American Journal of Transplantation 2010; 10: 1686–1694
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2010.03149.x

Pediatric Health-Related Quality of Life: Feasibility, Reliability and Validity of the PedsQL™ Transplant Module

J. Weissberg-Benchell[a,*], T. E. Zielinski[b], S. Rodgers[c], R. N. Greenley[d], D. Askenazi[e], S. L. Goldstein[f], E. M. Fredericks[g], S. McDiarmid[h], L. Williams[i], C. A. Limbers[j], K. Tuzinkiewicz[c], S. Lerret[k], E. M. Alonso[c] and J. W. Varni[l]

[a] *Department of Child and Adolescent Psychiatry,* [b] *Division of Kidney Diseases and* [c] *Department of Pediatrics, Children's Memorial Hospital, Chicago, IL*
[d] *Department of Psychology, Rosalind Franklin University of Medicine and Science, Chicago, IL*
[e] *Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL*
[f] *Department of Pediatrics, Renal Section, Baylor College of Medicine, Houston, TX*
[g] *Department of Pediatrics, The University of Michigan Health System, Ann Arbor, MI*
[h] *Department of Pediatric Gastroenterology, University of California, Los Angeles, CA*
[i] *Department of Surgery, University of Nebraska Medical Center, Omaha, NE*
[j] *Department of Psychology, Texas A&M University, College Station, TX*
[k] *Department of Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI*
[l] *Department of Pediatrics, College of Medicine, Department of Landscape Architecture and Urban Planning, College of Architecture, Texas A&M University, College Station, TX*
* *Corresponding author: J. Weissberg-Benchell, jwbenchell@childrensmemorial.org*

The measurement properties of the newly developed Pediatric Quality of Life Inventory™ (PedsQL™) 3.0 Transplant Module in pediatric solid organ transplant recipients were evaluated. Participants included pediatric recipients of liver, kidney, heart and small bowel transplantation who were cared for at seven medical centers across the United States and their parents. Three hundred and thirty-eight parents of children ages 2–18 and 274 children ages 5–18 completed both the PedsQL™ 4.0 Generic Core Scales and the Transplant Module. Findings suggest that child self-report and parent proxy-report scales on the Transplant Module demonstrated excellent reliability (total scale score for child self-report $\alpha = 0.93$; total scale score for parent proxy-report $\alpha = 0.94$). Transplant-specific symptoms or problems were significantly correlated with lower generic HRQOL, supporting construct validity. Children with solid organ transplants and their parents reported statistically significant lower generic HRQOL than healthy children. Parent and child reports showed moderate to good agreement across the scales. In conclusion, the PedsQL™ Transplant Module demonstrated excellent initial feasibility, reliability and construct validity in pediatric patients with solid organ transplants.

Key words: Patient report outcomes, PedsQL™, pediatrics, quality of life, transplant

Received 26 October 2009, revised 21 March 2010 and accepted for publication 24 March 2010

Introduction

The World Health Organization (WHO) defines health as a 'state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity' (1). The growing literature in pediatric solid organ transplantation supports the WHO's definition of health through an increasing recognition of the interaction between physiologic, developmental, and psychosocial factors in overall patient outcomes. Assessment of a person's health-related quality of life (HRQOL) facilitates the evaluation of patient outcomes by providing a more thorough understanding of the child's and family's experience of solid organ transplant and its treatment. HRQOL has been defined as an individual's subjective experience of their illness, and the impact that illness and its treatment have on the individual's functioning in a variety of domains (2–5). The key domains of HRQOL include physical, psychological and social functioning (2,5) as well as the impact of illness on the ability to engage in activities of daily living (2,4).

Although researchers have begun to recognize the important role of HRQOL in evaluating the effectiveness of medical treatments in pediatric chronic conditions, relatively few studies have examined HRQOL in pediatric solid organ transplant recipients. Transplantation often leads to improved physical health. However, the impact of the medications, hospitalizations, clinic visits and invasive procedures, as well as the impact of living with the uncertainty

of graft survival and long-term health status may all affect an individual's HRQOL. Therefore, assessing an individual's HRQOL after solid organ transplant can help evaluate the relative efficacy of medical interventions (4) and facilitate improvement in medical decision-making.

HRQOL has been assessed using both generic and disease-specific measures. Generic measures allow for the assessment of common dimensions among both healthy and chronically ill children, and allow for comparisons across populations (6–9). However, generic measures may be insensitive to a number of important disease-specific issues (2,10). Disease-specific measures assess specific outcomes and allow for the assessment of clinically relevant issues within a particular illness-group (11). Varni et al. (5) propose a modular approach to HRQOL assessment that includes both generic and illness-specific measures.

Pediatric measures of transplant-specific HRQOL must be sensitive to developmental issues. Parent proxy-report measures have been used to avoid the problems inherent in obtaining pediatric patient self-report, but the accuracy of only using parent proxy-report measures has been questioned (12–14). Since the validity, reliability and meaningfulness of children's responses to any HRQOL measure may fluctuate over time (5), measures of disease-specific HRQOL in a pediatric population should include both child and parent reports to measure their perspectives on patient HRQOL.

