Risk Factors for Health-related Quality of Life Deterioration Following Pediatric Critical Illness

Elizabeth Yarnell Killien

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Noel S. Weiss

Frederick P. Rivara

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Abstract

Risk Factors for Health-related Quality of Life Deterioration Following Pediatric Critical Illness

Elizabeth Yarnell Killien

Chair of the Supervisory Committee:

Noel S. Weiss

Department of Epidemiology

Background: Many children experience declines in health-related quality of life (HRQL) after critical illness, but it is unknown what components of HRQL are most affected. We aimed to evaluate risk factors for deterioration between baseline and post-discharge HRQL status in the individual components of common HRQL measures among pediatric survivors of critical illness.

Methods: We conducted a retrospective cohort study of children ≤18 years admitted to the Seattle Children's Hospital pediatric and cardiac intensive care units from 12/2011-02/2017 on whom pre-admission baseline, admission, and post-discharge follow-up (median 42.0 days) PedsQL™ or FS II-R HRQL assessments had been obtained. We determined associations between patient and illness characteristics with failure to recover within 4.5 points of baseline HRQL at follow-up (the minimum clinically significant difference between two scores) using

multivariable generalized linear Poisson regression. We determined the individual score components of the PedsQL™ Infant Scales (age <2), PedsQL™ Generic Core Scales (age 2-18), and FS II-R (for children with severe developmental or functional disabilities) with the highest prevalence of decline from baseline to follow-up, and assessed factors associated with decline for each question.

Results: Failure to recover within 4.5 points of baseline HRQL status occurred in 24.7% of 736 study patients. Factors independently associated with failure to recover were older age (adjusted RR 1.02/year, 95% CI 1.00-1.05), primary admission diagnosis of an oncologic condition (aRR 1.89 relative to respiratory, 95% CI 1.07-3.34) or orthopedic surgery (aRR 1.68, 95% CI 1.04-2.70), and longer duration from discharge to follow-up HRQL assessment (aRR 0.91/week, 95% CI 0.86-0.95). Individual score components most affected for the PedsQL™ Infant Scales were primarily emotional (crying/fussing, difficulty sleeping, difficulty self-soothing, feeling tired, and feeling afraid). Children 2-18 years assessed with the PedsQL™ Generic Core Scales most commonly experienced declines in physical functioning (participating in active play/exercise, hurting, lifting something heavy, being unable to do things other children their age can do) and feeling angry. Children for whom the FS II-R was completed most commonly experienced declines in both emotional and physical domains (reacting by crying, not sleeping through the night, irritability, poor energy, and acting moody). Patient demographic characteristics, underlying medical complexity, primary admission diagnosis, and severity of illness were commonly associated with declines in individual score components.

Conclusions: One-quarter of children surviving critical care experienced a clinically significant deterioration in HRQL when assessed a median of six weeks post-discharge, and the individual components of HRQL that were most affected varied by patient age and diagnosis. Potential targets for intervention to improve HRQL outcomes for critically ill children include minimizing deconditioning, improving sleep quality, addressing fear, and adequately managing pain.

Introduction

Mortality associated with pediatric critical illness has fallen consistently over the past several decades, with overall in-hospital mortality now 2-3% of all pediatric intensive care unit (PICU) admissions in North America.[1] Accordingly, the number of patients surviving critical illness is rising. There has been growing awareness that many children who survive critical illness struggle to regain their pre-hospitalization health status, experiencing persistent physical, social, psychological, and cognitive declines.[2-5] Additionally, there is emerging emphasis on the importance of assessing post-discharge morbidity in pediatric critical care research as an outcome that is clinically meaningful, patient-centered, and that is particularly helpful in evaluating the impact of illnesses and therapies in populations where case-fatality is low.[6-9]

Health-related quality of life (HRQL) is a means of assessing the impact of health status on physical, mental, emotional, and social functioning.[10,11] HRQL in children is influenced by factors such as the ability to participate in peer groups, keep up with developmentally appropriate activities, and succeed in school, and encompasses aspects of perceived health, health behavior, and well-being.[12-14] HRQL is increasingly used as a comprehensive measure of health outcomes in PICU populations,[15] and has been identified by both families and healthcare professionals as the most important outcome to assess among PICU survivors.[16]

Impaired HRQL has been demonstrated in many children following critical illness,[10,15,17-27] with approximately one-quarter to one-third of PICU survivors experiencing impairments in overall HRQL when assessed between 6 months and 2 years after hospital discharge.[18,21,23] It has not been previously examined which components of HRQL contribute most to overall score declines, however, or what the risk factors are for declines in individual score components.

This investigation aimed to evaluate the frequency of and risk factors for deterioration between baseline and post-discharge HRQL status in the individual components of common HRQL measures in a cohort of pediatric survivors of critical illness. Improved understanding of the patient and illness characteristics associated with decline in HRQL after critical illness, and identification of the individual elements of HRQL that are most commonly affected, may aid in the development of targeted interventions to improve long-term outcomes among critically ill children.

Methods

Study design: This was a retrospective cohort study to evaluate HRQL outcomes among patients admitted to the Seattle Children's Hospital (SCH) Pediatric Intensive Care Unit (PICU) and Cardiac Intensive Care Unit (CICU) who were enrolled in the SCH Outcomes Assessment Program (OAP). The study was approved by the SCH Institutional Review Board.

Setting: SCH is a freestanding academic children's hospital with 334 inpatient beds, including 32 PICU beds and 16 CICU beds at the time of data collection.

Participants: We included all patients ≤18 years admitted to the SCH PICU or CICU from 12/1/2011 – 02/05/2017 who were enrolled in the SCH OAP and for whom baseline, admission, and follow-up HRQL assessments were completed. Only the first admission during the study period in which all three HRQL assessments were completed was included.

HRQL instruments: We measured HRQL using the Pediatric Quality of Life Inventory (PedsQL™) 4.0 Generic Core Scales,[28] the PedsQL™ Infant Scales,[29] and the Functional Status II-R (FS II-R) instrument.[30] The PedsQL™ measures HRQL in patients ≤18 years, with different versions by patient age: Infant (0-12 months), Older infant (13-24 months), Toddler (2-4 years), Young child (5-7 years), Child (8-12 years), and Adolescent (13-18 years). All versions are available as parent proxy-report, and the Child and Adolescent versions are also available as child self-report. The Generic Core Scales for patients ≥2 years consist of 23 questions assessing physical, emotional, social, and school functioning. The Infant Scales for patients <2 years consist of 36 questions for infants 0-12 months and 45 questions for older infants 13-24 months assessing physical symptoms and physical, emotional, social, and cognitive functioning.[29,31]

The PedsQL™ scales have demonstrated reliability and consistency of parent proxy-reporting across all age subgroups.[32] Multiple studies have established the use of recall to determine patients' baseline HRQL status,[33-35] and there is strong correlation among in-person, telephonic, and electronic modes of administration.[33] The PedsQL™ has been frequently used in the PICU setting[15] and demonstrates responsiveness to changes in patients' clinical status during and after PICU admission.[27]

The FS II-R instrument is a similar tool to measure HRQL in children, but was designed for children with significant chronic physical conditions or severe developmental delays. It consists of 14 items assessing physical, emotional, and behavioral functioning. It was developed to assess children across the entire spectrum of pediatric ages via parent proxy-reporting.[15] OAP research assistants review patient charts and administer the FS II-R if medical records document that the patient has a severe developmental delay or functional disability. If this is not documented, then families of patients enrolled in the SCH OAP are asked on a screening

questionnaire whether their child has a "severe physical or mental developmental delay or disability" and, if so, are directed to complete the FS II-R rather than the PedsQL™ for their child.

HRQL scoring: For both the PedsQL™ and FS II-R instruments, respondents are asked to report how frequently the child experienced problems for each of the questions in the one month prior to survey administration for baseline assessments and in the 7 days prior for acute assessments. Each item on the PedsQL™ Generic Core Scales and Infant Scales is scored from 0 ("never") to 4 ("almost always"). Each item on the FS II-R is scored from 0 ("never or rarely") to 2 ("almost always"). Items are then reverse scored and linearly transformed to a 0-100 scale. The total score is computed as the mean of the individual item scores and ranges from 0-100, with higher scores indicating better HRQL. The population mean score for the PedsQL™ is 84.1,[31] and the mean score among chronically ill children on the FS II-R is 86.8.[15] A change of ≥4.5 points between two scores on the PedsQL™ has been considered a clinically important difference.[31] As the PedsQL™ and FS II-R have similar mean scores and standard deviations, a change of ≥4.5 points between two scores was adopted by the SCH OAP as the minimum clinically important difference for the FS II-R as well.

HRQL collection: The SCH OAP collected PedsQL™ and FS II-R data for all consenting participants admitted to the SCH PICU and CICU from December 2011 to February 2017. Patients with all diagnoses were eligible for enrollment in the OAP, but HRQL assessments were typically only collected for a single admission and patients were not re-enrolled for future admissions. Only patients admitted to the ICU with new oncologic diagnoses were enrolled but

not patients who had already begun treatment. Patients were not eligible for inclusion if they had active Child Protective Services involvement, if the patient did not live with their legal guardian, if the nurse or physician did not feel that the family should be approached, or if the family had declined participation three times in the past or once within the past two months. Surveys were available in English, Spanish, Chinese, Russian, and Vietnamese.

