The Pediatric Quality of Life Inventory: Measuring Pediatric Health-Related Quality of Life from the Perspective of Children and Their Parents

James W. Varni, PhD[a,b,*], Christine A. Limbers, MS[c]

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- Pediatric Quality of Life Inventory
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The past decade has evidenced a dramatic increase in the development and use of pediatric health-related quality of life (HRQOL) measures in an effort to improve pediatric patient health and determine the value of health care services.[1,2] HRQOL is a multidimensional construct, consisting at the minimum of the physical, psychological (including emotional and cognitive), and social health dimensions delineated by the World Health Organization.[3] A number of authors have argued that improving

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The PedsQL is available at http://www.pedsql.org.

[a] Department of Pediatrics, College of Medicine, Texas A&M University, College Station, TX 77843, USA

[b] Department of Landscape Architecture and Urban Planning, College of Architecture, Texas A&M University, 3137 TAMU, College Station, TX 77843-3137, USA

[c] Department of Psychology, College of Liberal Arts, Texas A&M University, 4235 TAMU, College Station, TX 77843-4235, USA

* Corresponding author. Department of Landscape Architecture and Urban Planning, College of Architecture, Texas A&M University, 3137 TAMU, College Station, TX 77843-3137.

E-mail address: jvarni@archmail.tamu.edu (J.W. Varni).

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quality of life is the ultimate goal of health care.[4] Although the term ''quality of life'' (QOL) is sometimes used interchangeably with HRQOL, QOL is actually a broader construct that encompasses aspects of life which are not amenable to health care services. Thus, HRQOL has emerged as the most appropriate term for QOL health dimensions that are within the scope of health care services.[5]

During the past several years, legislative changes including the Pediatric Exclusivity Provision of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) have created both voluntary and mandatory guidelines for drug studies in children, resulting in a substantial increase in pediatric clinical trials. Nevertheless, although the above pediatric initiatives have opened the opportunity for children to be included in clinical trials, pediatric patients have not been afforded the right to self-report on matters pertaining to their health and well-being when evaluating the health outcomes of treatments in most pediatric clinical trials to date.[6] This fact stands in sharp contrast to the recent Food and Drug Administration (FDA) Draft Guidance for Industry for evaluating patient-reported outcome (PRO) instruments as health outcomes in clinical trials in which the FDA is quite definitive in stating that ''some treatment effects are known only to the patient.''[5] Thus, what has been an obvious recognition in clinical trials for adult patients, that is, that PROs are *patient self-reported* outcomes, has not received the same level of recognition in clinical trials for pediatric patients.[6]

PATIENT-REPORTED OUTCOMES

By definition, PROs are self-report instruments that directly measure the patient's perceptions of the impact of disease and treatment as clinical trial end points.[5] PROs include multi-item health-related quality of life (HRQOL) instruments, as well as single-item symptom measures (eg, pain visual analog scale [VAS]).[7–9]

It has been extensively documented in the PRO measurement of children with chronic health conditions and healthy children that information provided by proxy-respondents is not equivalent to that reported by the child.[10,11] The findings on the *proxy problem* ''indicate that parent reports cannot be substituted for child self-reports''[12] and evaluations of pediatric patients' perspectives regarding treatment outcomes should be included in pediatric clinical trials given the documented differences between child and parent report.

THE ROLE FOR PARENT PROXY-REPORT

Although pediatric patient self-report should be considered the standard for measuring perceived HRQOL,[13] there may be situations when the child is too young, too cognitively impaired, or too ill or fatigued to complete an HRQOL instrument, and parent proxy-report may be needed in such cases. Further, it is typically parents' perceptions of their children's HRQOL that influences health care use.[14,15] Thus, HRQOL instruments should be chosen that measure the perspectives of both the child and parent because these perspectives may be independently related to health care use, risk factors, and quality of care. Ideally, parent and child HRQOL instruments should measure the same constructs with parallel items to make comparisons between self and proxy report more meaningful.[16]

GENERIC AND DISEASE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS

Although there are a number of disease-specific instruments available, there are potential benefits of integrating generic and disease-specific approaches.[17–19]

Disease-specific measures may enhance measurement sensitivity for health domains germane to a particular chronic health condition, while a generic HRQOL measurement instrument enables comparisons across pediatric populations and facilitates benchmarking with healthy population norms. Thus, there is an emerging perspective that for pediatric chronic health conditions, both generic and disease-specific HRQOL measures should be administered so as to gain a more comprehensive evaluation of the patient's HRQOL.

