Online Only Supplementary Material

Wolfe J, Orellana L, Cook EF, Ullrich C, Kang T, Geyer R, Feudtner C, Weeks JC, Dussel V. Improving Care of Children with Advanced Cancer Using an Electronic Patient-Reported Feedback Intervention: Results from the PediQUEST Randomized Controlled Trial.

Contents:

This supplementary material has been provided by authors to give readers additional information about their work.

Instruments. Description of PediQUEST Surveys and Pilot Testing of PediQUEST-Surveys

PediQUEST-Surveys

PediQUEST technology consisted of a hand-held computer device containing software allowing the selection of a user specific survey aimed at tracking symptoms and quality of life. The hardware chosen for PediQUEST was the Acer TravelMate C104Ti, a Tablet PC with a 10.4" color, touch sensitive screen, which had a good ability to rapidly load graphs on the screen.

The PQ-Survey assessed symptoms, health related quality of life (HRQoL), and overall sickness. PQ-Survey had nine versions allowing for age and respondent appropriateness. Survey versions and modes of administration are explained in the Methods section of the paper and Box 1. Self-reports were available for children aged 5 years old and older, and proxy reports for parents of all children enrolled (2 years old and older). When a self-report version was available, the child was asked to complete PediQUEST. If the child was unable or unwilling to do so, the parent was asked to complete proxy forms on the child's behalf.

The instruments used in PQ-Surveys were selected after an extensive literature review. PQ-Surveys included four tools:

i) PediQUEST Memorial Symptom Assessment Scale (PQ-MSAS), adapted from previously validated MSAS child[1,2] and proxy[3] versions,

ii) Pediatric Quality of Life Inventory (PedsQL 4.0™),[4] a HRQoL tool with extensive validation,

iii) Faces Pain Scale-Revised (FPS-R),[5] used to measure current pain and not included in this analysis, and

iv) Sickness question, a single item score, developed de novo for the study.

In this section we will provide further details about PQ-MSAS, PedsQL 4.0™, and the overall sickness question. Any modification introduced to these instruments is explained below. Piloting of the new instruments (PQ-MSAS, PedsQL 4.0™, and Sickness question) is described in the next section:

1. <u>PediQUEST-Memorial Symptom Assessment Scale for children (PQ-MSAS)</u>

MSAS was originally designed as an adult patient-administered clinical tool to assess the symptoms experienced by cancer patients.[6] The adult version of the scale has been extensively validated and shown to be useful in the palliative care setting.[7-9] MSAS was the only multidimensional and multiple symptom instrument that had been adapted and validated for use in children. There are two validated child versions, MSAS 10-18[1] and MSAS 7-12.[2] A proxy version had been developed for report by nurses.[3] MSAS 10-18 and MSAS proxy contain 31 items, whereas MSAS 7-12 is shorter with only 8 items. Three domains are assessed: physical symptoms, psychological symptoms and global symptom distress. MSAS 10-18 reliability has been reported to be above 0.80 and its convergent validity is good.[1]

Three PQ-MSAS versions were adapted and shortened to make it more appropriate for the pediatric advanced cancer population: PQ-MSAS 13-18 (adapted from MSAS10-18), PQ-MSAS 7-12 (comprised of PQ-MSAS 7-12 (self-report) and PQ-MSAS proxy-supplemental), and PQ-MSAS proxy-full. The three versions of PQ-MSAS allowed the assessment of severity, frequency, and distress of 24 physical and psychological symptoms across the study age range.

The seven items removed from the original questionnaires were eliminated to reduce study burden and to focus on symptoms that are known to be distressful for children with advanced cancer.[10,11] Those removed included hair loss, headache, weight loss, dizziness, taste changes, mouth sores, and swelling of arms and legs. All the eliminated items were presented as a checklist in two "other symptom" questions. In PQ-MSAS 7-12, itch was removed and dyspnea incorporated (however, since this item was not child validated, a dyspnea item was left in the parent's supplemental questionnaire and used for analysis).