OAP staff approached parents of ICU patients within 72 hours of admission, and parents of enrolled participants were asked to score their child on either the PedsQL™ or FS II-R for both the month prior to ICU admission to establish a baseline and as of the time of hospital admission. Families were then contacted electronically or via telephone four to six weeks following hospital discharge to complete a follow-up PedsQL™ or FS II-R referring to the week prior to the assessment. Some families were contacted before four weeks, and OAP staff attempted to contact families for up to eight weeks following the initial attempt, and thus follow-up data were collected from two to 16 weeks following discharge. Approximately 80% of families who were approached consented to participate, and approximately 50% of consented families completed all three assessments. Patients without PedsQL™ or FS II-R data from all three time-points were excluded from our analysis. Children ≥8 years old were also eligible to complete a child self-report for the PedsQL™, but <5% of ICU patients did and thus child self-reports were excluded from our analysis.

Exposures: We queried the local Virtual Pediatric Systems[36] and OAP databases to determine patient and illness characteristics. Patient factors assessed included patient age, sex, race/ethnicity, language, baseline Pediatric Cerebral Performance Category (PCPC) score and Pediatric Overall Performance Category (POPC) score, Pediatric Medical Complexity Algorithm

(PMCA) category,[37] and parent age and education. PMCA category is a method of classifying baseline comorbidity status by categorizing patients as having non-chronic illness, non-complex chronic illness (isolated to a single organ system, e.g. asthma or diabetes), or complex chronic illness (progressive or affecting multiple organ systems, e.g. cancer). Illness factors assessed included the primary admitting diagnosis, type of admission (e.g. medical, scheduled surgery, acute surgery, congenital heart disease), presence of other active conditions (infection, oncologic, neurologic, psychiatric, chronic mechanical ventilation, solid organ transplant, other immunodeficiency), ICU admission severity of illness using the Pediatric Risk of Mortality score,[38] and ICU and hospital length of stay.

Outcomes: The primary outcome was failure to recover to overall baseline HRQL, defined as a decrease of ≥4.5 points on the total score from baseline to follow-up assessments for either the PedsQL™ or FS II-R. The secondary outcomes were any decline in score from baseline to follow-up for each of the 36 PedsQL™ Infant Scales questions, 23 PedsQL™ Generic Core Scales questions, and 14 FS II-R questions (e.g. baseline score of 2 [“sometimes a problem”] to follow-up score of 3 [“often a problem”]).

Statistical analyses: We calculated the median baseline, admission, and follow-up total HRQL scores for the entire cohort and determined the proportion of patients who failed to recover within 4.5 points of their baseline HRQL status at the time of follow-up. We assessed the prevalence of failure to recover to baseline stratified by survey version completed and time to follow-up. We determined associations between exposures and failure to recover in bivariate analyses using generalized linear Poisson regression models, comparing patients with failure to

recover to patients with a follow-up score within or above 4.5 points of baseline. We included variables with $p \leq 0.2$ on bivariate analyses in a backwards selection model-building process to develop a multivariable generalized linear Poisson regression model, adjusted for time to follow-up, using $p<0.05$ for variables to remain in the model.

We then determined the proportion of patients with any decline from baseline to follow-up for each survey question across the three survey types (PedsQL™ Infant Scales, PedsQL™ Generic Core Scales, and FS II-R). We determined the questions with the greatest proportion of patients who experienced declines for each of seven groups of active diagnoses (respiratory, medical cardiac disease, congenital heart disease, infectious, oncologic, neurologic, and surgical), and compared the frequency of decline for patients with and without each diagnosis using chi-squared and Fisher's exact tests. We then used generalized linear Poisson regression to assess associations between exposures and score decline for the five individual questions with the greatest proportion of patients experiencing decline between baseline and follow-up for each of the three survey types. We first assessed bivariate associations between each risk factor and presence of decline for each of the 15 questions, and then built multivariable models for each question using a backwards stepwise selection process with a significance threshold of $p<0.05$ to be maintained in the model. All multivariable models were adjusted for time to follow-up as a continuous variable. We conducted all analyses using Stata/SE 14.2 statistical software.

Results

Population characteristics

A total of 736 unique ICU patients had complete baseline, admission, and follow-up HRQL assessments during the five-year study period and were included in the study cohort.

Compared to ICU survivors admitted during the same time period who were not enrolled in the OAP or had incomplete HRQL data, study patients were of similar age and gender and had similar baseline PCPC and POPC scores (Table 1). Study patients were more commonly non-Hispanic white and less commonly non-Hispanic black than non-study patients. The most common reason for admission was for acute medical diagnoses in both groups, but study patients were more likely to be admitted following scheduled surgeries than other ICU patients and were less likely to have active oncologic and psychiatric diagnoses. Study patients had slightly lower PRISM III scores and ICU length of stay, and less frequently experienced declines in PCPC and POPC scores from ICU admission to discharge.

Among study participants, 60.3% had complex chronic conditions, 27.3% had non-complex chronic conditions, and 12.4% had non-chronic conditions per PMCA category. Over three-quarters (76.3%) of respondents to HRQL baseline and admission surveys were the mothers of patients. Ninety percent of surveys were completed in English, while 9.1% were completed in Spanish and only four surveys were completed in other languages. In total, 33% of patients were surveyed using the PedsQL™ Infant Scales, 40% with the PedsQL™ Generic Core Scales, and 27% with the FS II-R. Time from discharge to follow-up assessment occurred at a median of 42.0 days after discharge (IQR 31.4-56.4).

Failure to recover to baseline HRQL

Failure to recover within 4.5 points of baseline HRQL at follow-up occurred in 24.7% of patients (n=182), of whom two-thirds (16.2% of total cohort, n=119) failed to recover within 9 points, twice the minimum clinically significant difference. When evaluated by version of HRQL survey completed, failure to recover was more common among older children and adolescents whose HRQL was evaluated using the PedsQL™ (29.9-34.9%) and patients whose HRQL was

evaluated using the FS II-R (31.0%). Failure to recover was less common among younger children using the PedsQL™. Children ages 5-7 years had the lowest prevalence of failure to recover at 15.5%, but also had the longest time to follow-up at a median of 49.6 days (IQR 36.6-63.5); infants <2 years had a similar median time to follow-up as the entire cohort and had a prevalence of 16.1-20.3% failure to recover (Figure 1).

The median HRQL scores for the entire cohort were 85.0 (IQR 73.1-93.0) at baseline, 53.2 (IQR 35.6-71.8) at admission, and 89.0 (IQR 76.7-95.9) at follow-up (Figure 2). In contrast, the median baseline score of patients who failed to recover to their baseline status after discharge was similar to the overall cohort (89.8, IQR 82.0-96.1), but fell further at admission to a median score of 43.9 (IQR 30.6-67.5) with a median follow-up score of 74.2 (IQR 58.3-82.9), a decline of median 15.6 points from baseline.

Prevalence of failure to recover was higher among patients with shorter durations from hospital discharge to follow-up, with 29.6-30.9% failure to recover among patients <6 weeks to follow-up and 14.5-15.2% failure to recover among patients with ≥8 weeks to follow-up (Figure 3). When stratified by the survey version completed, patients completing the FS II-R had the greatest amount of change in prevalence of failure to recover over time, with 40.9% of patients surveyed at 2-3 weeks after hospital discharge not returning to baseline HRQL and only 6.3% at ≥10 weeks. Patients completing the PedsQL™ Infant Scales had the least amount of change over time, with 19.4% of patients surveyed at 2-3 weeks after hospital discharge failing to recover to baseline and 15.0% failing to recover at ≥10 weeks.

Factors associated with failure to recover

We evaluated factors associated with failure to recover by comparing patients who did and did not recover by the time of follow-up across demographic (Table 2a) and illness (Table 2b) characteristics on bivariate and multivariable analyses. The only demographic factor associated with failure to recover on multivariable analysis was age, with an adjusted relative risk (aRR) of 1.02 per year (95% confidence interval [CI] 1.00-1.05). Neither PMCA category nor baseline PCPC or POPC were significantly associated with failure to recover to baseline HRQL. There was no association with the respondent's relationship to the patient, level of education, or the language in which the survey was completed.

The patient's primary admission diagnosis was strongly associated with failure to recover to baseline HRQL status, with decline most commonly occurring for patients admitted for oncologic conditions (47.6% failure to recover, aRR 1.89 relative to respiratory, 95% CI 1.07-3.34) and orthopedic surgery (45.7%, aRR 1.68, 95% CI 1.04-2.70). Patients with a PRISM score >15 had a higher likelihood of failing to recover, but this was based on only 10 patients and was not statistically significant. Neither ICU nor hospital length of stay were associated with failure to recover. Longer duration of time from hospital discharge to follow-up HRQL assessment was independently associated with a lower likelihood of failure to recover (aRR 0.91/week, 95% CI 0.86-0.95).

Decline by survey question

PedsQL™ Infant Scales: Of the 36 items surveyed for both infants ages 0-12 months and ages 13-24 months using the PedsQL™ Infant Scales, infants most commonly experienced decline between baseline and follow-up in emotional domains including 1) crying or fussing when left alone (28.1% of patients with decline); 2) difficulty sleeping at night (25.3%); 3)

difficulty soothing him/herself (24.5%); 4) feeling tired (22.8%); and 5) feeling afraid or scared (21.6%) (Figure 4a). Infants least commonly experienced declines in physical symptoms such as vomiting and difficulty breathing or swallowing, and social/cognitive domains including fixing attention on objects, making eye contact, and laughing or smiling.