PEDIATRIC QUALITY OF LIFE INVENTORY MEASUREMENT MODEL

Consistent with the measurement paradigm that generic and disease-specific HRQOL measures should be administered so as to gain a more thorough evaluation of the patient's HRQOL, the Pediatric Quality of Life Inventory (PedsQL) Measurement Model was designed as a modular approach to measuring pediatric HRQOL, developed to integrate the relative merits of generic and disease-specific approaches.[19] Although other pediatric HRQOL instruments exist, including generic measures and disease-specific measures,[2,20] it has been an explicit goal of the PedsQL Measurement Model[19] to develop and test brief measures for the broadest age group empirically feasible, specifically including child self-report for the youngest children possible.[13] The items chosen for inclusion were initially derived from the measurement properties of the child self-report scales, whereas the parent proxy-report scales were constructed to directly parallel the child self-report items. Thus, the development and testing of the PedsQL as a pediatric PRO explicitly emphasizes the child's perceptions. The PedsQL includes child self-report for ages 5 to 18 and parent proxy-report for ages 2 to 18.[21,22] For ages 8 to 18, the PedsQL is self-administered. For ages 5 to 7, the PedsQL is interviewer-administered.

The PedsQL 4.0 Generic Core Scales were designed for application in both healthy and patient populations,[21–23] whereas the PedsQL Disease and Condition Specific Modules were designed to measure HRQOL dimensions specifically tailored for pediatric patients with chronic health conditions.[24–31]

PEDIATRIC QUALITY OF LIFE INVENTORY 4.0 GENERIC CORE SCALES

The PedsQL 4.0 Generic Core Scales have resulted from an extensive iterative process over the past 25 years, involving numerous patient and parent focus groups and individual focus interviews, item generation, cognitive interviewing, pre-testing, and subsequent field testing following standardized protocols,[32–35] with international data on more than 35,000 healthy children and children with numerous pediatric chronic health conditions published or in press in more than 345 peer-reviewed journals since 2001. (A full listing of the updated peer-reviewed journal publications is available at www.pedsql.org.)

The PedsQL 4.0 Generic Core Scales distinguish between healthy children and children with pediatric chronic health conditions, have demonstrated sensitivity to disease severity and responsiveness through patient change over time, and evidence significant intercorrelations with disease-specific symptom scales (based on the conceptualization of disease-specific symptoms as causal indicators of generic HRQOL[36]).[21,22,25–28,31,37–49] Further, the PedsQL 4.0 has shown an impact on clinical decision making, demonstrating significant associations with quality of health care, barriers to health care, and prediction of health care costs over time.[40,50–52]

The items selected for the PedsQL 4.0 Generic Core Scales reflect those that are of universal concern across childhood age groups. Attempts were made to keep wording, and thus the content, as similar as possible across parallel forms, while being

sensitive to developmental differences in cognitive ability. For instance, the only differences between child and adolescent self-report is the use of ''kids'' for items in the Social Functioning Scale in the child self-report version and ''teens'' for those items in the adolescent self-report version, and ''It is hard to keep up with my peers'' for the adolescent self-report version rather than ''It is hard to keep up when I play with other kids'' for the child self-report version. Additionally, parent proxy-report for the toddler age range (ages 2–4) includes only three age-appropriate items for the School Functioning Scale and developmentally appropriate wording for some items in the other scales (eg, ''Participating in active play or exercise'' rather than ''Participating in sport activity or exercise''; ''Bathing'' rather than ''Taking a bath or shower by him or herself''; ''Worrying'' rather than ''Worrying about what will happen to him or her''). This scale construct consistency facilitates the evaluation of differences in HRQOL across and between age groups, as well as the tracking of HRQOL longitudinally. The PedsQL 4.0 Generic Core Scales is the only empirically validated generic pediatric HRQOL measurement instrument that we are aware of to span ages 2 to 18 for parent proxy-report and ages 5 to 18 for child self-report while maintaining item and scale construct consistency. Recent research with the PedsQL 4.0 Generic Core Scales has extended the age range to ages 19 to 25, with additional research in progress on the PedsQL Infant Scales for ages 1 to 24 months.

INTERNATIONAL TRANSLATIONS

There are now more than 65 international translations of the PedsQL 4.0 Generic Core Scales (see www.pedsql.org). Many of these translations were conducted by the Mapi Research Institute in Lyon, France, with the remaining translations conducted by research teams in countries worldwide. The Mapi Research Institute's translations are ''official'' PedsQL translations,[53] whereas the individual research teams' translations are considered preliminary national translations until further validated by the Mapi Research Institute's translation team.

PEDIATRIC QUALITY OF LIFE INVENTORY DISEASE- AND CONDITION-SPECIFIC MODULES

The PedsQL Disease and Condition-Specific Modules were designed to measure HRQOL dimensions specifically tailored for pediatric chronic health conditions, and currently include the PedsQL Asthma,[27,39] Arthritis/Rheumatology,[28] Brain Tumor,[29] Cancer,[26] Cardiac,[31,54] Cerebral Palsy,[24] End-Stage Renal Disease,[30] and Diabetes Modules,[25] as well as the generic PedsQL Multidimensional Fatigue Scale,[26,38] Pediatric Pain Questionnaire,[55] Family Impact Module,[56] and the Healthcare Satisfaction Module.[57,58] The PedsQL Module Scales were developed through focus groups, cognitive interviews, pre-testing, and field testing measurement development protocols.[32–35] New PedsQL Disease- and Condition-Specific Modules currently in various phases of development and testing include the PedsQL Organ Transplantation Module, Neuromuscular Module, and Sickle Cell Disease Module, with other modules in the planning and early development stages.