The lack of a valid and reliable transplant-specific HRQOL measure has hampered our ability to identify children at different levels of morbidity, determine the differential impact of various treatment regimens, predict which patients are at risk for emotional difficulties and/or poor regimen adherence, and identify emerging problems for long-term survivors. The development of such a transplant-specific measure would provide a more thorough understanding of the multidimensional nature of both the child's experience and the parent's perceptions of the child's experience regarding the impact of solid organ transplantation.

To address this critical, unmet need, this study investigates the initial feasibility, reliability and validity of the Pediatric Quality of Life Inventory™ (PedsQL™) 3.0 Transplant Module in a general population of children with solid organ transplants. Once the measurement properties of this newly developed measure are demonstrated in this diverse population of solid organ transplant patients, further studies can assess the clinical utility of the measure within organ specific transplant groups. For the present study, aimed at assessing the initial feasibility, reliability and validity of the PedsQL™ 3.0 Transplant Module, the PedsQL™ 4.0 Generic Core Scales was also administered. We hypothesized that the Generic Core Scales would distinguish between healthy children and children with solid organ transplants. We also hypothesized that greater transplant-specific symptoms or difficulties would be associated with lower generic HRQOL based on the impact of disease-specific symptoms on generic HRQOL.

Materials and Methods

Solid organ transplant sample

Eight hundred seventy-four families were invited to participate from seven sites across the United States. A total of 342 participants (274 children ages 5–18 years and 338 parents of children ages 2–18 years) completed the questionnaires, a response rate of 39%. The sample consisted of children who had received the following types of solid organ transplants: 184 (53.8%) liver, 90 (26.3%) kidney, 33 (9.6%) heart, 6 (1.8%) small bowel, and 27 (8.5%) multiple organs (heart and kidney = 2, liver and kidney = 2, liver, kidney and small bowel = 2, liver and small bowel = 21). The mean time since transplantation for the sample was 7.01 years (SD = 4.82; Range = 0.24–18.37). The average age of the 185 boys (54.1%) and 152 girls (44.4%) was 11.3 years (SD = 5.0). With respect to race/ethnicity, the sample contained 249 (72.8%) White non-Hispanic, 34 (9.9%) Hispanic, 30 (8.8%) Black non-Hispanic, 12 (3.5%) Asian/Pacific Islander and 17 (5.0%) Other or Missing. With respect to parent education, 12% did not complete high school, 18.8% had a high school degree, 29% completed some college, 24.5% had a college degree and 14.3% had a graduate degree. Family income showed 34% earning less than $50,000 per year, 38% earning between $51,000 and $100,000, 15% earning between $101,000 and $150,000 and 10% earning more than $151,000 per year.

Healthy Children Sample: PedsQL™ Generic Core Scales

The healthy children sample (n = 2039) was derived from the previously conducted PedsQL™ 4.0 initial field test (5) and a State's Children's Health Insurance Program (SCHIP) evaluation in California (15). Children were assessed either in physicians' offices during well-child visits, by telephone, or via a statewide mailing. The average age of the 1081 boys (53.0%) and 958 girls (47.0%) was 9.7 years (SD = 4.4; Missing = 3, 0.1%). With respect to race/ethnicity, the sample contained 1311 (64.3%) White non-Hispanic, 271 (13.3%) Hispanic, 232 (11.4%) Black non-Hispanic, 142 (7.0%) Asian/Pacific Islander and 83 (4.1%) Other ethnicities. Parental level of education was unavailable for the total sample, although the statewide SCHIP sample was representative of low-income families. The solid organ transplant sample was randomly matched to the healthy children sample by age, gender and race/ethnicity utilizing the SPSS Version 16.0 statistical software random sample case selection command (16).

Measures

PedsQL™ 3.0 Transplant Module: The PedsQL™ 3.0 Transplant Module was developed based on our research and clinical experiences with organ transplantation and other chronic conditions, and the instrument development literature (17–20). The Module Scales were developed through focus groups, cognitive interviews, pretesting and field-testing protocols (details contained in Appendix A). The child self-report items are listed in Appendix B.

The 46-item PedsQL™ 3.0 Transplant Module encompasses 8 Scales: 1) About My Medicines I (9 items; barriers to medical regimen adherence), 2) About My Medicines II (8 items; medication side effects), 3) My Transplant and Others (8 items; social relationships and transplant), 4) Pain and Hurt (3 items; physical discomfort), 5) Worry (7 items; worries related to health status), 6) Treatment Anxiety (4 items; fears regarding medical procedures), 7) How I Look (3 items; impact of transplant on appearance), and 8) Communication (4 items; communication with medical personnel and others regarding transplant issues). The format, instructions, Likert response scale, and scoring method for the PedsQL™ 3.0 Transplant Module

are identical to the PedsQL™ 4.0 Generic Core Scales, with higher scores indicating better HRQOL (5).

The Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5–18 years, and a parent proxy-report format for children ages 2–4 years. Child self-report forms are specific for ages 5–7, 8–12, and 13–18 years. Parent proxy-report forms are specific for children ages 2–4 (toddler), 5–7 (young child), 8–12 (child), and 13–18 (adolescent), and assess parents' perceptions of their child's HRQOL. The instructions ask how much of a problem each item has been during the past one month. A 5-point response scale is utilized across child self-report for ages 8–18 and parent proxy-report (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). To further increase the ease of use for the young child self-report (ages 5–7), the response scale is reworded and simplified to a 3-point scale (0 = not at all a problem; 2 = sometimes a problem; 4 = a lot of a problem). This simplification to a 3-point scale for the young child self-report is consistent with the PedsQL™ 4.0 Generic Core Scales as well as with all of the PedsQL illness-specific modules.