On multivariable analysis of the demographic and illness characteristics associated with decline for each of the five questions for which patients were most commonly affected, none of the risk factors tested were significantly associated with declines in fussing, sleeping, or tiredness (Table 3a). For difficulties with self-soothing, higher PRISM score (aRR 1.06/point, 95% CI 1.03-1.09) and race were both independently associated with risk of decline on multivariable analysis; all races/ethnicities were less likely to report difficulties with self-soothing compared to white patients, with significantly lower risk among Hispanic families (aRR 0.17, 95% CI 0.04-0.67). Higher PRISM score was also significantly associated with patients feeling more afraid after hospitalization (aRR 1.06/point, 95% CI 1.01-1.11), as was PMCA category with patients without chronic illness being more likely to feel afraid relative to patients with complex chronic conditions (aRR 2.37, 95% CI 1.25-4.49).

PedsQL™ Generic Core Scales: Of the 23 items surveyed for children ages 2-18 years using the PedsQL™ Generic Core Scales, children most commonly experienced declines in physical functioning including 1) participating in active play or exercise (26.8%); 2) hurting or aching (26.1%); 3) lifting something heavy (25.8%); and 4) being unable to do things other children their age can do (24.5%), followed by the emotional domain question of feeling angry (24.0%) (Figure 4b). Children least commonly experienced declines in social functioning

including getting along with other children, other children not wanting to be friends, or getting teased by other children.

Patient diagnosis was independently associated with decline in all five of the most affected PedsQL™ Generic Core Scales questions (Table 3b). For playing/exercising, a primary admission diagnosis for orthopedic surgery followed by oncology were the strongest risk factors for declines between baseline and follow-up. Shorter time to follow-up assessment was also independently associated with risk of decline (aRR 0.90, 95% CI 0.84-0.96). While primary admission diagnosis was not an independent risk factor for having more hurting/aching, any active oncologic or bone marrow transplant diagnosis was strongly associated with worsening pain (aRR 6.27, 95% CI 2.45-16.05). Race/ethnicity was also associated with pain, with both black (aRR 4.27, 95% CI 1.65-11.03) and Asian (aRR 3.52, 95% CI 1.08-11.51) patients significantly more likely to experience more hurting/aching after hospitalization relative to white patients.

Similar to playing/exercising, decline in patients' ability to lift something heavy was also associated with primary admission diagnosis for orthopedic surgery or oncology, and fewer weeks to follow-up (aRR 0.92, 95% CI 0.86-0.99). A primary admission diagnosis of an oncologic condition was the only risk factor associated with decline in patients' ability to do things their peers were doing (aRR 5.48 relative to respiratory, 95% CI 2.25-13.35). Finally, younger age (aRR 0.96/year, 95% CI 0.92-0.99) and primary admission diagnosis of either oncologic conditions (aRR 6.70 relative to respiratory, 95% CI 2.23-20.19) or other medical conditions (aRR 4.18, 95% CI 1.46-11.97) were associated with more feelings of anger at the time of follow-up.

FS II-R: Children for whom the 14-item FS II-R was completed most commonly experienced declines in both emotional and physical domains, including 1) reacting to little things by crying (29.3%); 2) not sleeping through the night (23.2%); 3) seeming unusually irritable (21.7%); 4) not seeming lively or energetic (21.0%); and 5) acting moody (20.5%) (Figure 4c). They least commonly experienced declines in social/cognitive domains including being interested in what is going on around them and responding to attention.

Factors associated with declines in FS II-R questions varied across the five questions assessed (Table 3c). Reacting to little things by crying was independently associated with younger age (aRR 0.93/year, 95% CI 0.88-0.97), female gender (aRR 1.72, 95% CI 1.11-2.67), and PRISM score >15 (aRR 2.52 relative to score <5, 95% CI 1.72-3.69). None of the risk factors tested were significantly associated with more difficulty sleeping through the night. Irritability was associated with admission for acute surgical problems (aRR 2.20 relative to medical, 95% CI 1.02-4.76) and active oncologic conditions or bone marrow transplants (aRR 2.39, 95% CI 1.09-5.22). Acute surgical admissions (aRR 4.76, 95% CI 2.17-10.45), PRISM score >15 (aRR 7.11, 95% CI 3.89-13.00), and longer hospital length of stay (aRR 1.01/day, 95% CI 1.002-1.01) were all independently associated with declines in energy. Finally, acting more moody was associated with male gender (aRR 1.97, 95% CI 1.10-3.52) and acute surgical admissions (aaRR 3.41, 95% CI 1.73-6.73).

HRQL decline by diagnosis

We evaluated the overall prevalence of failure to recover to baseline HRQL across seven categories of active diagnoses, and determined the individual questions across the three survey types with the greatest prevalence of decline for each diagnosis category. For the PedsQL™

Infant Scales (Table 4a), patients with active respiratory diagnoses had similar overall prevalence of failure to recover to baseline (17.7%) as the total cohort of patients assessed using the PedsQL™ Infant Scales (17.1%), and the four questions with most frequent declines were also among the most commonly affected questions for the entire infant cohort. Patients with respiratory diagnoses were significantly more likely to experience worsening wheezing after hospital discharge compared to infants without respiratory diagnoses (21.8% vs 12.2%, p=0.04). Patients with congenital heart disease had lower overall failure to recover (13.8%) than the overall infant cohort. Similar questions were most affected other than constipation, which was the third most commonly affected item for patients with congenital heart disease. Patients with active infections had similar overall failure to recover (17.7%), but significantly higher prevalence of worsened wheezing (23.8% vs 11.0%, p=0.01), difficulty breathing (13.1% vs 3.4%, p=0.006), and difficulty swallowing (12.9% vs 5.4%, p=0.04). Finally, patients admitted with surgical problems had the lowest frequency of overall failure to recover (13.0%), but were significantly more likely to have worsening fussiness after discharge (37.0% vs 22.1%, p=0.047) and commonly had worsened crankiness, difficulty soothing, feeling afraid, and crying a lot. There were not enough infants with medical cardiac disease, oncologic conditions, or neurologic conditions to assess these diagnostic categories for this age group.

For the PedsQL™ Generic Core Scales (Table 4b), patients with respiratory disease had lower prevalence of overall HRQL decline (16.1%) than the overall child/adolescent cohort (26.9%). They did not commonly experience declines in the physical functioning domains most frequently seen in the overall child/adolescent cohort, but had high prevalence of declines in missing school for not feeling well (22.9%) or for doctor's visits (22.2%). Medical cardiac disease patients also reported high prevalence of declines in missing school for doctor's visits

(44.4% vs 17.0, p=0.04) or not feeling well (44.4% vs 20.0, p=NS). Children and teens with congenital heart disease had high overall prevalence of failure to recover to baseline HRQL (37.5%), and had a higher prevalence than children without congenital heart disease of feeling more afraid after hospital discharge (38.8% vs 15.7%, p<0.001), having trouble sleeping (30.6% vs 17.1%, p=0.03), and having difficulty bathing (22.9% vs 9.6%, p=0.01). Patients with infections had similar prevalence of overall failure to recover (26.2%), and no questions that were significantly different in prevalence of decline, than patients without infections, but notably did have a high prevalence of worsened energy level (29.2%) and pain (27.7%).

Patients with oncologic conditions or bone marrow transplants had a higher prevalence of failure to recover to baseline HRQL relative to patients without these conditions (71.4% vs 22.7%, p<0.001), and had a higher prevalence of declines across a range of primarily physical and emotional domains. Patients with neurologic and neurosurgical conditions most commonly experienced worsening pain after hospital discharge (34.7%), though did not have any questions that were significantly different in prevalence of decline than patients without neurologic conditions. Patients with surgical diagnoses most commonly had declines across physical functioning categories, though notably also had a higher prevalence of declines in attention than patients without surgical conditions (23.8% vs 10.4%, p=0.009).

For patients assessed with the FS II-R, the overall prevalence of failure to recover to baseline HRQL varied by diagnosis category (Table 4c). Unlike for the other survey types, patients with infections were more likely to experience decline in overall HRQL compared to patients without infections (53.1% vs 28.7%, p=0.008). Patients with respiratory disease also had high prevalence of failure to recover to baseline HRQL (43.6%). There was less variation by question across the different diagnostic categories compared to the other survey types, with most

diagnostic categories having high prevalence of declines in crying, irritability, sleep, tiredness or energy, and moodiness. The only question with a statistically significant difference in prevalence between diagnostic groups was worsening irritability, which was more common among patients with respiratory disease than without (38.9% vs 18.5%, p=0.009). There were not enough patients with medical cardiac disease or oncologic conditions to assess these diagnostic categories for patients assessed using the FS II-R.

Discussion

In this five-year cohort study of 736 critically ill children, we evaluated the trajectory of children's HRQL status before, during, and after an ICU stay and provided a description of the individual HRQL score components that contributed most to declines in children's HRQL status after intensive care. While the majority of patients fully recovered to their baseline status after hospital discharge or even improved, one-quarter of patients experienced a clinically significant decline in HRQL from their pre-admission baseline to their post-discharge follow-up. The median decline in this group was 15.6 points below baseline, over three times the size of a minimum clinically significant difference. Evaluating how this group differs from the patients who recovered fully, and which specific elements of HRQL are most affected, may help identify targets for interventions to enhance post-discharge outcomes for at-risk children.

