Quality of Life (QOL) in Pediatric Cancer Patients: Related Demographic, Psychosocial, and Treatment Variables and Concordance Between Child and Parent Proxy Reports

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ABSTRACT

Title: Quality of Life (QOL) in Pediatric Cancer Patients: Related Demographic, Psychosocial, and Treatment Variables and Concordance Between Child and Parent Proxy Reports

Purpose: Survival rates of pediatric cancer have increased, so efficacy of treatment regimens has begun to focus on the psychosocial impact of cancer on a patient and his/her family, including child QOL. When a child is too young or too sick to report on his/her own QOL, parent proxy reports are utilized. The aims of the present study are to identify psychosocial, demographic, and treatment variables that affect a child's QOL, quantify concordance between child and parent proxy reports, and determine whether strength of concordance is related to time since diagnosis, child gender, or child age.

Methods: The "Psychosocial Assessment Tool" (PAT) (parents only) and QOL measures (parents and children) were completed within 2 weeks of diagnosis, and QOL measures (parents and children) again 6 months after diagnosis. We ran multivariate, linear regressions to investigate whether psychosocial variables measured by the PAT, child gender, child age, and intensity of the child's treatment regimen could predict any of 8 different child QOL outcomes (4 child reports and 4 corresponding parent proxy reports). To measure concordance, we used single measure intraclass correlation coefficients to quantify agreement. We also examined concordance after splitting our sample size by time since diagnosis, child gender, and child age.

Results: Higher scores on the PAT (indicating poorer psychosocial functioning) predicted three parent measures of child QOL but none of the child self reports. Males demonstrated an increased QOL relative to their female counterparts on 7/8 QOL measures. Child and parent proxy report of child QOL was moderate (or greater), similar across time points, gender, and age, with the exception of less than moderate concordance on the "psychosocial" QOL subscale for many subsets of parent-patient dyads. Almost universally, parent proxy reports underestimated a child's self report of QOL.

Discussion: These results suggest that psychosocial risk, as quantified by the PAT (a parent reported measure) might color a parent's perception of their child's QOL. Generally, moderate concordance existed in our patient population, but clinicians should be wary of the lower concordance rates on psychosocial domains of QOL. Lastly, it is important for clinicians to be conscious of the fact that parents tend to underestimate child QOL in comparison to the child's self report. These conclusions will help clinicians tailor appropriate and effective interventions to improve QOL in their pediatric cancer patients.

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GLOSSARY OF ABBREVIATIONS

CMTS = Caregiver Medical Traumatic Stress

ICC = Intraclass Correlation Coefficient

ITR = Intensity of Treatment Regimen

PAT = Psychosocial Assessment Tool

POSCS = Pediatric Oncology Supportive Care Study

PPPHM = Pediatric Psychosocial Preventative Health Model

QOL = Quality of Life

SECTION 1: INTRODUCTION

Assessing Psychosocial Risk in Pediatric Cancer Patients and Their Families: Pediatric Psychosocial Preventative Health Model and the Psychosocial Assessment Tool

The diagnosis and treatment of childhood cancer are distressing events that affect the entire family (Armstrong & Mulhern, 1999; Pai et al., 2008; Stuber, 1995). Considering that the ability to effectively cope with stress differs between families, researchers have developed the Pediatric Psychosocial Preventative Health Model (PPPHM), which classifies families entering the pediatric healthcare system by psychosocial risk (Kazak et al., 2007). The PPPHM stratifies families into three levels: Universal (those who experience initial distress that attenuates with time), Targeted (those who display acute distress in the setting of psychosocial risk factors), and Clinical (those who experience a high level of distress that is persistent, escalates over time, and is often associated with post traumatic stress symptoms) (Pai et al., 2008). In order to operationalize and designate families as belonging to one of these three categories of "psychosocial risk" in the PPPHM, clinicians use the Psychosocial Assessment Tool (PAT). The PAT includes many items, including those that assess family functioning, family structure and resources, social support, the child's emotional and behavioral concerns, and caregiver medical traumatic stress (CMTS) (Pai et al., 2008). The clinical importance of the PAT is grounded in the fact that once psychosocial risk is operationalized, higher levels of psychosocial care can be directed to the families that demonstrate the greatest need (Kazak et al., 2007). There is evidence-based support for the use of the PAT in clinical settings to improve quality of life (QOL) in pediatric cancer patients. One study in a pediatric oncology population found that providing information to a child's treatment team about a family's psychosocial risk around the time of diagnosis (in the form of a summary of the family's PAT) was associated with improved child QOL outcomes and parental anxiety 6 months later (Barrera et al., 2014).