Items are reverse-scored and linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate better HRQOL. The Total Scale Score is computed as the sum of all the items on the PedsQL™ 3.0 Transplant Module divided by the number of items answered. Scale Scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). If more than 50% of the items in the scale are missing, the Scale Score is not computed (21). This accounts for the differences in sample sizes for scales reported in the tables. Although there are other strategies for imputing missing values, this computation is consistent with the previous PedsQL™ peer-reviewed publications as well as other well-established HRQOL measures (5,22,23).

The PedsQL™ 4.0 Generic Core Scales: The 23-item PedsQL™ 4.0 Generic Core Scales encompass: 1) Physical Functioning (8 items), 2) Emotional Functioning (5 items), 3) Social Functioning (5 items), and 4) School Functioning (5 items) (5,14). To create the Psychosocial Health Summary Score, the mean is computed as the sum of the items divided by the number of items answered in the Emotional, Social, and School Functioning Scales.

The PedsQL™ Family Information Form: Parents completed the PedsQL™ Family Information Form which contains demographic information including the child's date of birth, gender, race/ethnicity, and parental education and occupation information (5).

Procedures: Participants were children ages 5–18 years who had received a solid organ transplant and parents of children ages 2–18 years who had received a solid organ transplant at 7 clinical centers across the United States (Children's Memorial Hospital, Chicago, n = 122; University of Alabama, Birmingham, n = 30; University of Michigan, Ann Arbor, n = 49; Nebraska Medical Center, University of Nebraska, Omaha, n = 79; Texas Children's Hospital, Houston, n = 13; University of California, Los Angeles, n = 32; Children's Hospital of Wisconsin-Milwaukee, n = 17). The Children's Memorial Hospital site initially administered only the PedsQL™ 3.0 Transplant Module (n = 93), and then with a sample that excluded the original 93 respondents, an additional 29 completed both the Transplant Module and Generic Core Scales. The other 6 sites administered the Transplant Module and Generic Core Scales at the same time. This explains the larger sample size for the Transplant Module in the tables.

All eligible patients at each clinical site were invited to participate in the study. Participants completed the PedsQL™ 3.0 Transplant Module either during routinely scheduled clinic visits (n = 109) or via a mass mailing (n = 233) of transplant recipients from each clinical site. All parents completed the PedsQL™ Family Information Form. The human subject institutional review boards at each center approved the study.

Statistical analysis: Feasibility was determined from the percentage of missing values (23). Cronbach's coefficient alpha was utilized to determine scale internal consistency reliability (24). Scales with reliabilities of 0.70 or greater are recommended for comparing patient groups, while a reliability criterion of 0.90 is recommended for analyzing individual patient scores (25,26).

Construct validity for the Generic Core Scales was determined utilizing the known-groups method (27). The known-groups method compares scale scores across groups known to differ in the health construct being investigated. Generic Core Scales scores in groups differing in known health condition (healthy children and children with a solid organ transplant) were computed using independent samples t-tests. We hypothesized that the Generic Core Scales would distinguish between healthy children and children with solid organ transplants based on previous PedsQL™ findings in other pediatric chronic conditions (28–30). Effect sizes were calculated to determine the magnitude of the differences (31). Effect size as utilized in these analyses was calculated by taking the difference between the healthy sample mean and the organ transplant sample mean, divided by the pooled standard deviation. Effect sizes for differences in means are designated as small (.20), medium (.50), and large (.80) in magnitude (18).

An analysis of the intercorrelations among the Generic Core Scales and Summary Scores with the Transplant Module Scale Scores was used to examine construct validity for the Transplant Module. Computing the intercorrelations among scales provides initial information on the construct validity of an instrument (26). We hypothesized greater disease-specific symptoms or problems would correlate with lower overall generic HRQOL based on the conceptualization of disease-specific symptoms as causal indicators of generic HRQOL (32). Pearson Product Moment Correlation coefficients are designated as small (.10–.29), medium (.30–.49), and large (≥.50) (31).

A principal components factor analysis of the PedsQL™ 3.0 Transplant Module extracting eight factors and one factor was also conducted. Item loadings were assessed to determine if each subscale loaded onto a distinct factor or if a total Transplant Module score best represented the data. A cut-off value of 0.30 was utilized.

Intraclass Correlation Coefficients (ICCs) were used to determine agreement between child self-report and parent proxy-report (33). The ICC provides an index of absolute agreement as it takes into account the ratio between subject variability and total variability (33,34). ICCs are designated as ≤0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.81–1.00 excellent agreement (35,36). Statistical analyses were conducted using SPSS Version 16.0 for Windows (16).