We found that older age, admission diagnoses of oncologic or orthopedic conditions, and shorter time to follow-up were independently associated with overall HRQL deterioration. Older age has previously been demonstrated to be a risk factor for poor HRQL compared to population norms among pediatric ICU patients.[21,39,40] This may suggest greater resilience among younger children recovering from illness, less morbidity from illnesses requiring hospitalization for

younger patients (e.g., bronchiolitis), or that rapidly developing infants and toddlers may manifest impact on HRQL by lack of developmentally expected progression of skills rather than decline. We did observe a trend towards more frequent HRQL decline with higher PRISM score, which is consistent with the results of some prior studies[19,23,26] but not others.[17,41]

We did not find that PMCA category was associated with decline in HRQL, though patients assessed with the FS II-R measure, intended for patients with significant chronic illness, had higher prevalence of HRQL decline than patients for whom the PedsQL™ was used. Prior studies have repeatedly found children with chronic comorbidities to have worse HRQL after critical illness.[10,19,21,27] We also did not find that prolonged ICU or hospital stay was associated with HRQL decline, in contrast to previous findings;[10,22] this may be due to the short median length of stay in our cohort.

Our evaluation of how the individual components of HRQL contribute to overall declines offers potentially important insights into the domains most affected across different age groups and diagnoses. We found that infants most commonly experienced deterioration in emotional functioning, while older children and teens were most commonly affected by declines in physical functioning. Children with significant chronic illness or development delay for whom the FS II-R was completed experienced declines across both physical and emotional domains. Overall, social and cognitive domains were less commonly affected across all three survey measures.

While declines in physical functioning among children and teens were most common among patients undergoing orthopedic and other surgical procedures, patients with medical diagnoses also experienced high prevalence of physical impairment and pain. Acute loss of skeletal muscle mass contributes to ongoing physical disability that is known to be common among survivors of critical illness.[42,43] Early and more aggressive physical therapy and passive

range of motion introduced in the ICU may reduce ICU neuropathy and other musculoskeletal complications. Early mobilization programs are now being developed and have been found to be feasible to implement in pediatric ICU settings,[44] and larger-scale studies are evaluating the impact of such programs.

Sleep disturbances were common across all ages and multiple different diagnosis categories. While sleep is known to be severely disturbed in the hospital, post-discharge sleep quality has not been well-described. Other emotional symptoms, including difficulties with self-soothing and fussiness for infants, anger in children and teens, and crying, irritability, and moodiness in children assessed with the FS II-R were also common. It is possible that sleep disturbances either contributed to greater emotional lability in patients, or that difficulty with sleep was a manifestation of emotional and psychiatric sequelae of the ICU stay. Nearly one-third of children surviving critical illness report delusional memories, which are associated with an increased risk of post-traumatic stress disorder.[45] Interventions that improve sleep quality may reduce cognitive and psychiatric sequelae of ICU care.[46,47]

Fear was another domain that was commonly experienced across different age groups and diagnoses. Infants with higher severity of illness were more afraid after hospitalization, which may be associated with undergoing more invasive procedures; it has been previously demonstrated that children who are younger, more severely ill, and who experience more invasive procedures have more medical fear and post-traumatic stress.[48] Infants without chronic illness were also more likely to feel afraid relative to patients with complex chronic conditions; this may be due to these patients having less familiarity with healthcare settings. Among older children, fear was especially common among patients with congenital heart disease, supporting the possibility that fear may be associated with exposure to invasive procedures.

Pain was the second most commonly reported problem among children and teens, and was experienced by patients with medical as well as surgical and oncologic diagnoses. Black and Asian patients were more likely to experience worsened pain after hospitalization relative to white patients, raising the question of whether pain may be undertreated in these populations. Pain may also be under-recognized in infants; while it was not commonly reported to be a problem, infants with surgical problems had high frequency of worsening fussiness, crankiness, difficulty soothing, and crying which could be manifestations of pain in this age group. Previous studies have demonstrated that inadequate pain and sedation management while in the ICU is associated with adverse post-discharge outcomes,[39] and ongoing pain after discharge may have a similar effect.

Limitations

There were several limitations to this study. Only a sample of SCH ICU patients were enrolled in the Outcomes Assessment Program, and our cohort had lower illness severity, shorter ICU length of stay, and were less commonly admitted with acute medical problems and oncologic conditions than the general population of children admitted to the ICU at our institution.

Additionally, assessment of patients' baseline HRQL status was based on recall, which is inherently subject to bias. The direction of recall bias in this situation is unknown and likely variable; some families may recall their child to have had a better prior HRQL in comparison to the acute illness than they actually did,[49] while others may be influenced by the acute illness or a potential prodrome such that they recall their child's baseline status to be worse than it actually

was. While several studies have demonstrated construct validity of the PedsQL™ for evaluating baseline HRQL based on recall,[33-35] this has not been prospectively studied.

A final limitation was that follow-up was relatively short-term and was performed at variable time-points from discharge, introducing the potential for sampling-time bias and preventing direct comparison across patients at equivalent intervals between discharge and follow-up. Our data suggest an improvement in HRQL with further time from discharge, though this was assessed cross-sectionally and not longitudinally as patients had different follow-up intervals.

Conclusions

These data demonstrate that nearly one-quarter of children surviving ICU care experience a clinically significant deterioration in HRQL from their baseline status at the time of post-discharge follow-up. This study adds a comprehensive evaluation of how individual components of HRQL contribute to overall declines, and helps identify targets for potential interventions. Minimizing deconditioning, improving sleep quality, addressing fear, and adequately managing pain both while in the ICU and after discharge may help improve HRQL outcomes for critically ill children.

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Table 1: Characteristics of intensive care unit (ICU) survivors enrolled in the Outcomes Assessment Program (OAP) with complete health-related quality of life (HRQL) data compared to ICU survivors not enrolled in the OAP or with incomplete HRQL data

Patient characteristic	**HRQL data**[a] No. (%); n=736	**No HRQL data**[b] No. (%); n=6421
Age, years, median (IQR)	3.3 (0.8-9.4)	3.7 (0.6-12.0)
Gender, male	417 (56.7)	3457 (53.8)
Race		
Non-Hispanic White	413 (56.1)	3527 (54.9)
Non-Hispanic Black	24 (3.3)	447 (7.0)
Hispanic	119 (16.2)	935 (14.6)
Asian	62 (8.4)	589 (9.2)
Other/unknown	118 (16.0)	923 (14.4)
Baseline PCPC score		
1	585 (79.5)	5195 (80.9)
2	59 (8.0)	511 (8.0)
3	67 (9.1)	548 (8.5)
4	25 (3.4)	167 (2.6)
Baseline POPC score		
1	277 (37.6)	2220 (34.6)
2	180 (24.5)	1546 (24.1)
3	253 (34.4)	2423 (37.7)
4	26 (3.5)	232 (3.6)
Unit		
Pediatric ICU	552 (75.0)	5129 (77.6)
Cardiac ICU	184 (25.0)	1478 (22.4)
Diagnosis category		
Medical	309 (42.0)	3360 (52.3)
Congenital heart disease	130 (17.7)	1068 (16.6)
Acute surgical	31 (4.2)	401 (6.3)
Scheduled surgical	266 (36.1)	1592 (24.8)
Primary admission diagnosis[c]		
Congenital heart disease	130 (17.7)	1068 (16.3)
Respiratory	113 (15.4)	963 (15.0)
Craniofacial/Otolaryngology surgery	103 (14.0)	559 (8.7)
Infectious	99 (13.5)	870 (13.6)
Neurosurgery	62 (8.4)	426 (6.6)
Cardiovascular	46 (6.3)	395 (6.2)
Orthopedic surgery	46 (6.3)	164 (2.6)
Endocrine	34 (4.6)	304 (4.7)
Neurologic	30 (4.1)	443 (6.9)
Other medical	22 (3.0)	531 (8.3)
Oncologic	21 (2.9)	374 (5.8)
Other surgical	18 (2.4)	187 (2.9)
Solid organ transplant	12 (1.6)	137 (2.1)
Active diagnoses[d]		
Any infection	203 (27.6)	1626 (25.3)
Neurologic condition	196 (26.6)	1703 (26.5)
Oncologic condition	23 (3.1)	734 (11.4)

Tracheostomy/chronic mechanical ventilation	15 (2.0)	187 (2.9)
Solid organ transplant	14 (1.9)	188 (2.9)
Other immunodeficiency	4 (0.5)	48 (0.8)
Psychiatric condition	3 (0.4)	211 (3.3)
Bone marrow transplant	2 (0.3)	66 (1.0)
PRISM III score, median (IQR)	1.5 (0-4)	2 (0-5)
ICU length of stay, days, median (IQR)	1.59 (0.94-2.94)	1.70 (0.91-4.47)
Decline in PCPC, ICU admission to discharge	4 (0.5)	129 (2.0)
Decline in POPC, ICU admission to discharge	45 (6.1)	560 (8.7)

HRQL, health-related quality of life; IQR, interquartile range; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category; ICU, intensive care unit; PRISM, Pediatric Risk of Mortality

[a] Only first ICU admission with HRQL data included; [b] Only first ICU admission during date range included; [c] Primary diagnosis as recorded in Virtual Pediatric Systems database; [d] All active diagnosis for hospital encounter as recorded in Virtual Pediatric Systems database; categories not mutually exclusive