PQ-MSAS proxy-full was used by parents of 2-6 year-olds and when the child did not want to self-report. PQ-MSAS proxy-supplemental was administered to parents of 7-12 years old to assess the 16 symptoms not included in PQ-MSAS 7-12 and the dyspnea item. Items and time frame of proxy versions (originally MSAS proxy asked about symptoms during the last day of life of the patient) were modified to match PQ-MSAS 13-18 which asks

about symptoms over the past week. Necessary wording changes were introduced so that the questions addressed parents appropriately (originally developed for nurses).

Conceptual equivalence and score equivalence between the three PQ-MSAS versions (7-12, 13-18, and full-proxy) is assumed. Permission for all changes and use of the scale was obtained from the author (personal communication with JJ Collins).

MSAS Scoring: In its original form, MSAS uses a 0-3 scale for young children and a 0-4 scale for older children and proxy versions.[1] PQ-MSAS scores were standardized to 0-100 scales (100 worst) to increase comparability across age groups and with HRQoL scores. As recommended by authors the following average scores were calculated: individual symptom scores (average of the 3 sub-questions for each symptom (frequency, severity distress)), MSAS total score (average of all symptom scores), MSAS physical subscale (average of 8 physical symptoms), and MSAS psychological subscale (average of 6 psychological symptoms). Denominators are based on the number of answered, i.e. not missing, questions answered. Total and subscale scores were calculated if at least 50% of the items were not missing.

2. Pediatric Quality of Life Inventory Generic Core Module (PedsQL 4.0™)

This is a standardized patient self-report and parent-report instrument designed to systematically assess pediatric patient's HRQoL outcomes. The PedsQL 4.0™ consists of a 22-item core measure of HRQoL. Four proxy and three self-report age-adapted versions are available (age groups are 2-4, proxy only; 5-7, 8-12 and 13 and over, each with a self-report and proxy version available). Both English and Spanish versions of this scale have undergone extensive validation across a number of different diseases for the age range 2-18 years.[4,12-15] Patient-parent concordance was high (0.48-0.56) and for both patient and parent forms, internal consistency was strong (0.88 for self-reports and 0.93 for proxy-reports). Because of good psychometric properties, this instrument is recommended for use at the individual patient analysis level as well as for group comparisons. The only addition to PedsQL 4.0™ for the PediQUEST study was a question about whether the child has been attending school lately to allow for better interpretation of the data.

PedsQL 4.0™ Scoring: Each item is scored 0-25-50-75-100. As recommended by authors the following average scores were calculated: PedsQL 4.0™ Total QoL score: calculated as the average of all item scores; PedsQL 4.0™ Physical subscale (average of 8 physical items); PedsQL 4.0™ Psychosocial, Emotional, Social, and School subscales (each one averages the respective subsections of the tool). Range for all scores: 0-100 (0 worst). Denominators are based on the number of answered, i.e. not missing, questions answered. Total and subscale scores were calculated if at least 50% of the items were not missing.

3. Sickness question (Sickness)

This single item was developed de novo for the study to evaluate overall sickness. The question asked "Overall, how have you/your child been feeling during the past week?"
Two response scales were used: a three point faces scale (Sickness-Faces) was presented to children 5 to 6 years old and a Visual Analog Scale (Sickness-VAS) that was presented to children 7 years old and older and all parents. Anchors for both scales are "Not sick at all" and "Very sick."

Pilot Study Results:
Since PediQUEST was compiled and adapted from existing instruments and included a de novo sickness item, we conducted pilot testing through the adaptation process and development of the computerized survey. Protocol was approved by Dana-Farber Children's Hospital Cancer Center (DFCHCC)'s IRB.

Study Procedures: The pilot study included two phases. In phase 1 we tested the adaptations introduced to the PQ-Survey using paper and pencil versions and modifications were introduced as necessary. In phase 2, we tested acceptability and ease of use of the computerized versions of PQ-survey. For both phases, participants completed the PQ-Survey once and were subsequently asked to answer a short cognitive debriefing questionnaire addressing comprehensibility, need for clarification, willingness to complete the instrument on a regular basis, and respondent burden, as well as identification of difficult questions. In the case of the computerized survey we also asked about acceptability, burden and ease of use. Time to completion was tracked.