Child QOL

Considering that survival rates of pediatric cancer have increased, efficacy of treatment regimens has begun to focus on the psychosocial impact of cancer on a patient and his/her family (Feeny et al., 1999). In addition to the PAT, QOL measures are often

used to quantify the physical and psychological impact of a cancer diagnosis and treatment. QOL is defined as "a construct made up of several dimensions, including individuals' physical functioning, psychological state, social functioning, and physical discomfort" (Ivan & Glazer, 1994). QOL measures give a more complete picture of a child's psychosocial functioning from the time of diagnosis through treatment.

QOL in pediatric cancer patients is a function of many variables, including family structure, family resources, and parent stress levels (Curbow & Somerfield, 2005; Litzelman et al., 2011, Roddenberry & Renk, 2008). Family resources (including both social and financial) have been known to positively affect a family's adaptational response to stress (Curbow & Somerfield, 2005). CMTS is defined as "a set of psychological and physiological responses of children and their families to pain, injury, serious illness, medical procedures, and invasive or frightening treatment experiences" (National Child Traumatic Stress Network, 2003). Examining CMTS is an important step in guiding intervention development (Kazak et al., 2006), as studies have shown that the stress endured by parents of chronically ill children may have adverse implications in child and family adjustment throughout the treatment process (Abad, 2008; Litzelman et al., 2011; Roddenberry & Renk, 2008; Vance et al., 2001) as well as over the long term (Meeske et al., 2007; Kazak & Barakat, 1997). Poorer family functioning outcomes, such as reduced communication, poorer behavioral control (nonadherence to a set of rules), and reduced social adjustment have also been associated with increased parent stress levels (Colletti et al., 2008; Schaefer, 1983; Streisand, Kazak, & Tercyak, 2003). From a clinical psychiatric standpoint, children are significantly more likely to experience anxiety and depression if one or more parent also experiences these symptoms (Merrill et al., 2007). Taken in sum, these pervasive implications suggest that caregiver stress is an important factor that governs the extent to which a family is able to cope with a child's disease and treatment. From a clinical psychosocial standpoint, understanding a caregiver's level of stress can guide appropriate intervention development (Kazak et al., 2006).

Intensity of treatment regimen has, in the past, been hypothesized to affect behavioral outcomes in pediatric cancer patients, but studies to date have not supported such a relationship (Noll et al., 1997) and data on the relationship between intensity of treatment regimen and child QOL is limited (Noll et al., 1997).

Ultimately, an increase in understanding of factors which reveal or predict family functioning and a child's QOL can help clinicians to better provide psychosocial services to families to aid in long term adjustment and better psychological outcomes for the child and his/her family (Kazak, 2004). Furthermore, the assessment of a child's QOL in light of these variables at the time of diagnosis would allow physicians to determine psychosocial risk and initiate an early intervention.

Concordance Between Parent and Child Reports of a Child's QOL

We have established that an accurate assessment of a family's psychosocial risk and child's QOL is of great importance. In cases where a child is not able to report on his or her own QOL, clinicians rely on parent proxy reports (Russell et al., 2006), so understanding concordance between parent and child QOL reports becomes essential.

Studies have shown varying levels of agreement between parent and child reports of child QOL in both medical and non-medical settings. In one study, which examined concordance between parent and child QOL reports in a pediatric cancer population, poor to moderate agreement between parent and child reports was found (Vance et al., 2001), but there are reports that parent and child reports of child QOL in oncology populations might actually be higher than in non-cancer populations (Russell et al., 2006). With regards to populations outside of pediatric oncology, a study involving pediatric patients who had sustained a traumatic brain injury was notable for poor concordance of health related QOL (Pieper & Garvan, 2015).