The PedsQL Disease- and Condition-Specific Modules are composed of parallel child self-report and parent proxy-report formats, exactly like the PedsQL 4.0 Generic Core Scales. This exact matching format greatly facilitates the integration of the generic and disease-specific scales as originally envisioned in the PedsQL Measurement Model. Each Module contains disease-specific scales that are scored individually, and used as required to achieve the goals and objectives of a particular study. For instance, in a randomized clinical trial testing a new pharmaceutical intervention for pediatric asthma, the 11-item PedsQL Asthma Module Asthma Symptoms Scale

would be integrated with the 23-item PedsQL 4.0 Generic Core Scales when the intent of the intervention is to improve asthma symptom control and overall generic HRQOL. In this hypothetical study, for example, it would not be required, nor advised, to include all of the other Asthma Module Scales, such as the Worry and Communication Scales, as these constructs were not the primary objective of the intervention, although the Asthma Treatment Problems Scale might be indicated if barriers to medication adherence were of empiric interest. Thus, the primary outcome measures in this hypothetical randomized clinical trial would be the Asthma Symptoms Scale and the Generic Core Total Scale Score, with the individual Scale Scores from the generic core instrument as secondary outcomes.

This strategy of selecting individual Module Scales depending on the intent of the randomized clinical trial serves to reduce respondent burden and the costs of the trial, and may increase ''statistical efficiency'' by empirically determining the number of patients needed in a clinical trial through examining subscale intercorrelations, standard deviations, and predicted relative effects.[59] Vickers[59] has delineated a useful strategy for determining the statistical implications of selecting an individual subscale or a combination of subscales as the primary outcome in a randomized trial. When subscales measure distinctly different constructs, the cost/benefit ratio of combining them into a composite score must be carefully considered given the potentially significant implications for respondent burden, the number of patients needed given a specified effect size, and the associated costs. Thus, in the case of the Asthma Module, for example, although there may be a rationale for combining the Asthma Symptoms Scale and the Asthma Treatment Problems Scale into a single composite score, Vickers' statistical efficiency strategy might inform the decision-making process by demonstrating the relative effect sizes for either the Scales individually or as a combined subscale composite score based on the existing data from these Asthma Module Scales. It is likely that for a clinical trial concerned with asthma symptom control, using the Asthma Symptoms Scale as the primary outcome would be more conceptually precise and demonstrate greater statistical efficiency rather than creating a composite score by combining two subscales.

In sum, the PedsQL Disease- and Condition-Specific Modules have been developed to provide disease- and condition-specific Scales that can be individually used for a particular randomized trial, rather than necessitating the costs and respondent burden of requiring that all of the Scales in a particular Module are included. This flexibility is meant to increase the efficiency of determining the efficacy and effectiveness of an intervention with an integrated set of generic and disease-specific HRQOL constructs and scales. Greater detail on the measurement properties of each of the Modules is contained in the published peer-reviewed journal articles cited in the reference list, including age-specific findings. These Modules are briefly described next.

PEDIATRIC QUALITY OF LIFE INVENTORY ASTHMA MODULE

The 28-item PedsQL Asthma Module encompasses 4 Scales[27,39]: (1) Asthma Symptoms (11 items), (2) Treatment Problems (11 items), (3) Worry (3 items), and (4) Communication (3 items). The Asthma Symptoms Scale includes such items as ''It is hard to take a deep breath''; ''I feel wheezy''; ''My chest hurts or feels tight''; ''I cough''; ''I get out of breath.'' The Treatment Problems Scale includes such items as ''My medicines make me feel sick''; ''I have trouble using my inhaler''; ''I forget to take my medicines''; ''I don't like to carry my inhaler.''

PEDIATRIC QUALITY OF LIFE INVENTORY ARTHRITIS/RHEUMATOLOGY MODULE

The 22-item PedsQL Arthritis/Rheumatology Module Scales encompass[28]: (1) Pain and Hurt (4 items), (2) Daily Activities (5 items), (3) Treatment (7 items), (4) Worry (3 items), and (5) Communication (3 items). The Arthritis/Rheumatology Module Scales include such items as ''I ache or hurt in my joints and/or muscles''; ''I have trouble eating with a fork and knife''; ''My medicines make me feel sick''; ''I worry about my illness.''

PEDIATRIC QUALITY OF LIFE INVENTORY BRAIN TUMOR MODULE

The 24-item PedsQL Brain Tumor Module encompasses 6 Scales[29]: (1) Cognitive Problems (7 items), (2) Pain and Hurt (3 items), (3) Movement and Balance (3 items), (4) Procedural Anxiety (3 items), (5) Nausea (5 items), and (6) Worry (3 items). The Brain Tumor Module Scales include such items as ''It is hard for me to learn new things''; ''I get headaches''; ''It is hard for me to keep my balance''; ''It is hard for me to pay attention to things.''