Subjects: Patients were recruited at DFCHCC clinic in May 20-22, 2003 (phase 1) and December 16-17, 2004 (phase 2). During phase 1 of the pilot, 21 eligible families were approached, and 13 consented to participate (participation rate 62%). A total of 19 participants (11 parents and 8 children) completed a paper and pencil PQ-survey and a debriefing questionnaire. During phase 2 of the study, 13 eligible families were approached, and all agreed to participate (participation rate 100%). Three families began answering PQ-Survey but were unable to complete it due to their clinic schedule (and were therefore excluded from analysis). A total of 17 participants (10 parents and 7 children) from these 10 families completed computerized surveys and answered the debriefing questionnaire. Table A1summarizes age, gender, and type of instrument completed by children and parents in the two phases of the study.

Table A1. Characteristics of Children and Type of PQ-Survey Piloted

Age group	Gender		Type of PQ-Survey piloted						Total
			Paper and Pencil			Computerized			
	F	M	SR	Parent-Suppl	Full-Proxy	SR	Parent-Suppl	Full-Proxy	
2-4	0	4	0	0	2	0	0	2	4
5-6	2	3	2	2	1	2	2	0	5
7	3	2	2	2	0	3	3	0	5
8-12	3	2	2	2	1	2	2	0	5
13-20	0	4	2	0	1	0	0	1	4
Total	**8**	**15**	**8**	**6**	**5**	**7**	**7**	**3**	**23**

SR: PediQUEST-Survey Self-report versions. Questionnaire completed by child; see previous section for details on self-report surveys.
Parent-Suppl: PQ-Survey Parents-Supplemental Version. Used in children aged 5-12. (These children answered a shorter version of the PQ-Survey and parents were asked to complete the PQ-"supplemental" version which included PQ- MSAS items that were not available in the child SR version, as well as the sickness question, to allow for consistent measurement across the entire age range).
Full-proxy: PQ-Survey Parent's Full-Proxy version included all PQ-Survey items. Parents of 2-4 year olds answered this survey. Full-proxy versions existed for all age groups for parents of children who did not want or did not feel well enough to self-report.
Online-only material

Results:
Phase 1: The paper and pencil version of PediQUEST was well understood by children of all eligible age groups. Median time to completion was 16 minutes. Almost all respondents found PediQUEST "easy" or "very easy", "not boring at all" or "a little boring", of appropriate length, and reported no problem with completing it on a regular basis. All children understood the instructions at once. One item, lack of appetite, was modified to increase comprehensibility.

Phase 2: Median time to completion of the computerized PQ-Survey was 13 minutes (range 8-20). This included both parent and child responses when appropriate.
Overall, the questionnaire was well understood and accepted. All respondents who completed the debriefing survey found PediQUEST "easy" or "very easy" to complete. Regarding respondent burden, almost all said it was "not boring at all" or "a little boring", of appropriate length, and reported no problem with completing it every week. None found any question uncomfortable.

Specific issues with piloted instruments:

1. PQ-MSAS: Twenty-two of the 27 symptoms addressed, were reported by at least one patient (see below Table A2). Five symptoms were not reported by anyone. All response options of the different sub-questions (frequency, severity and distress) were used. At least half of the children reported having lack of energy, nausea, and/or sleep disturbance. Two patients reported a total of three "other symptoms." These included: fever, hair loss, and mouth sores. Two 2-4 yo parents had difficulty determining if behavioral issues are a result of treatment or typical age appropriate issues. After consulting with MSAS author it was decided not to introduce any changes.