The level of concordance between parent and child reports of a child's QOL has been shown to be impacted by many variables, including child age, child sex, and the type of QOL examined. Parent-child concordance has been shown in several studies to be inversely related to child age (Buck et al., 2012; Tluczek et al., 2013), potentially due to the fact that older children might consciously attempt to protect their parents from their own struggles or concerns about their illness (Russell et al., 2006). With regards to sex, some studies have shown greater discordance between male patients and their parents (Tluczek et al., 2013), but others have shown that males actually display better levels of concordance with their parents (Buck et al., 2012). Concordance has been shown to vary with the type of QOL being assessed. For example, parents were less reliable when rating their child's

internalizing (emotional) QOL as compared to the child's externalizing problems (e.g., acting out or aggression) (Quay & La Greca, 1986, as cited in Vance et al., 2001). However, one study actually noted that the lowest levels of parent-child concordance with respect to child QOL were with regards to physical functioning and physical limitations, in which parents overestimated QOL (Russell et al., 2006).

With regards to directionality, parents may have the tendency to rate their child's QOL as worse than the children, themselves, do (Theunissen et al., 1998; Tluczek et al., 2013; Vance et al., 2001), even in non-oncology populations (Feichtl et al., 2010), but this underestimation is not always significant (Russell et al., 2006). Timing of treatment has also been shown to affect concordance between parent and child QOL ratings. For example, one study showed that parents of pediatric cancer patients tended to underestimate their child's QOL shorter out from treatment, but overestimate their child's QOL further out from treatment (Roddenberry & Renk, 2008). Still, information about variables contributing to parent-child agreement levels remains limited (Upton, Lawford, & Eiser, 2008).

In light of the clinical importance of optimizing QOL in pediatric cancer patients and understanding the concordance between child and parent proxy reports, this study will examine:

Primary Aim #1: Quantify QOL in pediatric cancer patients undergoing treatment, and identify psychosocial, demographic, and treatment variables that are associated with a child's QOL at 6 months after diagnosis. We hypothesize that increased psychosocial risk, measured by the PAT, is likely to be associated with decreased QOL by both parent and child report. More specifically, family structure, family resources, and CMTS at the time of diagnosis (Roddenberry & Renk, 2008; Vance et al., 2001) might also independently predict a child's QOL at 6 months after diagnosis, with more disrupted family structure, fewer family resources, and increased CMTS predicting a lower QOL in the child. We also anticipate that the intensity of a child's cancer treatment regimen (ITR) will be inversely related to QOL.

Primary Aim #2: Characterize the concordance between child QOL reports and parent proxy reports. Studies have shown variable strength of concordance (Russell et al., 2006). In conjunction with the literature (Vance et al., 2001), we anticipate that child and parent assessments of child QOL will not be unanimously concordant. With regards to directionality, studies have shown that parents tend to underestimate their child's QOL, so for any non-concordant parent-patient dyads, we would predict a similar directionality in our study (Russell et al., 2006).

Secondary Aim #1: Given that existing literature has not clearly established factors that consistently predict concordance between child and parent-proxy QOL reports, we will identify associated variables related to concordance in our study population. Based on the literature, concordance should have an inverse relationship with child age (Buck et al., 2012; Pieper & Garvan, 2015; Tluczek et al., 2013), be unrelated to child sex (Buck et al., 2012; Feichtl et al., 2010; Pieper & Garvan, 2015; Tluczek et al., 2013), and be better for externalizing variables (ex-physical functioning) than for internalizing variables (ex-emotional functioning) (Russell et al., 2006, Vance et al., 2001). Timing (i.e., at diagnosis or at 6 months out from diagnosis) is more likely to affect directionality of concordance than the magnitude of concordance, with studies showing that parents tend to underestimate their child's QOL shorter out from treatment, but overestimate their child's QOL further out from treatment (Roddenberry & Renk, 2008).

