inactive Disease		Active vs Inactive Disease	Active Disease vs Healthy Controls,	Inactive Disease vs Healthy Controls,
	N	Mean (SD)	N	Mean (SD)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Child self-report							
Total score	18	80.98 (16.83)	29	85.62 (11.84)	–4.64 (–13.93, 4.66)	–2.93 (–11.31, 5.45)	1.71 (–2.81, 6.23)
Physical health	18	83.53 (17.63)	29	86.07 (13.60)	–2.54 (–12.48, 7.40)	–4.24 (–13.01, 4.53)	–1.70 (–6.88, 3.48)
Psychosocial health	18	79.62 (17.80)	29	85.56 (12.11)	–5.94 (–15.71, 3.83)	–2.21 (–11.07, 6.65)	3.73 (–0.89, 8.35)
Emotional functioning	18	75.69 (20.54)	29	84.83 (13.46)	–9.13 (–20.33, 2.06)	–3.52 (–13.74, 6.70)	5.62 (0.48, 10.76)
Social functioning	18	89.44 (14.54)	29	92.59 (10.40)	–3.14 (–11.20, 4.92)	4.47 (–2.77, 11.71)	7.62 (3.64, 11.60)
School functioning	18	75.28 (20.97)	29	79.31 (20.60)	–4.03 (–16.71, 8.65)	–6.03 (–16.47, 4.41)	–2.00 (–9.85, 5.85)
Parent/proxy report							
Total score	20	80.63 (19.34)	32	84.44 (14.60)	–3.81 (–14.06, 6.44)	–1.66 (–10.72, 7.40)	2.15 (–3.12, 7.42)
Physical health	20	79.22 (21.58)	31	85.80 (14.61)	–6.58 (–17.80, 4.63)	–4.86 (–14.97, 5.25)	1.72 (–3.65, 7.09)
Psychosocial health	20	81.39 (20.97)	32	84.14 (14.54)	–6.16 (–19.02, 6.70)	0.15 (–4.99, 5.29)	2.90 (–2.35, 8.15)
Emotional functioning	20	77.88 (24.57)	31	84.03 (17.24)	–6.16 (–18.02, 6.70)	–3.32 (–14.82, 8.18)	2.83 (–3.50, 9.16)
Social functioning	20	88.00 (17.35)	31	90.78 (12.97)	–2.77 (–11.98, 6.44)	4.95 (–3.18, 13.08)	7.73 (2.96, 12.50)
School functioning	19	77.02 (25.56)	31	80.86 (17.31)	–3.85 (–17.44, 9.75)	–1.25 (–13.58, 11.08)	2.59 (–3.77, 8.95)

Table 4. PedsQL rheumatology module and disease status in polyarticular JIA.

	Polyarticular JIA		Polyarticular JIA: Active Disease		Polyarticular JIA: Inactive Disease		Active Disease versus Inactive Disease,
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	Difference (95% CI)
Child self-report							
Pain and hurt	51	74.52 (23.48)	18	73.98 (24.28)	29	78.46 (21.25)	–4.47 (–18.62, 9.67)
Daily activities	51	94.31 (9.90)	18	93.06 (11.26)	29	95.86 (9.07)	–2.81 (–9.22, 3.61)
Treatment	51	78.04 (16.70)	18	76.70 (19.99)	29	79.16 (15.50)	–2.46 (–13.74, 8.83)
Worry	51	75.33 (26.77)	18	71.77 (32.35)	29	78.73 (24.04)	–6.96 (–25.05, 11.12)
Communication	51	81.63 (20.98)	18	84.72 (18.35)	29	79.19 (22.48)	5.53 (–6.61, 17.67)
Parent/proxy report							
Pain and hurt	56	76.25 (23.57)	20	73.15 (23.83)	32	80.09 (21.55)	–6.94 (–20.21, 6.32)
Daily activities	56	89.82 (16.29)	20	88.00 (17.19)	32	91.41 (16.33)	–3.41 (–13.13, 6.32)
Treatment	56	75.93 (20.68)	20	73.68 (23.09)	32	76.77 (20.35)	–3.09 (–15.84, 9.66)
Worry	51	80.88 (24.23)	18	78.71 (26.85)	29	83.63 (23.10)	–4.92 (–20.49, 10.65)
Communication	51	77.48 (27.47)	18	73.14 (31.38)	29	78.22 (26.05)	–5.07 (–23.09, 12.95)