Table A2. Frequency of Symptoms Reported using PQ-MSAS in Pilot PQ-Survey Study							
Symptom	**No. of pts (n=10)**	**No. w/ High distress**	**No. w/ Moderate Distress**	**Symptom**	**No. of pts (n=10)**	**No. w/ High distress**	**No. w/ Moderate distress**
Lack of energy	5	0	1	Skin changes	2	0	0
Nausea	5	0	1	Worrying	2	0	1
Sleep disturbances	5	**1**	1	Concentration	1	0	0
Cough	4	0	1	Constipation	1	0	0
Diarrhea	4	0	0	Don't look like themselves	1	0	0
Drowsy	4	0	1	Dyspnea	1	0	0
Pain	4	**1**	1	Itch	1	0	0
Irritability	3	0	1	Swallowing difficulties	1	0	0
Vomiting	3	0	0	Bleeding	0		
Dry Mouth	2	0	1	Numbness or tingling	0		
Feeling nervous	2	0	0	Seizures	0		
Lack of appetite	2	0	0	Sweat	0		
Other symptoms	2	0	1	Urinary problems	0		
Sadness	2	0	0				

Online-only material

2. PedsQL 4.0™: was well understood by children and parents of all age groups. PedsQL4.0™ Total score dispersion was wide, ranging from 50 to 85. Physical health scores were lower on average than the PedsQL 4.0™ study[4] (64.2 in this pilot vs. 72.2 in the original study). Average psychosocial and total scores were also lower than those from the original study (68 and 66.6 respectively for the pilot vs. 72.62 and 72.20 for the original). One 8-12yo child had difficulty comprehending "I hurt or ache" and also mentioned not liking to think about the issues that were address in the survey. One MSAS 7yo had difficulty with "how much trouble" questions. After consulting with PedsQL 4.0™ author, and based on the fact that the scale was widely validated, the decision was not to introduce any changes.

3. Sickness question: the question was well understood by children and parents of all age groups. Parents used the entire range of the Visual Analog Scale and children tended to report lower (better) scores. The average sickness score reported by parents was 27; 8 for children (n=5); and 25 for the 2 children 5 to 6 years old. No further issues were identified with this item.

Methods. Design rationale, Description of Outcomes, and Statistical Analysis Considerations.

Design Rationale:

The study was designed as a 1:1 parallel randomized controlled trial (RCT). Specifically, we compared routine completion of the electronic PQ-Survey (control arm, ePRO monitoring) with ePRO monitoring + feedback (intervention arm). The intervention consisted of providing summary reports to parents and providers + email alerts that were sent, when certain symptom and QoL thresholds were reached, to primary providers, and pain, palliative care, and psychosocial teams. One of the main problems with this design is the lack of a true control group (with no ePRO monitoring). Velikova[16] in a similar RCT in adult patients did not detect differences between the attention-control arm (ePRO monitoring) and the intervention arm (ePRO monitoring + feedback). However, they did find an effect when comparing both these arms against a true control arm (no PRO monitoring), a "measurement effect."

We faced two hindrances to incorporating a true control group (third arm): the small size of the population and the lack of other well validated PRO measures (needed to conduct a three-arm study). A two-arm study including a true control group as the comparator also seemed inappropriate given that a measurement effect was already described. As a compromise, we planned to review medical records among non-enrolled (if we were able to gain consent for their review) to compare documented symptoms and symptom treatments with those of enrolled participants. We anticipated that this third group, even with its limitations, would allow us to see differences in patterns of care that would speak to the measurement effect. However this strategy proved not feasible as non-enrolled subjects did not give us permission to review their records.

We also recognized the risk for contamination of the intervention given that physicians may care for patients in both arms. This risk was not easy to overcome given patients also see more than one physician during their care. The only solution would have been to run a cluster randomized trial (clustering by site), but this was not feasible due to practical considerations and budgetary constraints.

Description of Outcomes:
As this is a pilot study and given the lack of data regarding score distribution, we proposed to operationalize one of our primary outcomes (child distress) using two approaches: a) the proportion of patients with unrelieved symptoms (any symptom/s reported as causing moderate to high distress in 2 consecutive PediQUEST administrations) and b) trends over time of the MSAS and Sickness scores. Post hoc, it was evident that the data collection did not consistently include consecutive measurements which limited the feasibility of the first analysis and for this reason the main analyses was conducted only using score trends.