SECTION 2: STUDENT ROLE

My role in this project consisted of the following responsibilities:

- Performing a literature review on my topic of interest (QOL in pediatric cancer patients, concordance between child and parent proxy reports of child QOL)
- Developing my specific research questions, study aims, and hypotheses in the context of the existing literature
- Working with my PI as well as members of our research and statistics teams to devise a most effective statistics plan to answer our research questions, as well as

interpret the results of our analyses and how our study conclusions fit within the existing literature

SECTION 3: METHODS

Pediatric Oncology Supportive Care Study (POSCS)

The POSCS is a prospective longitudinal cohort study that is exploring the associations between psychosocial risk assessment, QOL, psychosocial service utilization, and medical treatment intensity in pediatric cancer patients undergoing treatment. Subjects eligible for the study include children ages 2-25 who are diagnosed with a hematologic, solid tumor, or neurologic malignancy and are undergoing chemotherapy at Dana-Farber Cancer Institute (DFCI)/Children's Hospital Cancer Center. The present study drew from the POSCS dataset.

Participants:

Participants in the study were newly diagnosed pediatric cancer patients and their English-speaking parents or legal guardians (69 mothers, 19 fathers). In our patient population, 52 patients were diagnosed with a hematologic malignancy, 28 had solid tumors, and 7 had neurologic malignancies. The 88 patients (47 males, 41 females) ranged in age from 2-20 years. Mean age was 10.02 years. Please refer to Table 1 for demographic characteristics and diagnostic group breakdown. Identifying information was kept confidential through the use of study subject ID numbers.

IRB/Ethical Considerations:

This study has IRB approval through the DFCI.

Measures:

Psychosocial Assessment Tool 2.0 (PAT 2.0):

The PAT is a 15-item, self report survey that has been validated as a screening tool to assess psychosocial risk in families of pediatric cancer patients. This measure has

demonstrated internal consistency, test-retest reliability, and content validity (Pai et al., 2008). It is a self-report measure, completed by a parent, that consists of 15 item sets, each dichotomously scored as 0 (no risk) or 1 (risk). Designated items are combined to yield the following subscales: family structure and resources, social support, the child's emotional and behavioral concerns, siblings' emotional and behavioral concerns (if applicable), family functioning, caregiver stress reactions (caregiver medical traumatic stress), and family beliefs. Each subscale is additive towards a total raw score, ranging from 0-7, with higher scores signifying increased psychosocial risk (0-.99=universal, 1-2.99=targeted, >3=clinical). This measure will yield our "PAT Total," "PAT Family Structure and Resources" and "PAT Caregiver Stress Reactions" scores for the present study.

PedsQL™ 4.0 Short Form 15 Generic Core Scales

The PedsQL Generic short form is a 15 item form designed to measure health related QOL in both clinical and healthy populations. Similar to the longer form of the survey, it has yielded comparable reliability and validity (Chan et al., 2005). Each item on the survey asks respondents to indicate to what extent the item has been problem for the child in the past month and is scored on a 5-point likert scale for a total score ranging from 0-100 (with higher scores representing higher QOL). The PedsQL Generic can be completed by both children and parents to yield child self reports as well as parent proxy reports. Scoring yields a total score as well as scores for each of the following subscales: Physical Functioning, Emotional Functioning, Social Functioning, School Functioning, and Psychosocial Health. There are Child report measures are separated into developmentally appropriate formats for ages 5-7, 8-12, and 13-17. Parent-proxy report measures include measures for ages, 2-4, 5-7, 8-12, and 13-17. Both a self-report and parent proxy-report were completed by each participating family.

PedsQL™ 3.0 Cancer Module

The PedsQL Cancer Module assesses health related QOL specific to cancer symptoms. It is a 27 item measure that yields eight subscales including Pain and Hurt, Nausea, Procedural Anxiety, Treatment Anxiety, Worry, Cognitive Problems, Perceived Physical Appearance, and Communication. Similar to the PedsQL Generic form, the Cancer Module is scored on a

scale of 0-100 (with higher scores denoting higher QOL) and is separated into developmentally appropriate formats with the exception of including an additional self report and parent-proxy report for patients ages 18-25. This measure has demonstrated good internal consistency reliability and construct validity (Varni et al., 2002). Both a self-report and parent proxy-report were completed by each participating family.