Table 5. PedsQL multidimensional fatigue scale in polyarticular JIA: comparison to a healthy control population[17]. healthy control sample recruited from an orthopedics clinic.

	Polyarticular JIA		Healthy Controls		Comparison,
	N	Mean (SD)	N	Mean (SD)	Difference (95% CI)
Child self-report					
Total fatigue	51	78.92 (15.45)	52	80.49 (13.33)	–1.57 (–7.22, 4.08)
General fatigue	51	83.01 (16.22)	52	85.34 (14.95)	–2.33 (–8.43, 3.77)
Sleep/rest fatigue	51	73.35 (20.32)	52	75.00 (18.76)	–1.65 (–9.30, 6.00)
Cognitive fatigue	51	79.90 (20.57)	52	81.14 (17.43)	–1.24 (–8.70, 6.22)
Parent/proxy report					
Total fatigue	55	81.08 (18.40)	102	89.63 (11.38)	–0.06 (–4.55, 4.43)
General fatigue	51	81.13 (21.42)	102	89.30 (13.33)	–8.17 (–14.71, 1.63)
Sleep/rest fatigue	55	80.60 (23.03)	102	88.86 (14.72)	–8.26 (–15.09, –1.43)
Cognitive fatigue	55	81.52 (23.93)	102	90.72 (15.15)	–9.20 (–16.28, –2.12)

Table 6. PedsQL multidimensional fatigue scale in polyarticular JIA: comparisons by disease activity status.

	Polyarticular JIA: Active Disease		Polyarticular JIA: Inactive Disease		Active vs Inactive Disease	Active Disease vs Healthy Controls,	Inactive Disease vs Healthy Controls,
	N	Mean (SD)	N	Mean (SD)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Child self-report							
Total fatigue	18	76.38 (17.05)	29	80.18 (14.87)	–3.80 (–13.72, 6.13)	–4.11 (–13.22, 5.01)	–0.31 (–6.98, 6.36)
General fatigue	18	81.25 (16.99)	29	84.20 (15.95)	–2.95 (–13.06, 7.17)	–4.09 (–13.35, 5.17)	–1.14 (–8.39, 6.11)
Sleep/rest fatigue	18	69.21 (22.92)	29	75.83 (19.60)	–6.62 (–19.89, 6.65)	–5.79 (–18.13, 6.55)	0.83 (–8.13, 9.79)
Cognitive fatigue	18	77.77 (20.71)	29	80.17 (21.23)	–2.40 (–15.11, 10.31)	–3.37 (–14.57, 7.83)	–0.97 (–10.26, 8.32)
Parent/proxy report							
Total fatigue	20	82.50 (19.84)	31	81.31 (17.29)	1.19 (–9.79, 12.16)	–7.13 (–16.64, 2.38)	–8.32 (–15.01, –1.63)
General fatigue	20	81.87 (21.56)	31	82.25 (19.48)	–0.39 (–12.44, 11.67)	–7.43 (–17.80, 8.94)	–7.05 (–14.61, 0.51)
Sleep/rest fatigue	20	80.84 (19.75)	31	81.72 (22.85)	–0.88 (–13.02, 11.26)	–8.02 (–17.63, 1.59)	–7.14 (–15.96, 1.68)
Cognitive fatigue	20	84.80 (23.07)	31	79.97 (22.88)	4.82 (–8.5, 18.15)	–5.92 (–17.05, 5.21)	–10.75 (–19.60, –1.90)

functioning (0.311), worry (0.378), and communication (0.357). Correlations between children with active disease and their parent/proxy tended to be higher. The majority of correlations for this group were good.