We had also proposed examining the MSAS-Global distress index (GDI) score because we believed that of all MSAS scores, this would better capture child distress. However, the GDI score changes were comparable to what was observed with MSAS total and other subscale scores so for the sake of simplicity, we decided to use the more inclusive scores and limit the number of tests performed.

Statistical Analysis Considerations:
Outcome Measurement Plan and assumptions about missing data: Because PRO collection times were based on a pragmatic approach, i.e. collected when participants came to clinic or ward and the visit met pre-specified eligibility criteria (see below*), longitudinal data were unbalanced by design. The proportion of administered surveys over total eligible visits was 62.4% and was stable over the first 20-weeks. Most of the missed measurement occasions

were due to technical problems (32.9%), such as the RA missing the patient window during the encounter or system problems to detect the patient's visit, and were assumed as missing completely at random (MCAR). Only 2.8% of eligible PQ-Survey administrations were not administered because the child reported feeling too ill or upset, and in 1.9% of eligible occasions the patient declined to answer (empirical observation during the study suggests that patients declined because they were in a very good health state and felt they had nothing to report on). Missed occasions due to patient illness/emotions or declinations could have introduced bias into the effect estimates, however, because their distribution across study arms was almost identical we can assume that the risk for such bias is limited. Further, it seems that positive and negative reports were missed at comparable rates. Based on these considerations no statistical approach for dealing with missing data was used for the unbalanced longitudinal data.

*PQ-Survey visit eligibility: A clinic visit was considered eligible only if a provider was seen and the date was at least one week later than a prior PQ-survey or from another eligible visit. If a participant was an inpatient, PQ-surveys were attempted at most once a week on the ward. If a patient did not have clinic visits or admissions for a month or more, a monthly eligible PediQUEST date was assigned.

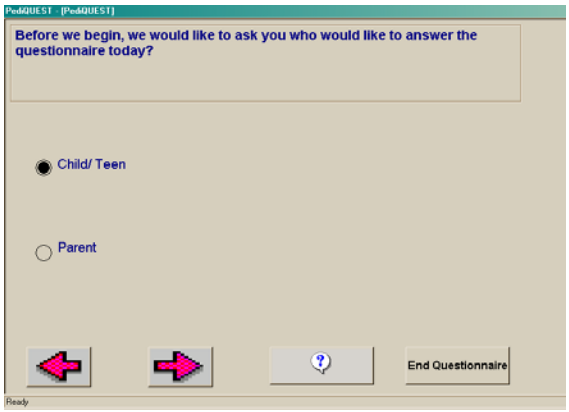
Sample Size estimation: The estimation of the sample size for a study with repeated measurements is based on the effect size (difference between the two trends/slopes) and the covariance matrix which depend on the within-subject correlation, the number of repeated measurements, and the frequency and distance of the observation times.[17] Although we primarily used previously validated instruments, there are no estimates of their distribution in pediatric populations with advanced cancer, nor any estimates of their variation over time. As a result, practical rather than statistical considerations drove the target sample size which was proposed as 120 patients and parents. Study results would assist in generating estimates of scores distributions and intra subject variability useful for future sample size calculations. Enrollment was closed in all three participating sites in June 2009, with 104 patients enrolled. The decision to stop enrollment before the target sample was achieved was based on practical considerations: enrolment of incident advanced cancer cases was slow and it was assumed that additional information ascertained from enrolling the remaining 16 patients would be limited.

Multiple comparisons adjustments: We chose not to correct for multiple comparisons to minimize the risk of false negative results. We report all individual p-values and confidence intervals for the estimated effects, so readers can informally account for multiple comparisons (Table A3). We considered that a false negative result would be more harmful to the field than a false positive one. False negative results may discourage further investigation of an intervention that involves minimal risk and may bring benefits to a population that is in deep need of attention. ePRO interventions have already shown such potential in adults and are being subject of further studies to understand how to maximize their benefits.