Intensity of Treatment Rating Scale (ITR-2)

The ITR-2 is a measure of intensity of pediatric cancer treatment. It classifies 34 types of cancer and treatments into four levels of increasing intensity: least intensive (Level 1) to most intensive (Level 4). Ratings are made based on treatment modality (chemotherapy, radiation, surgery) as well as stage/risk level of disease, extracted from a patient's medical record. The ITR-2 has demonstrated content validity and inter-rater reliability (Werba et al., 2007).

Instrument Administration

At Dana Farber Cancer Institute, the PAT 2.0 is administered to patients' caregivers as part of routine clinical care for psychosocial assessment within 2 weeks of diagnosis. Consent for the POSCS study and completion of time 1 QOL measures took place within 6 weeks of the patient's diagnosis. Participation in the study included a medical record review of the PAT 2.0, as well as the administration of two versions of the PedsQL (Generic and Cancer Modules), which assessed QOL via a patient self-report and a parent proxy report. These QOL measures were repeated at the 6-month time point post diagnosis, as well. As per above, the ITR score was derived from chart review for inclusion in the 6-month data set.

Data collection and management were executed using the "Research Electronic Data Capture" (REDcap) method in collaboration with the Pediatric Clinical Translational Investigative Program (CTIP). IBM SPSS Statistics Version 22 was utilized for data analyses.

Data Analysis

Primary Aim #1: Quantify QOL in pediatric cancer patients undergoing treatment, and identify psychosocial, demographic, and treatment variables present at the time of diagnosis

(PAT Total score, PAT "Family Structure and Resources" subscale, PAT "Caregiver Stress Reactions" subscale, child age, child sex, and intensity of treatment regimen (ITR)) that are associated with a child's QOL at 6 months after diagnosis. Here, QOL includes child reports and parent proxy reports of the following four QOL measures: Generic Total score, Generic "Psychosocial" subscale, Generic "Physical Functioning" subscale, and Cancer Total score.
In order to test this aim, three separate multivariate linear regression models were constructed with the following independent variables:

1) PAT Total Score, child age, child gender, ITR
2) PAT "Family Structure and Resources" subscale, child age, child gender, ITR
3) PAT "Caregiver Stress Reactions" subscale, child age, child gender, ITR

The dependent variables for each of the aforementioned groups of independent variables were each of the following measures of child QOL:

1) Generic Total (child report)
2) Generic Total (parent proxy report)
3) Generic "Psychosocial" subscale (child report)
4) Generic "Psychosocial" subscale (parent proxy report)
5) Generic "Physical Functioning" subscale (child report)
6) Generic "Physical Functioning" subscale (parent proxy report)
7) Cancer Total (child report)
8) Cancer Total (parent proxy report)

In summary, we ran a total of 24 multivariate linear regressions to investigate aim #1.

Primary Aim #2: Characterize the concordance between child QOL reports and parent proxy QOL reports at 6 months following diagnosis. QOL reports include the same as those aforementioned in "Primary Aim #1."
In order to examine level of concordance between child and parent proxy reports of child QOL, we obtained a single measures intraclass correlation coefficient (ICC) for each of the following pairs of child-parent proxy QOL reports (at 6 months following diagnosis):

1) Generic Total
2) Generic "Psychosocial" subscale
3) Generic "Physical Functioning" subscale

4) Cancer Total

Secondary Aim #1: Identify variables (age, sex, and time since diagnosis) that affect the level of concordance between parent proxy QOL reports and child QOL reports. QOL reports include the same as those aforementioned in "Primary Aim #1."