Table 2: Relative risk of failure to recover to baseline health-related quality of life by demographic and illness characteristics on bivariate and multivariable Poisson regression

2a: Demographic and respondent characteristics

Characteristic	Failure to Recover n (%)	Bivariate		Multivariable	
		RR	95% CI	RR	95% CI
Age		1.03 / yr	1.01-1.05	1.02 / yr	1.00-1.05
Gender					
Female	82 (25.7)	Ref			
Male	100 (24.0)	0.93	0.74-1.20		
Race					
White	104 (25.2)	Ref			
Black	8 (33.3)	1.32	0.73-2.39		
Hispanic	27 (22.7)	0.90	0.62-1.31		
Asian	19 (30.7)	1.22	0.81-1.83		
Other/mixed/unknown	24 (20.3)	0.81	0.54-1.20		
PMCA Category					
Non-chronic	24 (26.4)	Ref			
Non-complex chronic	40 (19.9)	0.75	0.49-1.27		
Complex chronic	118 (26.6)	1.01	0.69-1.47		
Baseline PCPC		1.02 / pt	0.88-1.20		
Baseline POPC		1.10 / pt	0.96-1.26		
Respondent gender					
Female	139 (25.2)	Ref			
Male	39 (23.6)	0.94	0.69-1.28		
Respondent education					
8th grade or less	5 (20.8)	Ref			
Some high school	13 (31.0)	1.49	0.60-3.66		
High school graduate	24 (18.9)	0.91	0.38-2.14		
Some college/two-year college	55 (23.6)	1.13	0.50-2.56		
Four-year college degree	39 (24.8)	1.19	0.52-2.73		
Graduate/professional degree	44 (30.3)	1.46	0.64-3.30		
Respondent relationship					
Mother	140 (25.1)	Ref			
Father	38 (23.5)	0.93	0.68-1.28		
Other relative or guardian	2 (20.0)	0.80	0.23-2.78		
Survey language					
English	167 (25.1)	Ref			
Spanish	14 (20.9)	0.83	0.51-1.35		
Other	1 (25.0)	1.00	0.18-5.47		

RR, relative risk; CI, confidence interval; PMCA, Pediatric Medical Complexity Algorithm; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category

2b: Illness characteristics

Characteristic	Failure to Recover n (%)	Bivariate RR	Bivariate 95% CI	Multivariable RR	Multivariable 95% CI
Unit					
Pediatric ICU	414 (25.0)	Ref			
Cardiac ICU	44 (23.9)	0.96	0.71-1.29		
Diagnosis category					
Medical	73 (23.6)	Ref			
Congenital heart disease	36 (27.7)	1.17	0.83-1.65		
Acute surgical	9 (29.0)	1.23	0.68-2.21		
Scheduled surgical	64 (24.1)	1.02	0.76-1.37		
Primary admission diagnosis					
Respiratory	26 (23.0)	Ref		Ref	
Cardiac	44 (25.0)	1.09	0.71-1.66	1.12	0.74-1.72
Infectious	28 (28.3)	1.23	0.78-1.95	1.18	0.74-1.86
Oncologic	10 (47.6)	2.07	1.18-3.63	1.89	1.07-3.34
Orthopedic	21 (45.7)	1.98	1.25-3.15	1.68	1.04-2.70
Neurologic/Neurosurgical	19 (20.7)	0.90	0.53-1.52	0.83	0.49-1.41
Other medical	10 (17.9)	0.78	0.40-1.50	0.73	0.38-1.40
Other surgical	24 (18.1)	0.78	0.48-1.29	0.84	0.51-1.37
Any infection	54 (26.6)	1.11	0.84-1.46		
Infection type					
Bronchiolitis/pneumonia	21 (22.6)	Ref			
Central nervous system	2 (22.2)	0.98	0.27-3.55		
Other viral	21 (26.6)	1.18	0.70-1.99		
Other bacterial	10 (45.5)	2.01	1.11-3.65		
Neurologic condition	50 (25.5)	1.04	0.79-1.38		
Oncologic condition/BMT	13 (52.0)	2.19	1.48-3.26		
Chronic ventilation	1 (6.7)	0.27	0.04-1.77		
Solid organ transplant	4 (28.6)	1.16	0.50-2.68		
PRISM III category					
<5	151 (25.0)	Ref			
5-10	23 (23.0)	0.92	0.63-1.35		
11-15	3 (13.0)	0.52	0.18-1.51		
>15	5 (50.0)	2.00	1.06-3.77		
ICU length of stay		1.01/day	0.99-1.03		
Hospital length of stay		1.00/day	0.99-1.01		
Weeks to follow-up from discharge		0.90/week	0.85-0.95	0.91/week	0.86-0.95
Weeks to follow-up from admit		0.94/week	0.89-0.99		

RR, relative risk; CI, confidence interval; ICU, intensive care unit; BMT, bone marrow transplant; PRISM, Pediatric Risk of Mortality

Table 3: Multivariable analyses of associations between risk factors and decline in individual survey questions. Analyses for the five questions with the greatest proportion of patients experiencing decline between baseline and follow-up for each survey type are shown. All analyses were adjusted for weeks to follow-up.

3a: PedsQL™ Infant Scales (0-24 months old)

Question	Risk Factor	Relative Risk	95% CI
Fussing when left alone	*No significant associations*		
Difficulty sleeping	*No significant associations*		
Difficulty soothing self	**PRISM Score**	1.06	1.03-1.09
	Race		
	White	Ref	
	Hispanic	0.17	0.04-0.67
	Asian	0.67	0.30-1.52
	Other	0.68	0.37-1.25
Feeling tired	*No significant associations*		
Feeling afraid	**PRISM Score**	1.06	1.01-1.11
	PMCA Category		
	Non-chronic	2.37	1.25-4.49
	Non-complex chronic	1.20	0.64-2.24
	Complex chronic	Ref	

PMCA, Pediatric Medical Complexity Algorithm; PRISM, Pediatric Risk of Mortality

3b: PedsQL™ Generic Core Scales (2-18 years old)

Question	Risk Factor	Relative Risk	95% CI
Playing or exercising	**Primary admission diagnosis**		
	Respiratory	Ref	
	Cardiovascular	1.77	0.75-4.15
	Infectious	2.00	0.80-4.99
	Oncologic	4.63	1.97-10.86
	Orthopedic	5.99	2.74-13.10
	Neurologic/Neurosurgical	1.88	0.79-4.48
	Other medical	1.25	0.45-3.53
	Other surgical	1.23	0.42-3.65
	Weeks to follow-up	0.90	0.84-0.96
Hurting or aching	**Race**		
	White	Ref	
	Black	4.27	1.65-11.03
	Hispanic	1.14	0.37-3.51
	Asian	3.52	1.08-11.51
	Other	2.22	0.73-6.78
	Oncologic condition/BMT	6.27	2.45-16.05
Lifting something heavy	**Primary admission diagnosis**		
	Respiratory	Ref	
	Cardiovascular	2.45	1.01-5.98
	Infectious	2.16	0.80-5.84
	Oncologic	4.46	1.68-11.87
	Orthopedic	6.28	2.61-15.14
	Neurologic/Neurosurgical	1.71	0.65-4.51
	Other medical	1.26	0.40-3.97
	Other surgical	1.71	0.58-5.03
	Weeks to follow-up	0.92	0.86-0.99
Unable to do things	**Primary admission diagnosis**		
	Respiratory	Ref	
	Cardiovascular	2.00	0.81-4.94
	Infectious	1.82	0.64-5.17
	Oncologic	5.48	2.25-13.35
	Orthopedic	2.10	0.60-7.40
	Neurologic/Neurosurgical	2.22	0.88-5.58
	Other medical	1.98	0.73-5.42
	Other surgical	1.39	0.44-4.32

Feeling angry	**Age**	0.96	0.92-0.99
	Primary admission diagnosis		
	Respiratory	Ref	
	Cardiovascular	2.48	0.87-7.10
	Infectious	2.32	0.74-7.22
	Oncologic	6.70	2.23-20.19
	Orthopedic	1.13	0.14-9.33
	Neurologic/Neurosurgical	2.60	0.89-7.59
	Other medical	4.18	1.46-11.97
	Other surgical	2.47	0.78-7.82

BMT, bone marrow transplant

3c: FS II-R

Question	Variable	Relative Risk	95% CI
Reacting by crying	**Age**	0.93	0.88-0.97
	Female gender	1.72	1.11-2.67
	PRISM Score		
	<5	Ref	
	6-10	0.73	0.37-1.47
	11-15	0.72	0.14-3.78
	>15	2.52	1.72-3.69
Not sleeping through night	*No significant associations*		
Unusually irritable	**Diagnosis category**		
	Medical	Ref	
	Acute surgical	2.20	1.02-4.76
	Scheduled surgical	0.51	0.18-1.43
	Congenital heart disease	0.71	0.40-1.28
	Oncologic condition/BMT	2.39	1.09-5.22
Not energetic	**Hospital length of stay**	1.01	1.002-1.01
	PRISM Score		
	<5	Ref	
	6-10	1.05	0.41-2.66
	11-15	0.94	0.15-5.88
	>15	7.11	3.89-13.00
	Diagnosis category		
	Medical	Ref	
	Acute surgical	4.76	2.17-10.45
	Scheduled surgical	1.66	0.82-3.39
	Congenital cardiac	0.86	0.24-3.04
Acting moody	**Male gender**	1.97	1.10-3.52
	Diagnosis category		
	Medical	Ref	
	Acute surgical	3.41	1.73-6.73
	Scheduled surgical	0.73	0.37-1.44
	Congenital cardiac	1.30	0.61-2.77

PRISM, Pediatric Risk of Mortality; BMT, bone marrow transplant

Table 4: Frequency of failure to recover to baseline health-related quality of life by diagnosis category, stratified by survey type completed. The number of patients and median time to follow-up are indicated for each diagnosis category. The five survey questions with the greatest proportion of patients experiencing decline from baseline to follow-up are listed for each category. Questions in each diagnosis category with a significantly higher proportion of patients experiencing decline compared to patients without that diagnosis are indicated with an asterisk (*). Questions not among the five most common for decline for the diagnosis category but with significantly more frequent decline than patients without that diagnosis are also listed.