DISCUSSION

Despite the relatively low levels of disease and disability in this cohort, children with inactive disease and their parents/proxies reported higher quality of life than did the children with active disease on the PedsQL Generic Core Scales, and their scores were similar to those of healthy controls. Similarly, children with inactive disease and their parents/proxies reported higher scores on the domains of the PedsQL Rheumatology Module than did children with active disease and their parents/proxies. However, the children in this cohort and their parents/proxies reported lower scores on all domains of the PedsQL Multidimensional Fatigue Scale than did healthy controls, regardless of disease activity status.

Although a significant number of publications have assessed quality of life in JIA and the associations between HRQOL and disability, few published data are available regarding the association between levels of disease activity and quality of life in children with JIA. Previous cross-sectional studies of children with multiple JIA subtypes have indicated no association between number of active joints and HRQOL, as measured by the PedsQL Generic Core Set and the PedsQL Rheumatology Module, but a moderate correlation between disability and the PedsQL Rheumatology Module[18,19]. Our data also indicate that disability, as measured by the CHAQ, is most strongly correlated with the PedsQL Generic Core Scales and the PedsQL Rheumatology Module. A recent report of a cohort of 60 children with multiple JIA subtypes found a moderate correlation between the CHAQ and psychological functioning, but no association between psychological function and individual measures of disease activity, including the physician global assessment of disease activity and total active joint count[20]. In contrast, 2 trials of disease modifying antirheumatic drugs, including methotrexate and corticosteroids, specifically examined HRQOL as a primary endpoint[21,22]. Children in these studies reported improved HRQOL and also had an overall decreased active joint count or decreased physician assessment of disease severity during the study period, indicating the value of prospective study in the correlation of HRQOL and measures of disease activity. Our current data support the findings from these prospective studies. It is possible that differences in function associated

Table 7. Pearson correlations between child self-report and parent/proxy report scale.

	Total Sample	Inactive Disease	Active Disease
PedsQL generic core scales			
Total score	0.713	0.667	0.759
Physical health	0.657	0.621	0.622
Psychosocial health	0.629	0.568	0.774
Emotional functioning	0.571	0.311	0.802
Social functioning	0.556	0.663	0.628
School functioning	0.614	0.448	0.777
PedsQL rheumatology module			
Pain and hurt	0.671	0.626	0.670
Daily activities	0.718	0.835	0.556
Treatment	0.577	0.460	0.758
Worry	0.537	0.378	0.772
Communication	0.429	0.357	0.692
PedsQL multidimensional fatigue scale			
Total fatigue	0.641	0.583	0.723
General fatigue	0.679	0.640	0.743
Sleep/rest fatigue	0.566	0.554	0.621
Cognitive fatigue	0.533	0.611	0.375

with multiple levels of disease activity may be too small to detect, and the use of dichotomized disease activity status increased our ability to detect differences in HRQOL in this cross-sectional study.