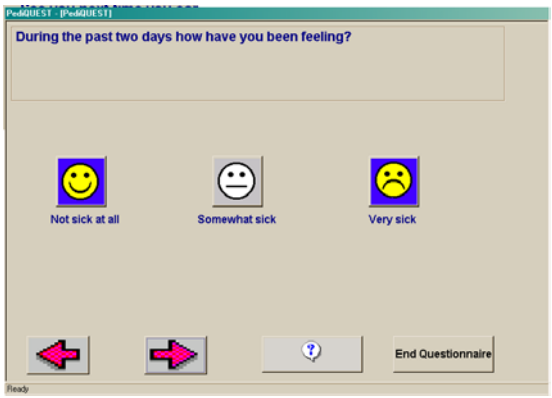
Figure A1. PediQUEST-Survey Screenshots

Sample screenshots of the different scales and response option types of the PediQUEST application are presented below.

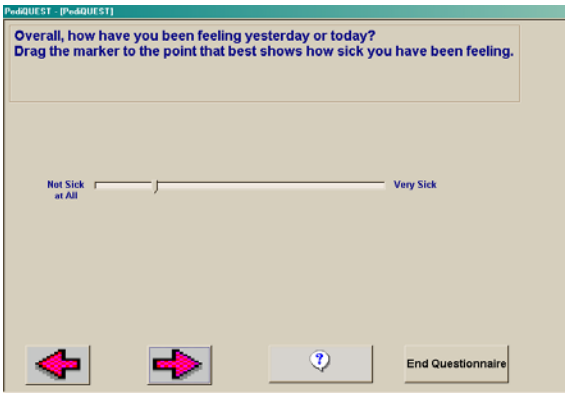
Respondent item



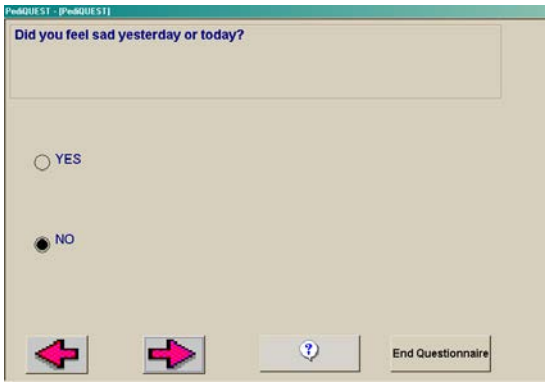
Sickness question
Faces scale (Children 5-6 year olds)



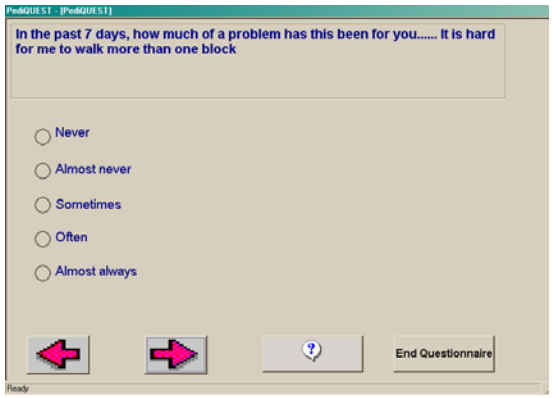
Sickness question
Visual Analog Scale (Children 7yo)[a]



PQ-MSAS 7-12 item [a]
(lead question- sadness)



PedsQL4.0™ 13-18 years old item [b]



[a]: Older children and parents screen was identical except for time frame ("past week")
[b]: PedsQL4.0™ 5-7 years old version used three point faces scales
Abbreviations: PQ-MSAS, PediQUEST-Memorial Symptom Assessment Scale; PedsQL4.0™, Pediatric Quality of Life Inventory.
Online-only material

Figure A2. PediQUEST-Sample Report

The sample report shows how QoL and symptom data were presented to parents and providers.
Total QoL scores for the last 5 PQ-surveys were graphed on the left, and subscale scores (physical, emotional, social, and school) on the right. Similarly, the symptom section showed the evolution of the average symptom scores on the left and the respective item scores (frequency, severity and distress) on the right. Only present symptoms were graphed. The report ended with a brief summary highlighting current scores (provided a range of QoL scores for children with cancer), and observed changes. Provider and families' reports were almost identical except for the last page which had a list of resources that was adapted to the recipient.