PEDIATRIC QUALITY OF LIFE INVENTORY CANCER MODULE

The 27-item PedsQL Cancer Module encompasses 8 Scales[26]: (1) Pain and Hurt (2 items), (2) Nausea (5 items), (3) Procedural Anxiety (3 items), (4) Treatment Anxiety (3 items), (5) Worry (3 items), (6) Cognitive Problems (5 items), (7) Perceived Physical Appearance (3 items), and (8) Communication (3 items). The Cancer Module Scales include such items as ''I hurt a lot''; ''I become sick to my stomach when I have medical treatment''; ''I get scared when I have to have blood tests''; ''I worry about the side effects from medical treatments''; ''It is hard for me to pay attention to things''; ''I don't like other people to see my scars.''

PEDIATRIC QUALITY OF LIFE INVENTORY DIABETES MODULE

The 28-item PedsQL Diabetes Module encompasses 5 Scales[25]: (1) Diabetes Symptoms (11 items), (2) Treatment Barriers (4 items), (3) Treatment Adherence (7 items), (4) Worry (3 items), and (5) Communication (3 items). The Diabetes Module Scales include such items as ''I feel thirsty''; ''I get irritable''; ''It is hard for me to take insulin shots''; ''It is hard for me to exercise''; ''I worry about long-term complications from diabetes.''

PEDIATRIC QUALITY OF LIFE INVENTORY CARDIAC MODULE

The 27-item PedsQL Cardiac Module encompasses 6 Scales[31,54]: (1) Heart Problems and Treatment (7 items), (2) Treatment II (5 items), (3) Perceived Physical Appearance (3 items), (4) Treatment Anxiety (4 items), (5) Cognitive Problems (5 items), and (6) Communication (3 items). The Cardiac Module Scales include such items as ''My chest hurts or feels tight when I do sports activity or exercise''; ''I wake up at night with trouble breathing''; ''My heart medicine makes me feel sick''; ''It is hard for me to remember what I read.''

PEDIATRIC QUALITY OF LIFE INVENTORY CEREBRAL PALSY MODULE

The 35-item PedsQL Cerebral Palsy Module encompasses 7 Scales[24]: (1) Daily Activities (9 items, eg, ''It is hard for me to button my shirt''), (2) School Activities (4 items, eg, ''It is hard for me to use a mouse for the computer''), (3) Movement and Balance (5 items, eg, ''It is hard for me to move one or both of my legs''), (4) Pain and Hurt (4 items,

eg, ''I ache or hurt in my joints and/or muscles''), (5) Fatigue (4 items, eg, ''I feel tired''), (6) Eating Activities (5 items, eg, ''It is hard for me to eat with a spoon and/or fork''), and (7) Speech and Communication (4 items, eg, ''It is hard for other people to understand my words'').

PEDIATRIC QUALITY OF LIFE INVENTORY MULTIDIMENSIONAL FATIGUE SCALE

The 18-item PedsQL Multidimensional Fatigue Scale encompasses 3 Scales[26,38]: (1) General Fatigue Scale (6 items, eg, ''I feel tired''; ''I feel too tired to do things that I like to do''), (2) Sleep/Rest Fatigue Scale (6 items, eg, ''I feel tired when I wake up in the morning''; ''I rest a lot''), and (3) Cognitive Fatigue Scale (6 items, eg, ''It is hard for me to keep my attention on things''; ''It is hard for me to think quickly'').

RESPONSIVENESS OF THE PEDIATRIC QUALITY OF LIFE INVENTORY

Improvement in HRQOL is a primary goal in the management of acute and chronic health conditions. As such, determining a HRQOL measure's capacity to detect change in clinical trials and intervention studies is important. Responsiveness is the psychometric property associated with an instrument's ability to measure meaningful or important change.[60] The responsiveness of a measurement instrument is demonstrated through a longitudinal analysis of changes within patients in whom a change is anticipated as a result of, for example, an intervention of known or expected efficacy.[61,62] Responsiveness is a particularly important issue when selecting an HRQOL measure, because instruments that are highly responsive allow clinical trials and intervention studies to be conducted with fewer patients.[63]

The PedsQL has demonstrated responsiveness to evidenced-based interventions and access to health care. **Table 1** illustrates examples of the published data on responsiveness of the PedsQL 4.0 Generic Core Scales and Disease-Specific Modules.

As an example, the PedsQL Generic Core Scales and Asthma Module have demonstrated responsiveness to evidence-based chronic disease management. Specifically, Mangione-Smith and colleagues[64] conducted a national effectiveness trial in pediatric asthma following the Chronic Care Model and the Breakthrough Series collaborative team approach. The Chronic Care Model identifies 6 elements of the health care system such as organization/leadership, patient self-management, delivery system design, health care provider decision support, informational technology, and links to community resources that can be used to optimized chronic disease care.[64] The Breakthrough Series collaborative process emphasizes a team approach to continuous quality improvement in patient chronic disease management.[64] In this effectiveness study,[64] pediatric patients with asthma receiving care from clinics participating in the collaborative intervention had significant improvements in processes of care variables, such as monitoring their peak flows and having a written asthma action care plan. Patients in the intervention group demonstrated higher generic and asthma-specific scores on the PedsQL Generic Core Scales and the PedsQL Asthma Module. This real-world effectiveness trial suggests the potential utility of the PedsQL as a HRQOL outcome measure in clinical practice settings.