4a: PedsQL™ Infant Scales (0-24 months old)

	Respiratory n=80; 40.5 days		**Congenital heart disease** n=30; 39.1 days		**Infectious** n=86; 40.5 days		**Surgical** n=46; 41.5 days	
Overall % with failure to recover to baseline	17.7%		13.8%		17.7%		13.0%	
Questions with greatest % of patients declining	Fussing when alone	26.6	Difficulty soothing	25.0	Difficulty sleeping	25.0	Fussing when alone	37.0*
	Difficulty sleeping	24.7	Difficulty sleeping	24.1	Fussing when alone	24.7	Feeling cranky	33.3
	Feeling afraid	23.1	Being constipated	23.3	Wheezing	23.8*	Difficulty soothing	26.7
	Feeling tired	22.1	Feeling afraid	21.4	Feeling afraid	22.2	Feeling afraid	26.1
	Wheezing	21.8*	Fussing when alone	17.9	Feeling cranky	22.2	Crying a lot	24.4
Additional questions with significantly more frequent decline					Difficulty breathing	13.1*		
					Difficulty swallowing	12.9*		

4b: PedsQL™ Generic Core Scales (2-18 years old)

	Respiratory n=56; 38.5 days		**Cardiac** n=16; 40.5 days		**Congenital heart disease** n=49; 40.6 days		**Infectious** n=65; 37.6 days	
Overall % with failure to recover to baseline	16.1%		18.8%		37.5%		26.2%	
Questions with greatest % of patients declining	Missed school	22.9	Doctor's visits	44.4*	Feeling afraid	38.8*	Low energy	29.2
	Doctor's visits	22.2	Missed school	44.4	Lifting	31.3	Hurting	27.7
	Low energy	20.0	Hurting	31.3	Feeling angry	30.6	Doctor's visits	22.9
	School activities	19.1	Unable to do things	31.3	Trouble sleeping	30.6*	Worrying	21.5
	Forgetting things	16.7	Lifting	25.0	Exercising	30.4	Missed school	21.3
Additional questions with significantly more frequent decline					Bathing	22.9*		

	Oncologic/BMT n=14; 37.0 days		**Neurologic / Neurosurgical** n=52; 39.6 days		**Surgical** n=110; 40.5 days	
Overall % with failure to recover to baseline	71.4%*		23.1%		27.3%	
Questions with greatest % of patients declining	Running	71.4*	Hurting	34.7	Exercising	32.7
	Exercising	69.2*	School activities	28.6	Lifting	31.4
	Feeling sad	64.3*	Exercising	28.0	Unable to do things	30.1
	Trouble sleeping	64.3*	Unable to do things	27.1	Hurting	29.5
	School activities	60.0*	Paying attention	25.0	School activities	28.2
Additional questions with significantly more frequent decline	Lifting	57.1*			Running	26.0*
	Unable to do things	53.9*			Paying attention	23.8*
	Keeping up	53.9*				
	Hurting	50.0*				
	Low energy	50.0*				
	Feeling angry	50.0*				
	Walking	42.9*				
	Worrying	42.9*				
	Chores	35.7*				

4c: FS II-R

	Respiratory n=39; 40.5 days		**Congenital heart disease** n=23; 38.6 days		**Infectious** n=32; 40.1 days	
Overall % with failure to recover to baseline	43.6%		30.4%		53.1%*	
Questions with greatest % of patients declining	Reacting by crying	41.2	Reacting by crying	34.8	Not sleeping through night	32.3
	Unusually irritable	38.9*	Acting moody	30.4	Reacting by crying	30.0
	Not contented	29.0	Not communicating	22.7	Feeling tired	29.0
	Not sleeping through night	25.0	Feeling tired	17.4	Unusually irritable	29.0
	Feeling tired	23.7	Not contented	17.4	Acting moody	28.1
Additional questions with significantly more frequent decline						

	Neurologic / Neurosurgical n=21; 40.5 days		**Surgical** n=83; 39.6 days	
Overall % with failure to recover to baseline	28.6%		34.9%	
Questions with greatest % of patients declining	Unusually irritable	33.3	Reacting by crying	30.1
	Not sleeping through night	28.6	Not energetic	26.5
	Acting moody	23.8	Not contented	25.6
	Not communicating	23.8	Not sleeping through night	25.3
	Not occupying self	23.8	Feeling tired	22.2
Additional questions with significantly more frequent decline				

Figure 1: Proportion of patients who experienced failure to recover to their baseline health-related quality of life status at the time of follow-up, stratified by survey version completed.

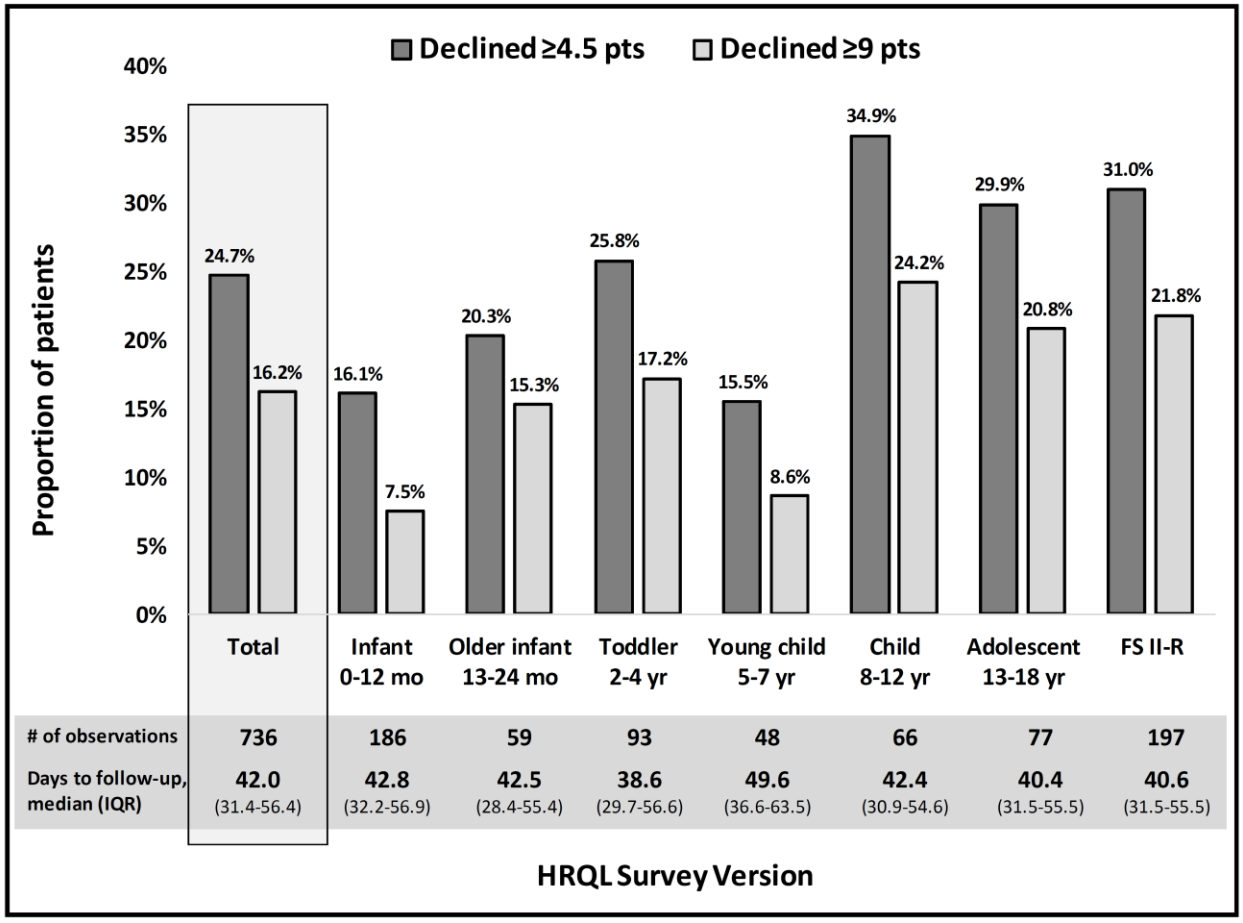


Figure 2: Distribution of HRQL scores at baseline, admission, and follow-up assessments for the entire cohort and for those who failed to recover to baseline health-related quality of life.