Results

Feasibility: missing item responses

The percentage of missing item responses was 2.1% and 0.8%, respectively, for all scales for child self-report and parent proxy-report on the PedsQL™ 3.0 Transplant Module. For child self-report and parent proxy-report on the PedsQL™ 4.0 Generic Core Scales, the percentage of missing item responses was 1.7% and 0.4%, respectively, for all scales except the parent proxy-report School Functioning Scale. The percentage of missing items for

Table 1: PedsQL™ 4.0 Generic Core Scales scores and reliability for child self-report and parent proxy-report for solid organ transplant sample and comparisons with matched healthy children scores

Scale	Number of Items	Solid Organ Transplant			Healthy		Difference	Effect Size
		n	α	Mean ± SD	N	Mean ± SD		
Child self-report								
Total Score	23	199	0.91	76.09 ± 17.25	1302	85.66 ± 11.99	9.57*	0.75
Physical Health	8	199	0.85	81.06 ± 19.67	1299	89.53 ± 12.38	8.47*	0.62
Psychosocial Health	15	198	0.87	73.73 ± 17.22	1298	83.64 ± 13.60	9.91*	0.70
Emotional Functioning	5	198	0.79	73.90 ± 21.04	1302	81.50 ± 17.52	7.60*	0.42
Social Functioning	5	198	0.79	80.22 ± 20.65	1296	87.15 ± 15.77	6.93*	0.42
School Functioning	5	196	0.76	66.56 ± 21.95	1279	82.23 ± 16.29	15.67*	0.91
Parent proxy-report								
Total Score	23	247	0.94	74.93 ± 19.40	2017	85.41 ± 13.49	10.48*	0.74
Physical Health	8	247	0.91	79.10 ± 23.25	2017	88.26 ± 16.69	9.16*	0.52
Psychosocial Health	15	247	0.91	72.68 ± 19.53	2019	83.79 ± 13.94	11.11*	0.76
Emotional Functioning	5	247	0.84	74.13 ± 21.28	2017	82.24 ± 16.16	8.11*	0.48
Social Functioning	5	247	0.87	76.48 ± 23.80	2017	87.32 ± 16.68	10.84*	0.62
School Functioning	5	228	0.81	65.93 ± 24.86	1829	81.27 ± 17.96	15.34*	0.81

*$p < 0.001$ based on independent samples *t*-tests. Higher values equal better health-related quality of life. Effect sizes designated as small (0.20), medium (0.50) and large (0.80). α, Cronbach's coefficient alpha; SD, standard deviation.

the proxy-report School Functioning Scale was 0.8% (ages 5–18) and 42.9% (ages 2–4). This large percentage for toddlers (ages 2–4) may exist since instructions on the PedsQL™ toddler form ask parents to complete the School Functioning Scale if their child attends school or daycare and many toddlers do not attend school or daycare.

Internal consistency reliability

Table 1 presents internal consistency reliability coefficients for the Generic Core Scales. All child self-report and parent proxy-report scales on the Generic Core exceed the minimum reliability standard of 0.70 required for group comparisons. The Total Scale Scores for both child self-report and parent proxy-report exceeds the reliability criterion of 0.90 recommended for analyzing individual patient scores.

Internal consistency reliability coefficients for the Transplant Module are shown in Table 2. All child self-report and parent proxy-report scales on the Transplant Module exceed the minimum reliability standard of 0.70 required for group comparisons. The Total Scale Scores for both child self-report and parent proxy-report for the Transplant Module exceed the reliability criterion of 0.90 recommended for analyzing individual patient scores.

Construct validity

Table 1 presents the differences between healthy children and children with solid organ transplants. For each Generic Core Scale and Summary Score, children with solid organ transplants and their parents report statistically significant lower HRQOL than healthy children. The majority of effect sizes are in the medium range, supporting discriminant validity. The largest effect sizes are demonstrated on the School Functioning Scale for both child self-report (0.91) and parent proxy-report (0.81).

Table 3 presents the intercorrelations between the Generic Core Scales and summary scores with the Transplant Module. The majority of intercorrelations are in the medium to large range, supporting construct validity of the Transplant Module.

Factor analysis

A principal components factor analysis of the PedsQL™ 3.0 Transplant Module extracting eight factors and one factor revealed a one-factor solution best represented the data. While for the one-factor solution two of the items for child self-report and one item for parent proxy-report did not meet the 0.30 cut-off value, these items were retained given that the items were generated by focus groups and cognitive interviews of pediatric patients who had undergone solid organ transplantation and their parents and thus we felt these items were of clinical importance since they were identified by children and parents as being so. Based on these findings, a Total Transplant Module score was included in the analyses.

Parent/child agreement

ICCs between child and parent report are shown in Table 4. All of the ICCs are in the moderate to good agreement range for the PedsQL™ Scales. The greatest overall agreement is found on Total Generic Core Scale Score (0.71), School Functioning Scale (0.71), and About Medicines II Scale (0.71).