The PedsQL 4.0 Generic Core Scales has also demonstrated responsiveness to access to health care.[65] As part of a 2-year, prospective cohort study of enrollees in the California State Children's Health Insurance Program, parents and children completed the PedsQL 4.0 Generic Core Scales at enrollment and after 1 and 2 years in the program.[65] Realized access to care and forgone care were assessed through parents' reports of problems getting necessary care (''In the last 12 months, how

Table 1
Published studies demonstrating responsiveness of the PedsQL 4.0 Generic Core Scales and Disease-Specific Modules

Study	Patient Population/Treatment Condition	PedsQL Outcome(s)	Findings
Varni et al. (2002)[28]	34 pediatric patients with rheumatologic conditions ages 5–18 years receiving clinical care provided by a pediatric rheumatologist; the pediatric rheumatologist evaluated the child for the first time (ie, first visit as a new patient), with treatment then initiated at this visit (Visit 1), with two subsequent follow-up visits (Visits 2 and 3).	PedsQL 4.0 Generic Core Scales PedsQL 3.0 Rheumatology Module	For child self-report and parent proxy-report, the PedsQL Generic Core Total and Summary Scale Scores increased progressively from Visit 1 through Visit 3, with larger effect sizes at Time 3. Effect sizes were in the small range at Time 2, and in the medium to large effect size range at Time 3. The PedsQL 3.0 Rheumatology Module Scales demonstrated improvement over time primarily for Pain and Hurt, with small to medium effect sizes at Time 2, and large effect sizes at Time 3.
Varni et al. (2002)[40]	47 children ages 5–18 years presenting at a pediatric orthopedic clinic for the treatment of fractures	PedsQL 4.0 Generic Core Scales	The PedsQL 4.0 demonstrated responsiveness in the orthopedic clinic sample, with statistically significant changes in scores from the initial clinic visit for the treatment of a fracture to the subsequent follow-up (mean duration follow-up 7.53 months). At the follow-up evaluation, the recovered patients as a group demonstrated a return to health when compared with the healthy children scores.
Sallee et al. (2004)[73]	2968 children ages 6–12 years with a DSM-IV diagnosis of attention-deficit hyperactivity disorder participating in a prospective, open-label trial in which the baseline stimulant treatment regimen of immediate-release methylphenidate was converted to an approximately equivalent once-daily dose of extended-release mixed amphetamine salts	PedsQL 4.0 Generic Core Scales	For parent proxy-report, mean PedsQL 4.0 Generic Core Total Scale score at baseline was 74.5 compared with 81.0 ($P < .01$) after 7 weeks of treatment with extended-release mixed amphetamine salts (child self-report was not assessed in this study).

Mangione-Smith et al. (2005)[64]	385 asthmatic children receiving care at an intervention clinic and 126 receiving care at a control clinic (all children ages 2–17 years); intervention consisted of three 2-day educational sessions for quality improvement teams from participating sites followed by 3 "action" periods over the course of a year	PedsQL 4.0 Generic Core Scales PedsQL 3.0 Asthma Module	The overall process of asthma care improved significantly in the intervention group but remained unchanged in the control group ($P < .0001$); patients in the intervention group were more likely than patients in the control group to monitor their peak flows ($P < .0001$) and to have a written action plan ($P = .001$); patients in the intervention group had better PedsQL 4.0 Generic Core Total Scale scores (80 versus 77, $P = .05$) and asthma-specific quality of life related to treatment problems (89 versus 85, $P < .05$).
Schwimmer et al. (2005)[74]	Single-arm open-label pilot study of metformin 500 mg twice daily for 24 weeks in 10 obese nondiabetic children with biopsy-proven nonalcoholic steatohepatitis ages 8–17 years	PedsQL 4.0 Generic Core Scales	Participants self-reported a significant ($P < .01$) improvement in the mean PedsQL 4.0 Generic Core Total Scale score from baseline (69.00) to following treatment (81.00) at 24 weeks (only child self-report scores reported in manuscript).
Connelly and Rapoff (2006)[75]	40 children with a recurrent headache syndrome ages 7–12 years participating in a 4-week self-directed cognitive-behavioral pain management program	PedsQL 4.0 Generic Core Scales	At 3-month follow-up, participants receiving the self-directed cognitive-behavioral pain management intervention demonstrated significant improvements on the PedsQL 4.0 Generic Core Total Scale score ($P < .01$), Physical Functioning Scale ($P < .01$), and Psychosocial Summary score ($P = .01$; only child self-report scores reported in manuscript).
Felder-Puig et al. (2006)[76]	68 patients receiving allogeneic bone marrow or stem cell transplantation ages 4–18 years	PedsQL 4.0 Generic Core Scales PedsQL 3.0 Cancer Module	In all analyzed PedsQL domains on the Core and Cancer Module for child self-report and parent proxy-report (except for pain), PedsQL scores were significantly better ($P < .01$) at 1 year post transplant compared with the two measurement time points before bone marrow transplant.