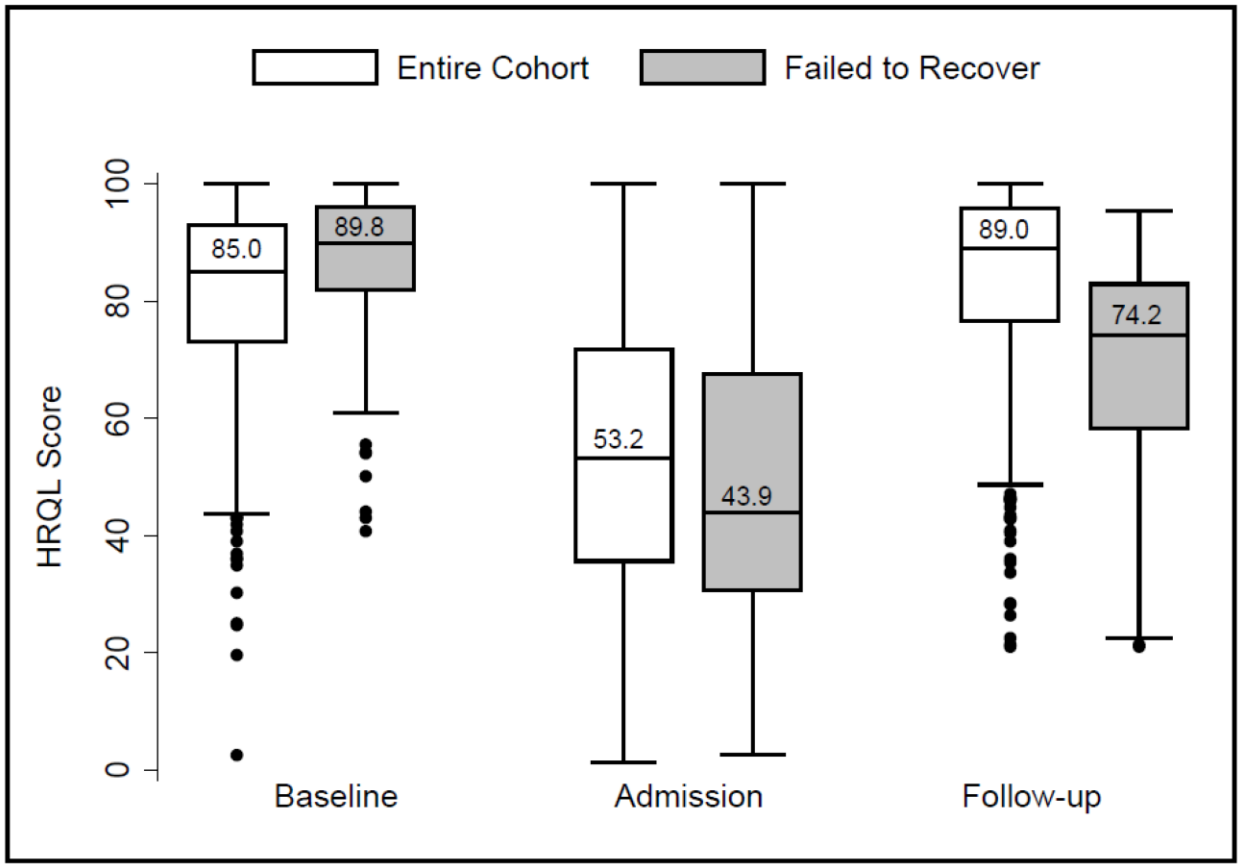


Figure 3: Prevalence of failure to recover to baseline health-related quality of life as a function of time to follow-up, in total and stratified by survey type completed

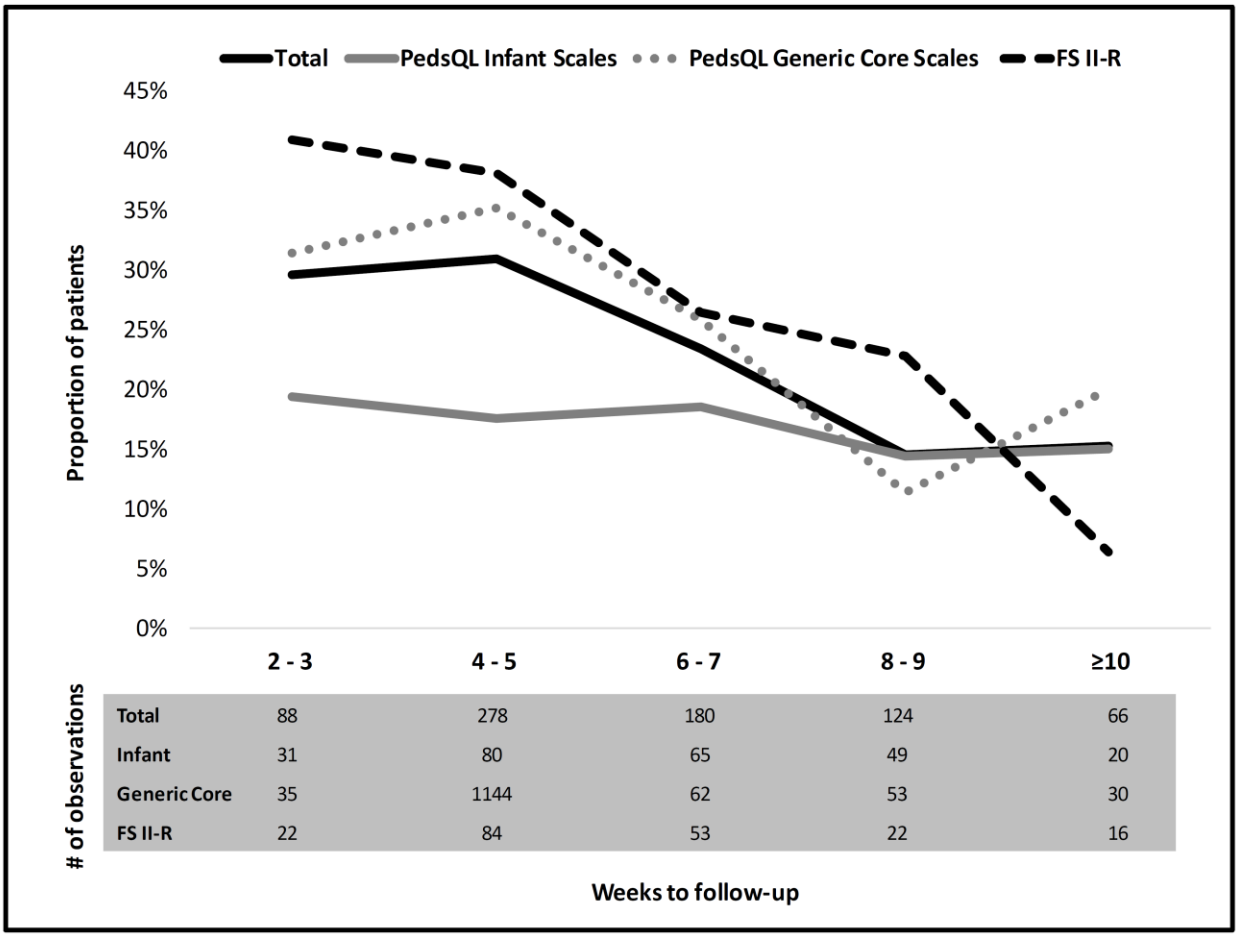
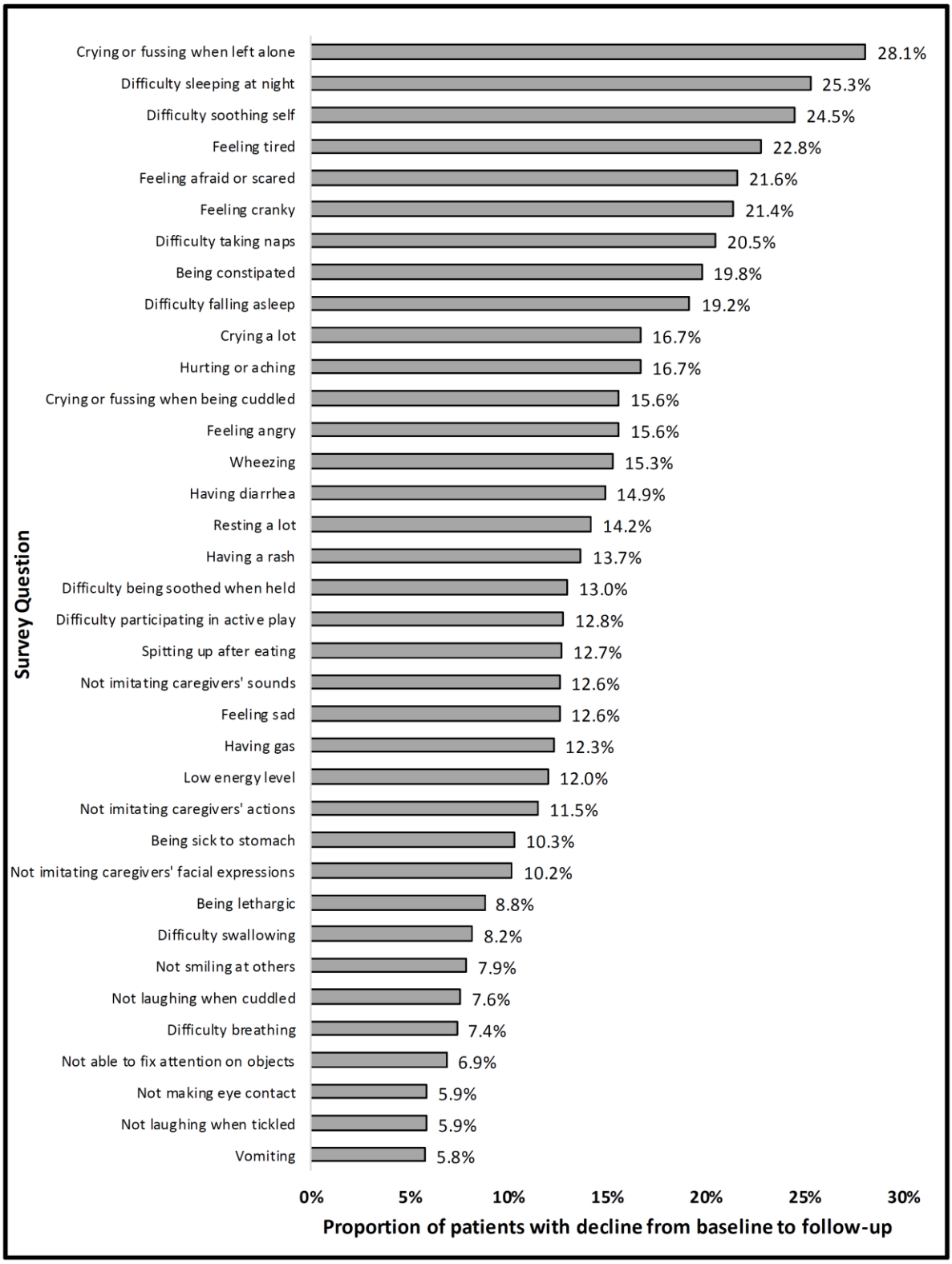
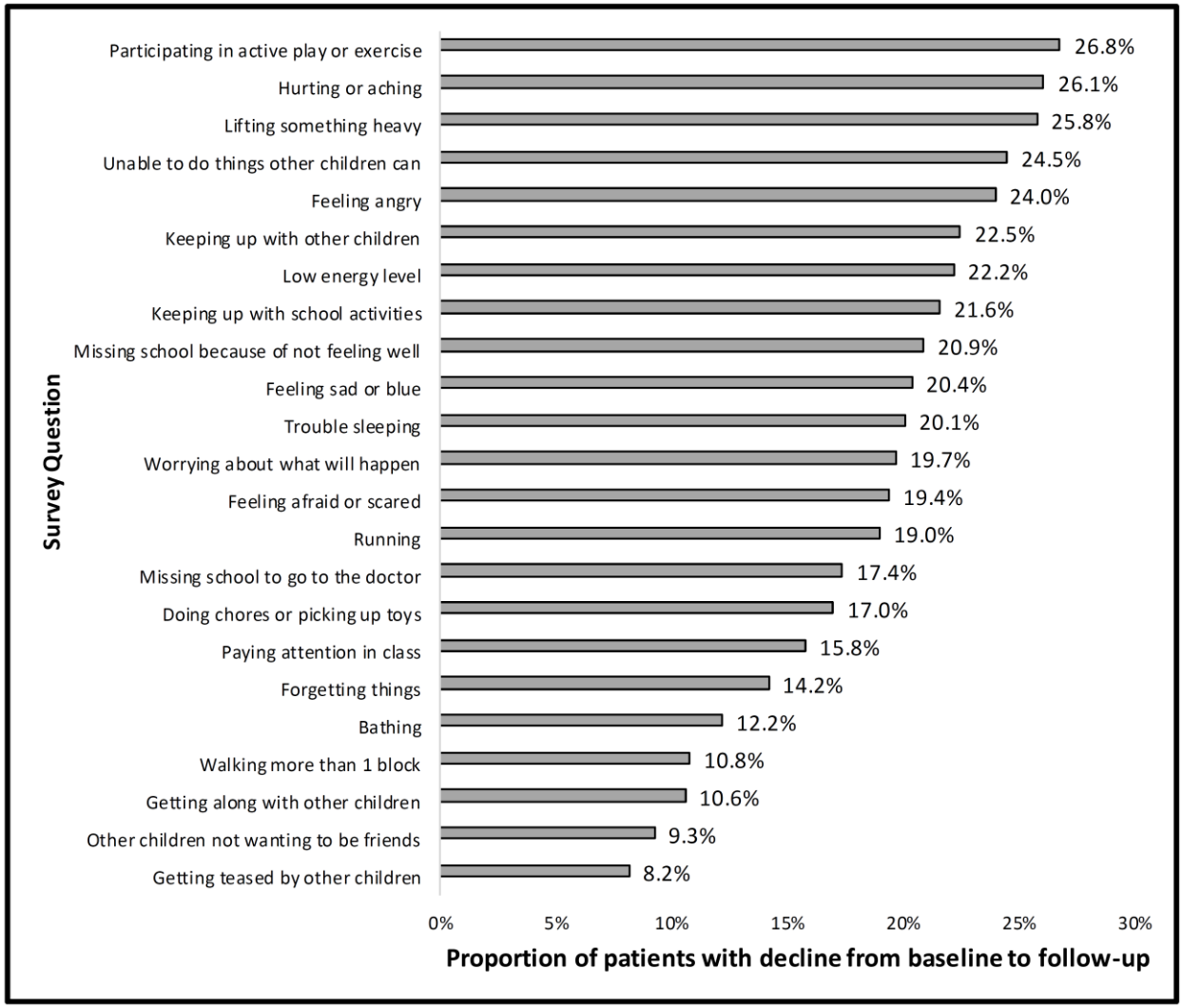