Discussion

The present study provides initial support for the feasibility, reliability and validity of the PedsQL™ 3.0 Transplant Module in a general population of children with solid organ transplants. Moreover, it provides support for the psychometric utility of the PedsQL™ 4.0 Generic Core Scales

Table 2: PedsQL™ 3.0 Transplant Module scores and reliability for child self-report and parent proxy-report

Scale	Number of Items	n	α	Mean ± SD
Child self-report				
Total Score	46	269	0.93	79.03 ± 14.36
About My Medicines I	9	272	0.77	83.08 ± 14.98
About My Medicines II	8	270	0.74	86.58 ± 16.19
My Transplant and Others	8	269	0.78	74.03 ± 19.77
Pain and Hurt	3	269	0.72	71.10 ± 23.43
Worry	7	268	0.88	79.44 ± 21.81
Treatment Anxiety	4	269	0.84	74.77 ± 27.23
How I Look	3	268	0.77	76.26 ± 26.76
Communication	4	268	0.80	76.84 ± 23.45
Parent proxy-report				
Total Score	46	338	0.94	79.43 ± 14.88
About His/Her Medicines I	9	336	0.84	84.77 ± 16.04
About His/Her Medicines II	8	336	0.77	83.74 ± 17.66
Transplant and Others	8	338	0.85	76.90 ± 19.78
Pain and Hurt	3	337	0.71	75.62 ± 20.99
Worry	7	337	0.91	78.05 ± 23.30
Treatment Anxiety	4	338	0.88	71.61 ± 27.45
Perceived Physical Appearance	3	337	0.80	78.76 ± 24.42
Communication	4	337	0.92	77.60 ± 26.61

Higher values equal better health-related quality of life. α, Cronbach's coefficient alpha; SD, standard deviation.

in children who have received a solid organ transplant. Both the Generic Core and the Transplant Module showed minimal missing values, supporting feasibility of the measures. Internal consistency for the Transplant Module Total Score exceeded the 0.90 criterion, and the factor analysis supported the use of a total score as a summary score for the primary analysis of HRQOL in children with solid organ transplants. The Transplant Module scale scores showed alpha coefficients ranging from 0.76 to 0.91, suggesting that each subscale can be used to examine specific

Table 3: Pearson's product moment correlations among PedsQL™ scales for child self-report (above diagonal) and parent proxy-report (below diagonal) for solid organ transplant sample

	T	PH	Psy	EF	SF	Sch	TS	AI	AII	TO	P	W	TA	PA	C
PedsQL™ Generic Core Scales															
Total Generic Core (T)	–	0.88	0.96	0.78	0.81	0.78	0.65	0.52	0.45	0.48	0.53	0.47	0.45	0.32	0.50
Physical Health (PH)	0.89	–	0.70	0.57	0.61	0.56	0.54	0.46	0.47	0.37	0.47	0.37	0.34	0.22[a]	0.37
Psychosocial Health (Psy)	0.95	0.71	–	0.81	0.84	0.81	0.68	0.53	0.40	0.53	0.51	0.52	0.45	0.38	0.52
Emotional Functioning (EF)	0.76	0.53	0.83	–	0.55	0.45	0.55	0.42	0.35	0.39	0.47	0.44	0.39	0.29	0.44
Social Functioning (SF)	0.86	0.69	0.86	0.57	–	0.52	0.61	0.48	0.31	0.52	0.34	0.48	0.39	0.34	0.51
School Functioning (Sch)	0.81	0.61	0.85	0.56	0.61	–	0.50	0.38	0.34	0.38	0.45	0.34	0.35	0.27	0.34
PedsQL™ Transplant Module															
Total Score (TS)	0.73	0.63	0.71	0.63	0.64	0.55	–	0.74	0.63	0.82	0.54	0.82	0.62	0.71	0.66
About Medicines I (AI)	0.57	0.51	0.53	0.50	0.45	0.43	0.71	–	0.44	0.58	0.40	0.49	0.32	0.42	0.44
About Medicines II (AII)	0.58	0.53	0.54	0.49	0.46	0.43	0.71	0.43	–	0.48	0.37	0.47	0.25	0.41	0.27
Transplant and Others (TO)	0.68	0.54	0.69	0.58	0.68	0.50	0.85	0.59	0.49	–	0.36	0.60	0.33	0.62	0.50
Pain and Hurt (P)	0.61	0.55	0.57	0.53	0.40	0.53	0.59	0.50	0.43	0.43	–	0.38	0.20[a]	0.30	0.22[a]
Worry (W)	0.46	0.41	0.43	0.40	0.39	0.32	0.77	0.43	0.47	0.54	0.37	–	0.44	0.59	0.46
Treatment Anxiety (TA)	0.40	0.36	0.38	0.33	0.37	0.30	0.60	0.26	0.29	0.45	0.24	0.47	–	0.38	0.50
Perceived Physical Appearance (PA)	0.48	0.39	0.49	0.48	0.43	0.33	0.70	0.40	0.43	0.61	0.42	0.50	0.32	–	0.42
Communication (C)	0.50	0.38	0.52	0.42	0.51	0.42	0.63	0.28	0.36	0.57	0.23	0.34	0.37	0.42	–

All values are statistically significant at $p < 0.001$ except for superscript 'a' which is statistically significant at $p < 0.01$.
Pearson's product moment correlations for child self-report are presented above the diagonal, parent proxy-report are presented below.
Pearson's product moment correlations are designated as small (0.10), medium (0.30) and large (0.50).
T = Total Generic Core; PH = Physical Health; Psy = Psychosocial Health; EF = Emotional Functioning; SF = Social Functioning; Sch = School Functioning; TS = Total Score; AI = About Medicines I; AII = About Medicines II; TO = Transplant and Others; P = Pain and Hurt; W = Worry; TA = Treatment Anxiety; PA = Perceived Physical Appearance; C = Communication.