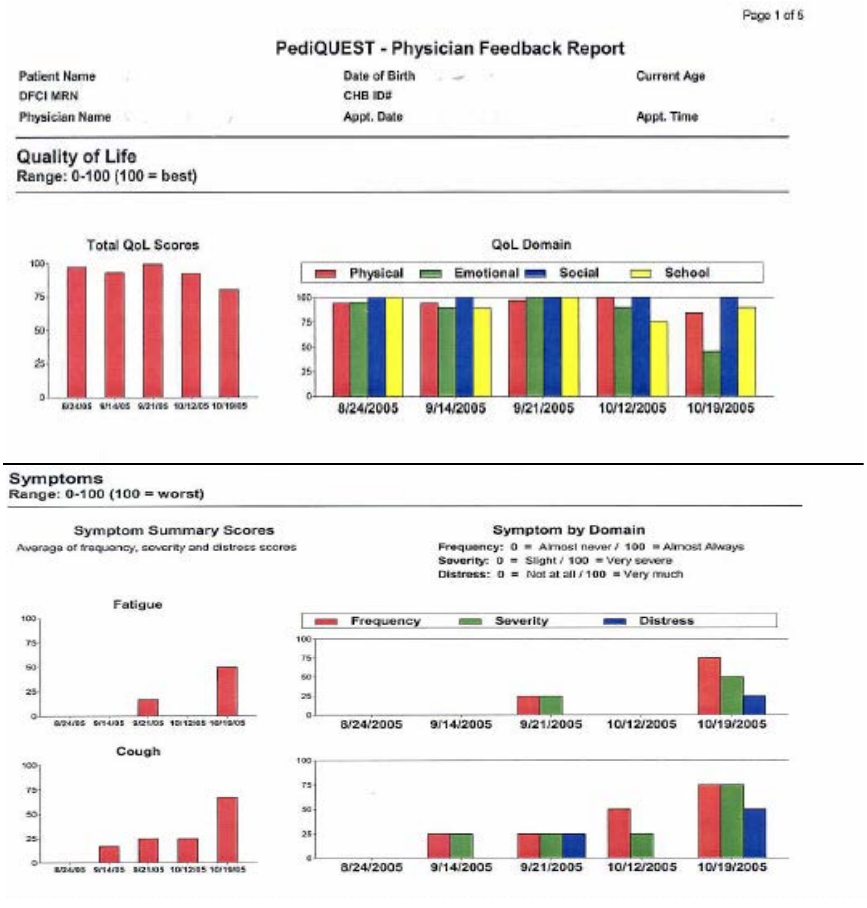


Table A3. Main and Subgroup Analysis of Patient Outcomes

Table A3. Main and Subgroup Analysis of Patient Outcomes

	Main Analysis				Subgroup Analysis			
	All Children[a]		Survivors[b]		Children ≥8 years old[c]		Survivors ≥8 years old[d]	
Outcome	Mean Score Difference (95% CI)[e]	P Value	Mean Score Difference (95% CI)[e]	P Value	Mean Score Difference (95% CI)[e]	P Value	Mean Score Difference (95% CI)[e]	P Value
PQ-MSAS Score								
Total	-0.7 (-2.9; 1.6)	0.57	-1.4 (-3.5; 0.7)	0.18	-1.9 (-4.6; 0.7)	0.16	-2.2 (-4.8; 0.4)	0.10
Physical	0.4 (-3.1; 3.7)	0.84	-1.0 (-4.2; 2.1)	0.52	-1.0 (-5.1; 3.1)	0.63	-1.9 (-5.8; 2.0)	0.33
Psychological	-0.4 (-4.5; 3.6)	0.84	-0.9 (-5.2; 3.4)	0.67	-2.2 (-6.3; 1.9)	0.30	-2.0 (-6.4; 2.4)	0.37
PedsQL4.0™ Score								
Total	1.5 (-4.2; 7.2)	0.61	3.3 (-2.2; 8.8)	0.24	4.1 (-2.5; 10.7)	0.22	5.7 (-0.7; 12.1)	0.08
Physical	2.0 (-6.8; 10.8)	0.66	5.0 (-3.5; 13.6)	0.25	6.3 (-3.7; 16.3)	0.22	8.5 (-1.5; 18.4)	0.10
Emotional	3.9 (-1.7; 9.6)	0.17	6.0 (0.3; 11.7)	0.04	6.0 (-0.4; 12.3)	0.07	8.1 (1.8; 14.4)	0.01
Sickness Score	-1.7 (-7.9; 4.5)	0.59	-5.3 (-10.6; 0.0)	0.05	-4.9 (-12.1; 2.4)	0.19	-8.2 (-14.2; -2.2)	0.008