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Study	Patient Population/Treatment Condition	PedsQL Outcome(s)	Findings
Razzouk et al. (2006)[77]	Anemic patients ages 5–18 years receiving myelosuppressive chemotherapy for nonmyeloid malignancies, excluding brain tumors, received intravenous epoetin alfa (EPO) 600 units/kg to 900 units/kg (n = 111) or placebo (n = 111) once weekly for 16 weeks	PedsQL 4.0 Generic Core Scales	EPO-treated patients had greater increases in hemoglobin (Hb) overall (P = .002) and were more likely to be transfusion free after 4 weeks (38.7% versus 22.5%; P = .010); change in Hb was correlated with change in PedsQL 4.0 Generic Core Total Scale score in the EPO group (r = 0.242; P = .018), but was not in the placebo group (r =0.086; P = .430). Young children ages 5–7 years had the greatest Hb response (92.3% of 5- to 7-year-olds in the EPO group were Hb responders); consistent with these findings, mean patient-reported PedsQL 4.0 Generic Core Total Scale scores at the final visit were significantly greater in the EPO group among patients 5 to 7 years of age (88.0 versus. 78.1; P = .043), but not among patients 8 years to 12 years of age or 13 years to 18 years of age.
Seid et al. (2006)[65]	4925 children ages 2–16 years enrolled in the California State Children's Health Insurance Program	PedsQL 4.0 Generic Core Scales	Foregone health care in the past 12 months and problems getting health care in the past 12 months significantly reduce parent proxy-report PedsQL scores by 3.5 and 4.5 points (P < .001) and child self-report PedsQL scores by 3.2 and 4.4 points (P < .001).

Cuomo et al. (2007)[78]	57 ambulatory children ages 5–15 years with cerebral palsy undergoing multilevel soft tissue surgery to correct sagittal imbalance	PedsQL 4.0 Generic Core Scales	Significant improvements in the PedsQL 4.0 Generic Core Total Scale score and Physical Functioning score were evidenced for parent proxy-report ($P < .001$) approximately 12 months postoperative.
Fullerton et al. (2007)[79]	80 sixth- and seventh- graders at-risk-for-overweight and overweight Mexican American children participating in 6 months of intensive weight management or self-help	PedsQL 4.0 Generic Core Scales	Children in the intensive weight management program condition achieved significantly greater weight loss (z BMI, -0.13; $P < .001$) and significantly greater PedsQL Physical Functioning improvements than those in the self-help condition at 6 months ($P < .05$). PedsQL Physical Functioning increases were associated with z BMI reduction ($P < .05$; only child self-report scores reported in manuscript).
Holterman et al. (2007)[80]	10 morbidly obese adolescents ages 14–17 years receiving laparoscopic adjustable gastric banding (LAGB)	PedsQL 4.0 Generic Core Scales	In the 8 patients with impaired HRQOL at baseline, the mean PedsQL 4.0 Generic Core Total Scale score rose from 62.6 at baseline to 75.6 ($P > .05$) 83.9 ($P = .03$), and 78.5 ($P = .06$) at 3, 6, and 9 months postoperative. For parent proxy-report, the mean PedsQL 4.0 Generic Core Total Scale score rose from 54.0 at baseline to 66.8 ($P < .002$) 74.8 ($P < .002$), and 72 ($P < .002$) at 3, 6, and 9 months postoperative.

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Table 1
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Study	Patient Population/Treatment Condition	PedsQL Outcome(s)	Findings
Banks et al. (2008)[81]	29 pediatric oncology patients ages 2–18 years undergoing an intravenous chemotherapy cycle (intravenous chemotherapy given during week 1)	PedsQL 4.0 Generic Core Scales PedsQL 3.0 Cancer Module	From week 1 to week 4 for parent proxy-report, the PedsQL 4.0 Generic Core Total Scale score demonstrated a mean change of 17 points and the Cancer Module Total Scale score demonstrated a 12-point change (child self-report was not assessed in this study).
Cheuk et al. (2008)[82]	24 transfusion-dependent thalassemic patients who survived matched sibling hematopoietic (SCT) and 74 patients treated conventionally with transfusion and iron chelation	PedsQL 4.0 Generic Core Scales	PedsQL revealed posttransplant patients rated better for running ($P = .001$) and sports ($P = .038$) after adjustment for comorbidities.
de Vries et al. (2008)[83]	41 children ages 2–18 years with acute lymphoblastic leukemia undergoing dexamethasone treatment alternating 2 weeks on and 5 weeks off (6 mg/m^2/day)	PedsQL 3.0 Cancer Module	Halfway as well as at the end of treatment, parents rated their child's overall HRQOL to be more impaired during periods on dexamethasone as compared with periods off dexamethasone; at time 2 during dexamethasone, scores on the PedsQL were significantly lower for the subscales Pain ($P = .04$), Worry ($P = .02$) and Cognition ($P = .01$).
Nuboer et al. (2008)[84]	38 children ages 4–16 years with type 1 diabetes undergoing insulin pump treatment versus. four times daily injections lasting 3.5 months	PedsQL 4.0 Generic Core Scales	Pump treatment resulted in decreased symptomatic hypoglycaemia and lowered hemoglobin A1c by 0.22%; consistent with these findings, within-patient comparisons of the two treatment modalities showed significant improvement in PedsQL scores after pump treatment.