Table 4: Intraclass correlations (ICC) between child self-report and parent proxy-report on the PedsQL™ 4.0 Generic Core Scales and the PedsQL™ 3.0 Transplant Module

Scale	Parent-Child Agreement ICC
PedsQL™ Generic Core Scales	
Total Generic Core	0.71*
Physical Health	0.69*
Psychosocial Health	0.68*
Emotional Functioning	0.62*
Social Functioning	0.59*
School Functioning	0.71*
PedsQL™ Transplant Module	
Total Score	0.66*
About Medicines I	0.67*
About Medicines II	0.71*
Transplant and Others	0.62*
Pain and Hurt	0.60*
Worry	0.52*
Treatment Anxiety	0.59*
Perceived Physical Appearance	0.52*
Communication	0.43*

*$p < .001$. ICCs are designated as $\leq$0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement and 0.81–1.00 excellent agreement.
ICC = Intraclass correlation.

domains of transplant-specific HRQOL as well as using the total score for an overall assessment of transplant-specific HRQOL.

Consistent with our hypotheses, the Generic Core Scales differentiated HRQOL between children receiving a solid organ transplant and children who are healthy. Children with solid organ transplants reported lower HRQOL than did healthy children, with school functioning showing the greatest differences between healthy and transplanted children. The differences in reports regarding school functioning may be a result of neurocognitive issues related to the child's transplant procedure, current medical condition, and/or medication regimen. Alternatively, differences in school function may also be related to missing days of school for clinic or lab visits, hospitalizations, or intercurrent illnesses. The difficulties in school functioning reported by transplant recipients suggest that clinicians should attend to the child's academic functioning and should encourage families to advocate for their child's academic support.

Children with solid organ transplants showed moderate to good agreement with their parent's scores, with the strongest agreement in the area of medication side-effects. This finding suggests that both parents and their children are keenly aware of the negative impact of medication side effects. Studies suggested that side effects may be a key factor in medication nonadherence (37), so careful attention to concerns about medication side effects during clinic visits is warranted.

The present study has several strengths, including the rigorous methods used to construct the measure, the large sample size, the broad age-range of participants, the diversity of the population (73% Caucasian), the nation-wide representation of the participants (7 clinical sites from across the country), and the assessment of recipients of four different transplanted organs.

Limitations include the lack of information on families who chose not to participate in the study, which may limit the generalizability of the findings. While our response rate was expected for the mode and method of survey administration utilized (one-time only mailing) (38), it may limit the generalizability of our findings. In addition, a high proportion of the parents in the present sample had at least some postsecondary education, which may not be representative of the general adult population in the US, and may further limit the generalizability of these findings. Feasibility in the present study was assessed solely by the percentage of missing values; future investigations should also evaluate the feasibility of these measures with regard to completion time and nonresponse rate. In addition, we did not collect test-retest reliability data. However, test-retest reliability may not be as useful in determining reliability of the Transplant Module as measuring internal consistency reliability, since fluctuations in the children's health status may influence their HRQOL. The only measure used to assess construct validity was the PedsQL™ Generic Core Scales. Other measures assessing such constructs as depression, anxiety, family communication, and adherence to medical regimens were not collected for this study (to reduce participant burden), and future comparisons among these measures may add important information regarding the construct validity of the Transplant Module.

Testing of the PedsQL™ Transplant Module with larger organ-specific populations is a necessary step in the iterative validation process for this new measure. In order to assess the clinical utility of this newly developed measure, these future studies should also assess the similarities and differences among the different solid organ transplant groups. Such an analysis was beyond the scope this study. Future studies should also assess such important medical factors as graft-function, medications prescribed (e.g. prednisone, tacrolimus, prograf), number of rejection episodes, length of time since transplant, and hospitalization days. Concurrently assessing important psychosocial factors such as peer relationships, extracurricular activities and emotional functioning will also add invaluable information regarding the clinical utility of this measure. Such clinically vital information, in conjunction with this newly developed, psychometrically sound measure of transplant-specific quality of life, will facilitate the development of appropriate prevention and intervention programs. The development of this new PedsQL™ 3.0 Transplant Module should help clinicians identify children at different levels of morbidity, identify the differential impact of various treatment regimens, identify those children at risk for emotional

difficulties, and identify emerging problems for long-term survivors. Use of the measure in clinical trials could facilitate a more thorough understanding of the multidimensional nature of both the child's experience and the parent's perceptions of their child's experiences regarding the impact of solid organ transplantation on generic and disease-specific HRQOL and facilitate medical decision-making.

Acknowledgments

This research was supported by grants from the Children's Memorial Hospital Shaw Research Grant from the Walden W. & Jean Young Shaw Foundation, the Foley Family Foundation and from the Siragusa Foundation.

Competing Interests

Dr. Varni holds the copyright and the trademark for the PedsQL™ and receives financial compensation from the Mapi Research Trust, which is a nonprofit research institute that charges distribution fees to for-profit companies that use the Pediatric Quality of Life Inventory™.