[a] Control n=49, Intervention n=49

[b] Children who survived beyond 20 Weeks; Control n=48, Intervention n=40

[c] Control n=35, Intervention n=35

[d] Children ≥8 years old who survived beyond 20 Weeks; Control n=34, Intervention n=30

[e] Intervention effect estimated under a mixed linear model with treatment and time (weeks from study entry) as fixed terms, and a random intercept (subject).

Abbreviations: PQ-MSAS, PediQUEST-Memorial Symptom Assessment Scale; PedsQL4.0™, Pediatric Quality of Life Inventory.

Online-only material

References

1. Collins JJ, Byrnes ME, Dunkel IJ, et al: The measurement of symptoms in children with cancer. J Pain Symptom Manage 19:363-77, 2000
2. Collins JJ, Devine TD, Dick GS, et al: The measurement of symptoms in young children with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7- 12. J Pain Symptom Manage 23:10-6., 2002
3. Drake R, Frost J, Collins JJ: The symptoms of dying children. Journal of Pain & Symptom Management 26:594-603, 2003
4. Varni JW, Burwinkle TM, Katz ER, et al: 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 94:2090-106, 2002
5. Bieri D, Reeve RA, Champion GD, et al: The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. Pain 41:139-50., 1990
6. Portenoy RK, Thaler HT, Kornblith AB, et al: The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer 30A:1326-36, 1994
7. Vogl D, Rosenfeld B, Breitbart W, et al: Symptom prevalence, characteristics, and distress in AIDS outpatients. J Pain Symptom Manage 18:253-62, 1999
8. Stromgren AS, Groenvold M, Pedersen L, et al: Symptomatology of cancer patients in palliative care: content validation of self-assessment questionnaires against medical records. Eur J Cancer 38:788-94, 2002
9. Chang VT, Thaler HT, Polyak TA, et al: Quality of life and survival: the role of multidimensional symptom assessment. Cancer 83:173-9., 1998
10. Wolfe J, Grier HE, Klar N, et al: Symptoms and suffering at the end of life in children with cancer. N Engl J Med 342:326-33., 2000
11. Hain RD, Patel N, Crabtree S, et al: Respiratory symptoms in children dying from malignant disease. Palliat Med 9:201-6, 1995
12. Seid M, Varni JW, Rode CA, et al: The Pediatric Cancer Quality of Life Inventory: a modular approach to measuring health-related quality of life in children with cancer. Int J Cancer Suppl 12:71-6, 1999
13. Varni JW, Seid M, Kurtin PS: 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 39:800-12, 2001
14. Varni JW, Burwinkle TM, Jacobs JR, et al: The PedsQL in type 1 and type 2 diabetes: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales and type 1 Diabetes Module. Diabetes Care 26:631-7., 2003
15. Varni JW, Seid M, Smith Knight T, et al: The PedsQL in pediatric rheumatology: reliability, validity, and responsiveness of the Pediatric Quality of Life Inventory Generic Core Scales and Rheumatology Module. Arthritis Rheum 46:714-25., 2002
16. Velikova G, Booth L, Smith AB, et al: Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol 22:714-24, 2004
17. Yi Q, Panzarella T: Estimating sample size for tests on trends across repeated measurements with missing data based on the interaction term in a mixed model. Control Clin Trials 23:481-96, 2002