Figure 4: Proportion of patients with decline from baseline to follow-up in each survey question, by survey type completed

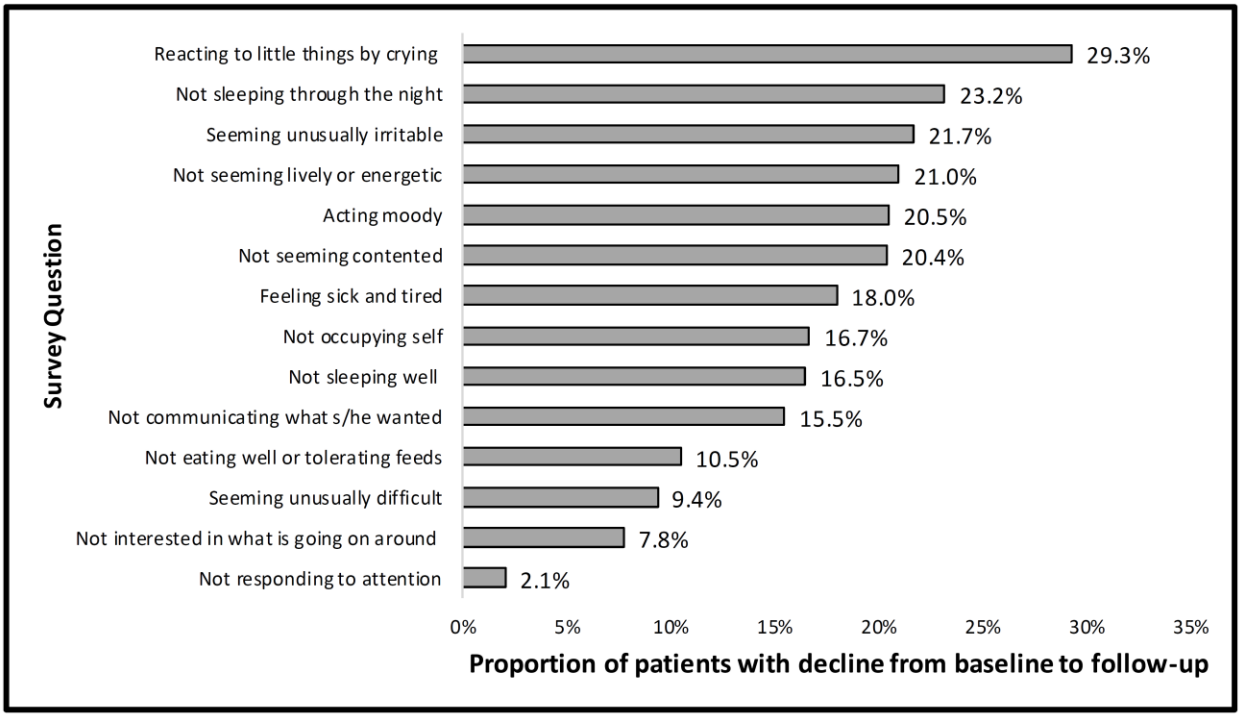
4a: PedsQL™ Infant Scales (0-24 months old)



4b: PedsQL™ Generic Core Scales (2-18 years old)



4c: FS II-R


Survey Question
Reacting to little things by crying
Not sleeping through the night
Seeming unusually irritable
Not seeming lively or energetic
Acting moody
Not seeming contented
Feeling sick and tired
Not occupying self
Not sleeping well
Not communicating what s/he wanted
Not eating well or tolerating feeds
Seeming unusually difficult
Not interested in what is going on around
Not responding to attention
29.3%
23.2%
21.7%
21.0%
20.5%
20.4%
18.0%
16.7%
16.5%
15.5%
10.5%
9.4%
7.8%
2.1%
0%
5%
10%
15%
20%
25%
30%
35%
Proportion of patients with decline from baseline to follow-up