References

1. World Health Organization. World Health Organization: Basic document. Geneva, Switzerland: WHO, 1948.
2. Cella DF. Quality of life outcomes: Measurement and validation. Oncology. 1996 10(11 Suppl.): 233–246.
3. Seid M, Varni JW, Rode CA, Katz ERs. The pediatric cancer quality of life inventory: A modular approach to measuring health-related quality of life in children with cancer. Int J Cancer 1999; 12(Suppl.): 71–76.
4. Spieth LE, Harris CV. Assessment of health-related quality of life in children and adolescents: An integrative review. J Pediatr Psychol 1996; 21: 175–193.
5. Varni JW, Seid M, Kurtin PS. The PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ version 4.0 Generic Core Scales in healthy and patient populations. Med Care 2001; 39: 800–812.
6. Drotar D. Relating parent and family functioning to the psychological adjustment of children with chronic health conditions: What have we learned? What do we need to know? J Pediatr Psychol 1997; 22: 149–165.
7. Palermo T, Long A, Lewandowski M, Drotar D, Quittner A, Walker LS. Evidence-based assessment of health related quality of life and functional impairment in pediatric psychology. J Pediatr Psychol 2008; 33: 983–996.
8. Quittner AL, Davis M, Modi A. Health related quality of life in pediatric populations. In: Roberts M, ed. Handbook of pediatric psychology. New York: Guilford Publications, 2003:696–709.
9. Schmidt S, Petersen C, Bullinger M. Coping with chronic disease from the perspective of children and adolescents—A conceptual framework and its implications for participation. Child: Care, Health Dev 2003; 29: 63–75.
10. Quittner AL, Sweeny S, Watrous M, et al. Translation and linguistic validation of a disease-specific quality of life measure for cystic fibrosis. J Pediatr Psychol 2000; 25: 403–414.
11. Holmbeck G, Wetchove V, Phillips W, et al. A multimethod, multi-informant, and multidimensional perspective on psychosocial adjustment in preadolescents with spina bifida. J Consult Clin Psychol 2003; 71: 782–796.
12. Achenbach T, McConaughy S, Howell C. Child/adolescent behavioral and emotional problems: Implications of cross-informant correlations for situational specificity. Psychol Bull 1987; 101: 213–232.
13. Guyatt G, Juniper E, Griffith L, Feeny D, Ferrie P. Children and adult perceptions of childhood asthma. Pediatrics 1997; 99: 165–168.
14. Varni JW, Seid M, Rode CA. The PedsQL™: Measurement model for the pediatric quality of life inventory. Med Care 1999; 37: 126–139.
15. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL™ 4.0 as a pediatric population health measure: Feasibility, reliability, and validity. Ambul Pediatr 2003; 3: 329–341.
16. SPSS. SPSS. 16.0 for Windows ed. Chicago: SPSS, Inc, 2008.
17. Aday LA. Designing and conducting health surveys: A comprehensive guide. 2nd Ed. San Francisco: Jossey-Bass, 1996.
18. Fowler FJ. Improving survey questions: Design and evaluation. Thousand Oaks, CA: Sage, 1995.
19. Krueger R. Focus groups: A practical guide for applied research. 2nd Ed. Thousand Oaks, CA: Sage Publications, 1994.
20. Schwarz N, Sudman N, eds. Answering questions: Methodology for determining cognitive and communicative processes in survey research. San Francisco: Jossey-Bass, 1996.
21. Fairclough DL. Design and analysis of quality of life studies in clinical trials: Interdisciplinary statistics. New York: Chapman & Hall/CRC, 2002.
22. Fairclough DL, Cella DF. Functional Assessment of Cancer Therapy (FACT-G): Non-response to individual questions. Qual Life Res 1996; 5: 321–329.
23. McHorney CA, Ware JE, Lu JFR, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care 1994; 32 40–66.
24. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika 1951; 16: 297–334.
25. Nunnally JC, Bernstein IR. Psychometric theory. 3rd Ed. New York: McGraw-Hill, 1994.
26. Pedhazur EJ, Schmelkin LP. Measurement, design, and analysis: An integrated approach. Hillsdale, NJ: Erlbaum, 1991.
27. Fayers PM, Machin D. Quality of life: Assessment, analysis, and interpretation. New York: Wiley, 2000.
28. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL™ in pediatric cancer: Reliability and validity of the Pediatric Quality of Life Inventory™ Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. Cancer 2002; 94: 2090–2106.
29. Varni JW, Burwinkle TM, Rapoff MA, Kamps JL, N. O. The PedsQL™ in pediatric asthma: Reliability and validity of the pediatric quality of life inventory™ generic core scales and asthma module. J Behav Med 2004; 27: 297–318.
30. Varni JW, Seid M, Knight TS, Burwinkle TM, Brown J, Szer IS. The PedsQL™ in pediatric rheumatology: Reliability, validity, and responsiveness of the Pediatric Quality of Life Inventory™ Generic Core Scales and Rheumatology Module. Arthritis Rheum 2002; 46: 714–725.
31. Cohen J. Statistical power analysis for the behavioral sciences. 2nd Ed. Hillsdale, NJ: Erlbaum, 1988.
32. Fayers PM, Hand DJ. Factor analysis, causal indicators and quality of life. Qual Life Res 6: 139–150. 1997; 6: 139–150.
33. McGraw KO, Wong SP. Forming inferences about some intraclass correlation coefficients. Psychol Methods 1996; 1: 30–46.