Parekh et al. (2008)[85]	25 patients ages 3–17 years with ureteropelvic junction obstruction undergoing pyeloplasty surgery	PedsQL 4.0 Generic Core Scales	6 weeks postoperative child Emotional Functioning (91.7) and Physical Functioning (90.3) improved significantly ($P < .05$) from preoperative scores; parent scores on Physical Functioning (88.4), Psychosocial Health (82.2), and Emotional Functioning (80.8) were significantly higher postoperative at 6 weeks.
Wade et al. (2008)[86]	Children and parents from 4 elementary schools with newly implemented school-based health centers and 4 elementary comparison schools	PedsQL 4.0 Generic Core Scales	There was a significant improvement in child self-reported HRQOL over the 3 years for school-based health center users compared with the comparison school group.
Yackobovitch-Gavan et al. (2008)[87]	71 obese adolescents ages 12–18 years participating in one of three 12-week diet regimens: low-carbohydrate low-fat, low-carbohydrate high-fat, or high carbohydrate low-fat diets	PedsQL 4.0 Generic Core Scales	A significant improvement in physical, emotional, school, and psychosocial functioning, as well as in the total PedsQL score was noted in the entire study population at the end of the interventions; a significant improvement in HRQOL was found in the low-carbohydrate low-fat group (emotional, school, and psychosocial functioning, and total PedsQL score) and in the high-carbohydrate low-fat group (physical, emotional, and psychosocial functioning, and total PedsQL score), but not in the low-carbohydrate high-fat group.

much of a problem, if any, was it to get care for your child that you or a doctor believed necessary?'' and ''In the past 12 months, has there been any time when you thought your child should get medical care, but did not?'').[65] Realized access to care during the prior year was related to HRQOL for each subsequent year. Foregone care and problems getting care were associated with decrements of 3.5 and 4.5 points on the PedsQL for parent proxy report ($P < .001$) and with decrements of 3.2 and 4.4 points on the PedsQL for child self-report ($P < .001$). Improved realized access resulted in higher PedsQL scores, continued realized access resulted in sustained PedsQL scores, and foregone care resulted in cumulative declines in PedsQL scores over time.

MINIMAL CLINICALLY IMPORTANT DIFFERENCE

Related to responsiveness is the minimal clinically important difference (MCID), which has been defined as the smallest difference in a score of a domain of interest that patients perceive to be beneficial and that would mandate, in the absence of troublesome side effects and excessive costs, a change in the patient's management.[66] The Standard Error of Measurement (SEM)[67] has been linked to the MCID, in which one SEM identified the MCID in responsiveness in an HRQOL measure.[68] Excellent agreement between the SEM and MCID has been shown.[68] As an illustration in a population-based study, the MCID for the PedsQL 4.0 has been determined through calculating the SEM. A 4.4 change in the PedsQL 4.0 Total Scale Score for child self-report has been determined as a minimal clinically meaningful difference, whereas a 4.5 change in PedsQL4.0 Total Scale Score for parent proxy-report was determined as a minimal clinically meaningful difference.[22] Thus, the MCID can provide a metric for determining meaningful change in a clinical trial, or in the planning stages of a clinical trial to determine the sample size needed to detect a meaningful clinical difference.

CUT-POINT FOR AT-RISK STATUS

Scores approximating 1 standard deviation below the population mean have been proposed as a meaningful cut-off point score for an at-risk status for impaired HRQOL relative to population means.[1,2] As an illustration, cut-off points for at-risk status for impaired HRQOL have been examined for the PedsQL 4.0 using the 1 standard deviation below the mean of the total population sample.[22] For child self-report, the PedsQL 4.0 Total Scale Score cut-off point score was 69.7 (parent proxy-report score of 65.4). To provide the context for these cut-off scores, it is useful to examine PedsQL 4.0 Total Scale Scores for children with physician-diagnosed chronic health conditions. For example, pediatric oncology patients receiving chemotherapy and radiation therapy self-report a PedsQL 4.0 Total Scale Score of 68.9 (parent proxy-report score of 67.0).[26] Similarly, children with rheumatic conditions (eg, juvenile rheumatoid arthritis) self-report a PedsQL 4.0 Total Scale Score of 72.1 (parent proxy-report score of 71.).[28] Thus, scores approximating 1 standard deviation below the population sample mean represent PedsQL 4.0 Total Scale Scores similar to children with severe chronic health conditions.