These data also support studies indicating that fatigue is an important component of HRQOL in children with JIA, and our study is the first to use the PedsQL Multidimensional Fatigue Score to assess the association between fatigue and disease activity. The recent American College of Rheumatology and European League Against Rheumatism consensus statement on reporting outcomes in adult RA clinical trials recommended that a measure of patient fatigue should be included in all future clinical trial reports, indicating that this may be an outcome of potential significance for JIA, as well[23]. Data from a group of children with a variety of rheumatic diseases indicated a statistically significant correlation between parent/proxy perception of disease severity and PedsQL Multidimensional Fatigue Scale. A prospective study of children with JIA that incorporated daily symptom logs found that child self-reported daily fluctuations in mood and stress led to changes in fatigue, pain, and stiffness[9]. However, disease activity was assessed at baseline only and it was unclear how baseline disease severity influenced these relationships during the study. Another study that compared polysomnography results among children with multiple JIA subtypes who had either active or inactive disease reported no significant difference between the 2 groups, likely due to the relatively low levels of disease activity in the cohort[10]. Fatigue was measured with a modified Sleep Self-Report questionnaire and, while there was no significant difference in fatigue between children with and without active disease, children with active disease were significantly more likely to find their fatigue bothersome. Our data indicate that, despite overall low levels of disability and low physician global assessment of disease activity, children with polyarticular JIA report increased fatigue as compared to healthy controls. Given its complexity and associations with additional factors, including pain, this component of HRQOL clearly remains an important outcome for prospective study.

Finally, our data indicated a trend toward better agreement between child self-report and parent/proxy report among children with active disease than among those with inactive disease. Studies of the PedsQL Generic Core Scales reported a good correlation between child self-report and parent/proxy report and an increase in this correlation associated with increased patient age[15]. Assessment of this correlation in a cohort of children with a variety of rheumatic diseases found statistically significant correlation between child self-report and parent/proxy report for all domains of the PedsQL Generic Core Scales. Studies evaluating this relationship specifically in JIA have reported a complex relationship between child self-report and parent/proxy report, despite overall good correlation between child self-report and parent/proxy reports on the PedsQL Generic Core Scales and PedsQL Rheumatology Module[18]. A study assessing a cohort of children with multiple JIA subtypes reported significant discrepancies between children and their parents in their reports of pain and disability, which seemed to be strongly associated with self-report of depressive symptoms by the child[24]. Nevertheless, a second report comparing parent and child responses on the Juvenile Arthritis Quality of Life Questionnaire reported good correlations between parent and child self-report in the majority of domains, including pain[25].

Our report is limited by the sample size that limited its statistical power and hence our ability to perform additional analyses, including adjustment for disease duration, pain, the pediatric core set components, and additional known predictors of disease severity and decreased HRQOL. The single-center design of the study and its exclusion of non-English speaking families may also restrict the generalizability of the results to other populations. For example, our cohort reported higher social functioning than the healthy controls, which may reflect that this cohort was relatively homogenous compared to the sample of healthy controls.

In addition, children and their parents/proxy were not physically separated for completion of questionnaires, which may have biased some responses. The relatively high proportion of RF-positive children in this sample (27%) may reflect the genetics of the population served by SCH or may reflect ascertainment bias, with RF-positive children more likely to have severe disease requiring close followup and therefore more likely to be retained in the cohort, potentially biasing the results toward children with more severe disease. Although there were clear trends in the differences between groups in this study, and the differences between children with active and inactive disease approached or were

similar to minimal clinically important differences larger studies are needed to assess the true magnitude of these differences and for statistical comparison of these differences to the definitions of minimal clinically important differences and significantly impaired quality of life for the PedsQL measures[15]. Further, the cross-sectional design limited our ability to determine the directionality of the relationship, and it may be that children with mild disease are more likely to achieve inactive disease and may report improved HRQOL independent of disease status. Longitudinal study incorporating these measures is required to assess this relationship.

Despite these limitations, our data are the first to indicate an improved health-related quality of life for children with inactive polyarticular JIA as compared to those with active disease, and support the use of this outcome measure in both clinical care and clinical trials. However, in this cohort, children reported increased fatigue as compared to healthy controls, regardless of disease activity, indicating that this outcome merits additional assessment and may be an important outcome to incorporate specifically into studies of HRQOL in these children, and an important target for therapeutic intervention. Additional study will be required to determine the etiology of fatigue in these children and its relationship with disease activity. Overall, our findings support continued longitudinal and prospective collection of data regarding HRQOL, fatigue, and disease activity in large cohorts of children with polyarticular JIA.

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