For this aim, separate single measures ICC's were run for each of the following patient-parent dyads for all four types of QOL reports (aforementioned in Primary Aim #2):

1) All patient-parent dyads at "time 1" (within 4 weeks of diagnosis)
2) All patient-parent dyads at "time 2" (at 6 months following diagnosis) – already acquired, per Primary Aim #2
3) Patient-parent dyads with female patients only at "time 2"
4) Patient-parent dyads with male patients only at "time 2"
5) Patient-parent dyads with patient age 5-7 years at "time 2"
6) Patient-parent dyads with patient age 8-12 years at "time 2"
7) Patient-parent dyads with patient age 13-17 years at "time 2"

SECTION 4: RESULTS

Descriptive Analysis

Means and standard deviations for all QOL outcome variables (both child and parent proxy reports) at 6 months out from diagnosis are presented in Table 2 along with means and standard deviations for independent variables in the current study, including PAT total score, PAT "Family Structure and Resources" subscale, PAT "Caregiver Stress Reactions" subscale, and ITR score. Also presented in the table are average means and standard deviations for QOL outcome variables as per Varni et al. (2002). As is evident from the table, the average QOLs for our sample of cancer patients, as reported by both patient and by parent proxy reports, are comparable to the results attained by Varni et al. (2002) in their study sample. QOL in our sample of cancer patients was lower than average QOL in healthy controls, but comparable to QOL in oncology patients reported by Varni et al., 2002.

Primary Aim #1: Variables Affecting Child QOL

To address primary aim #1, which investigated the association between psychosocial (PAT total score, PAT "Family Structure and Resources" subscale, PAT "Caregiver Stress Reactions" subscale), demographic (child gender, child age), and treatment (ITR) variables, linear regressions were run with each of the 8 QOL scales as outcome variables (Generic Total score, Generic "Psychosocial" subscale, Generic "Physical Functioning" subscale, and Cancer Total score each derived from both child report and parent proxy report).

Two linear regressions investigated the association between the PAT "family structures and resources" subscale and the PAT "Caregiver Stress Reactions" (respectively) while controlling for child age, child gender, and ITR. Results were notable in that for none of the QOL outcome variables did either of the PAT subscales emerge as an independent predictor.

In examining the association between PAT total score and the 8 aforementioned QOL outcomes while controlling for child age, child gender, and ITR, a linear regression yielded several notable results, displayed in Table 3. First, PAT total score emerged as a variable that was independently (and inversely) associated with three of the four parent proxy measures of child QOL including Generic Total ($F(4, 78) = 4.136$, $p=0.031$), Generic "Psychosocial" subscale ($F(4, 77) = 3.591$, $p=0.004$), and Cancer Total ($F(4, 81) = 7.515$, $p=0.001$). Second, child gender emerged as a variable significantly associated with 7/8 QOL outcomes including child reports of Generic Total ($F(4, 54) = 2.038$, $p=0.024$), Generic "Physical Functioning" subscale ($F(4, 55) = 1.211$, $p=0.046$), Cancer Total ($F(4, 56) = 1.881$, $p=0.016$) as well as all four parent proxy reports of child QOL including Generic Total ($F(4, 78) = 4.136$, $p=0.001$), Generic "Psychosocial" Subscale ($F(4, 77) = 3.591$, $p=0.005$), Generic "Physical Functioning" subscale ($F(4, 77) = 2.776$, $p=0.015$), and Cancer Total ($F(4, 81) = 7.515$, $p < 0.001$). In all cases, being a male pediatric cancer patient was associated with a higher QOL for each of the cases in which gender was a significant predictor of child QOL. Additionally, child age emerged as a significant predictor of child QOL on the Cancer Total measure as reported by the parent ($F(4, 81) = 7.515$, $p=0.003$). In this case, there was an inverse relationship between child age and parent report of the child's QOL such that parents reported older children as having a worse QOL on the Cancer Total scale as

compared to younger children. Perhaps most notably, ITR was not a significant predictor of any type of QOL as reported by either child or parent.