SENSITIVITY OF THE PEDIATRIC QUALITY OF LIFE INVENTORY

Although the responsiveness of a measurement instrument provides the opportunity to determine changes in individual patients or patient groups over time (prospective or longitudinal analysis), measurement sensitivity facilitates the identification of

differences among individual patients or patient groups at one point of time (cross-sectional analysis).[61,69] The sensitivity of a measurement instrument may be demonstrated through a cross-sectional analysis of differences between groups of patients with varying degrees of disease severity or through other group comparisons.[61] The PedsQL 4.0 Generic Core Scales has demonstrated sensitivity across disease severity for a number of pediatric chronic health conditions.[26,28,54,70,71] For example, Uzark and colleagues[54] conducted a cross-sectional analysis of health-related quality of life in children with varying severities of heart disease. Severity of heart disease was rated by a clinician blinded to the study outcomes and was categorized as (1) mild disease requiring no therapy or effectively treated nonoperatively (catheter therapy); (2) moderate disease surgically corrected (curative) or requiring no therapy; (3) surgical correction (one or more procedures) with significant residua or need for further surgery; (4) complex or severe disease, uncorrectable or palliated (includes single ventricle). Physical Functioning scores on the PedsQL 4.0 Generic Core Scales were significantly lower in children in disease category 3 or 4 compared with children in disease category 1 or 2 ($P < .01$) as rated by both children and parents. A significant difference in Psychosocial Health scores was demonstrated across disease severity categories ($P < .01$) with an incremental decrease in mean scores as disease severity increased.

PEDIATRIC QUALITY OF LIFE INVENTORY IN PEDIATRIC CLINICAL PRACTICE

Findings from the adult literature suggest that routine implementation of standardized HRQOL assessment may be a necessary but not sufficient condition for enhancing patients' HRQOL.[1] Incorporating specific resource management suggestions, such as appropriate referrals and tailored treatments are hypothesized to enhance the efficacy of HRQOL measurement by providing physicians and other health care professionals with viable options to identified problems.[1] In a recent study from the Netherlands,[72] adolescents with type I diabetes completed the PedsQL 4.0 Generic Core Scales and PedsQL Diabetes-Module on a computer before consultation with their pediatrician at three office visits within 12 months. PedsQL subscale scores were automatically calculated by a computer program and reports with the outcomes of the PedsQL were printed for the pediatrician and the adolescent to be discussed during the consultation.[72] Before beginning the study, pediatricians received a short training course on how to interpret and discuss PedsQL scores and were provided a small guide with instructions and a list of the individual items on the PedsQL subscale as a backup for discussing PedsQL scores. Pediatricians were instructed to start with discussing PedsQL 4.0 Generic Core scores, with Dutch norm scores as reference, and respectfully invite the adolescent to comment and discuss the outcomes.[72] Subsequently, the PedsQL Diabetes Module subscales were discussed, exploring possible solutions and actions.[72] At 12 months, mean scores on psychosocial well-being ($P < .001$), behavior ($P < .001$), mental health ($P < .001$), and family activities ($P < .001$) improved in the intervention group, except for adolescents with the highest A1C values.[72] Adolescents in the intervention group reported higher self-esteem at follow-up ($P = .016$), regardless of A1C, and were more satisfied with care ($P = .009$) than control subjects.[72]

SUMMARY

Health-related quality of life has been recognized as an important outcome, some contend *the* most important outcome for children's health care interventions.[4] The PedsQL Measurement Model was designed as a modular approach to measuring

pediatric health-related quality of life, developed to integrate the relative merits of generic and disease-specific approaches. The PedsQL 4.0 Generic Core Scales have been translated into more than 65 languages, with published data on more than 35,000 children and adolescents in more than 345 peer-reviewed journals since 2001 in healthy children and numerous pediatric chronic health conditions. The PedsQL Disease- and Condition-Specific Modules were designed to measure HRQOL dimensions specifically tailored for pediatric chronic health conditions. The PedsQL has demonstrated feasibility, reliability, validity, sensitivity, and responsiveness for child self-report ages 5 to 18 years and parent proxy-report ages 2 to 18 years, and has been shown to be related to other key constructs in pediatric health care such as access to needed care, health care barriers, predictive of health care costs, and quality of primary care. Future advances in the PedsQL Measurement Model include Web-based electronic administration (ePedsQL), integration into the electronic medical record, further efficacy and effectiveness outcome trials, and the development of the generic PedsQL Infant Scales for ages 1 month to 24 months as well as additional disease- and condition-specific modules for other pediatric chronic health conditions such as solid organ transplants and sickle cell disease.

Finally, how can HRQOL outcomes become incorporated into health care to improve quality? We propose that the advent of the electronic medical record provides the opportunity for the integration of HRQOL outcomes as a quality indicator of the appropriateness and safety of the care provided. Perhaps the time will finally arrive in the next 5 years to consider pediatric patients' and parents' perceptions of the child's health and well-being as essential outcomes in the evaluation of the quality of care provided. We suggest that part of the process of improving the quality of health care includes measuring HRQOL outcomes from the perspective of children and their parents on a routine basis, consistent with a consumer-based health care system approach.

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