34. Cremeens J, Eiser C, Blades M. Factors influencing agreement between child self-report and parent proxy-reports on the Pediatric Quality of Life Inventory™ 4.0 (PedsQL™) Generic Core Scales. Health Qual Life Outcomes 2006; 4: 1–8.
35. Bartko JJ. The intraclass correlation coefficient as a measure of reliability. Psychol Rep 1996; 19: 3–11.
36. Wilson KA, Dowling AJ, Abdolell M, Tannock IF. Perception of quality of life by patients, partners and treating physicians. Qual Life Res 2001; 9: 1041–1052.
37. Simons LE, Blount RL. Identifying barriers to medication adherence in adolescent transplant recipients. J Pediatr Psychol 2007; 32: 831–844.
38. Dillman DA. Mail and internet surveys: The tailored design method. 2nd Ed. New York: Wiley, 2000.

Appendix A

In Phase I of the instrument development for the PedsQL™ Transplant Module, an item pool designed to address HRQOL issues salient to pediatric transplant recipients and their families was created. To generate relevant items, fourteen focus groups were conducted. Participants in the focus groups included three separate groups of health-care team members from the liver, kidney and heart solid organ transplant teams at a large Midwestern pediatric hospital (n = 30). Separate groups of the parents of heart, kidney and liver transplant recipients (n = 32) and separate groups of children and teenagers (ages 8–18) who had received heart, kidney and liver transplants were also completed (n = 17).

Data collected from these focus groups were used to generate the items for the initial measure. The 46-item measure generated from the focus groups consisted of three versions: a young child self-report (5–7 year olds), a child self-report (8–12 year olds) and an adolescent report (13–18 year olds), with parallel parent proxy-report versions covering ages 2–18 to facilitate a family-centered approach to the assessment of HRQOL.

In Phase II, cognitive interviews were completed with 25 families to obtain feedback about each item from this newly generated measure. Feedback regarding the clarity of the wording, problems with administration and interpretation of instructions were sought. Nine families participated from the kidney transplant group, nine from the liver transplant group, and seven from the heart transplant group. Children's ages ranged from 5 to 18 years of age. Revisions of the measures were made based on the feedback from the children and their parents.

In Phase III, the revised 46-item questionnaire was administered to patients and their parents who were transplant recipients from a large Midwestern pediatric hospital who did not participate in either Phases I or II of the study. Ninety-one parents and 76 children completed the questionnaires. The Cronbach Alphas for this initial sample were good, ranging from.56-.86 for the child self-report measures, and from 0.57 to 0.90 for the parent-proxy measures, suggesting adequate internal consistency of the individual Transplant Module scales. Preliminary factor analyses suggested that most items performed well, with only four items showing low communalities.

The final phase, reported in this manuscript, involved recruiting a larger sample size from solid organ transplant recipients across the country to insure an appropriately representative sample to determine the feasibility, reliability, and validity of the PedsQL™ 3.0 Transplant Module.

Appendix B: PedsQL™ 3.0 Transplant Module Child Self-Report Item Content

About My Medicines I
1. My medicines make me feel sick
2. My medicines make me feel grumpy
3. I forget to take my medicines
4. It is hard for me to take my medicines
5. It is hard for me to swallow my medicines
6. I don't like the taste of my medicines
7. I don't like having to take my medication all the time
8. It is hard for me to fit my medicines into my day
9. I get mad when I have to take my medications

About My Medicines II
1. My medicines make my stomach/tummy bigger
2. My medicines make my face look puffy
3. My medicines make my teeth look different
4. My medicines make me gain weight
5. My medicines make me hairy
6. My medicines make my gums big
7. My medicines keep me from growing tall
8. My medicines give me pimples

My Transplant and Others
1. Other people treat me differently because of my transplant
2. I feel different than other kids my age because I've had a transplant
3. My parents don't let me do activities I want to do because of my transplant
4. Other people don't seem to understand what I've been through
5. I feel left out of things because of my transplant
6. It is hard for me to talk to other people about my transplant
7. My parents nag me about taking my medications
8. My doctors nag me about taking my medications

Pain and Hurt
1. I get stomachaches
2. I get headaches
3. I get backaches

Worry
1. I worry about side effects from medicines
2. I worry about whether or not my medicines are working
3. I worry that something is wrong when I don't feel well
4. I worry that my doctor will find something wrong with me
5. I worry about whether or not my transplant is working
6. I worry that I will have to have another transplant
7. I worry that I won't be able to do the things I used to because of my transplant

Treatment Anxiety
1. I get scared when I have to go to the doctor
2. I get scared when I have to go to the hospital
3. I get scared about having needle sticks (i.e. injections, blood tests, IV's)
4. I get scared when I have to have medical procedures (i.e. biopsy)

How I Look
1. I don't like other people to see my scars
2. I worry that my medicines will change the way I look
3. I am embarrassed when other people see my body

Continued.

Communication

1. It is hard for me to tell the doctors and nurses how I feel
2. It is hard for me to ask the doctors and nurses questions
3. It is hard for me to explain my transplant to other people
4. It is hard for me to understand what the doctors and nurses are telling me