Primary Aim #2: Concordance Between Child and Parent Proxy Reports of Child QOL

Concordance between child and parent proxy reports of child QOL at 6 months following initial cancer diagnosis, assessed by ICC's, were generally moderate to substantial (ICC greater than 0.4), using the cutoffs suggested by Landis & Koch (1977), from which Table 4 is adapted. One exception to the "moderate or greater" concordance between child and parent proxy QOL reports at 6 months following diagnosis, is the Generic "Psychosocial" subscale, which produced a single measures ICC of 0.290 ($F(54,54)= 3.234$, $p<0.001$), which is considered "fair" (Landis & Koch, 1977). ICC's for child and parent proxy reports for all four QOL outcomes (Generic Total, Generic "Psychosocial" subscale, Generic "Physical Functioning" subscale, and Cancer Total) are displayed in Table 5.

Secondary Aim #1: Relationship between Time Since Diagnosis, Child Gender, and Child Age on Strength of Concordance Between Child and Parent Proxy Reports of Child QOL

Concordance between child and parent proxy reports of child QOL was also analyzed in subgroups to examine the relationship between time since diagnosis, child gender, and child age on strength of concordance (Tables 6a-6c). With regards to time since diagnosis (Table 6a), the only difference in concordance that could be appreciated was that at initial diagnosis, child and parent proxy reports of child QOL on the Generic "Psychosocial" subscale were "moderately" concordant ($F(54,54)= 3.178$, $p<0.001$), and this concordance worsened at 6 months following diagnosis, at which point it became "fair" (as per above, $F(54,54)= 3.234$, $p<0.001$). In examining gender differences in parent-child concordance at 6 months following diagnosis (Table 6b), both females and male patients demonstrated moderate to substantial concordance with their parents on three of the four QOL measures (Generic Total, Generic "Physical" subscale, and Cancer Total). Concordance on the Generic "Psychosocial" subscale was less than 0.4, but the p-value was not significant for males or for females. In breaking down our patient population into three age categories (children

age 5-7 years, children age 8-12 years, and children age 13-17 years), we examined whether there were differences in concordance between parent and child reports of child QOL at 6 months following diagnosis that were related to child age (Table 6c). In terms of results, the parent-child concordance for each QOL measure was moderate to substantial, with a few exceptions. The Generic "Psychosocial" subscale for children ages 5-7 years yielded a low ICC (<0.4), but a p-value that was not significant. The Generic Total score for children ages 8-12 years also yielded a low ICC (<0.4), but again, the p-value was not significant. The Generic "Psychosocial" subscale for children ages 13-17 years yielded an ICC which was <0.4 and characterized as "fair" ($F(26,26)= 2.306$, $p=0.019$).

With regards to directionality of QOL rating discrepancies between parent and child, means and standard deviations for all discordant ICC's (<0.4) are displayed in Table 7. In all cases, the mean child QOL rating was higher than the mean parent proxy rating, with the exception of the Generic "Psychosocial" subscale for children age 5-7 years.

SECTION 5: DISCUSSION

Given that survival rates for pediatric cancer patients have increased through improved treatment efficacy, there has been more focus on improving child QOL (Feeny et al., 1999). Child QOL has been shown to be impacted by many variables, including parent distress levels (Abad, 2008; Litzelman et al., 2011; Roddenberry & Renk, 2008; Vance et al., 2001) as well as a family's access to financial and social resources (Curbow & Somerfield, 2005). When child reports cannot be utilized due to the child being too ill or too young to report on their own QOL, parent proxy reports are often utilized. However, research results are variable regarding whether these parent proxy reports are accurate and whether there are demographic or other variables that can affect the relationship between reports.

The present study sought to investigate factors related to child and parent proxy reports of QOL, characterize the concordance between child and parent proxy reports, and discern whether concordance levels are associated with time since diagnosis, child gender, or child age.

Factors Affecting Child QOL

In the present study, child QOL as reported by both child and parent was lower than average QOL in a healthy patient sample, but comparable to a cancer sample reported by Varni et al., 2002.

With regards to factors affecting child QOL, we tested three separate linear regression models which each included child age, child gender, ITR, and one PAT measure (either PAT "Family Structure and Resources" subscale, PAT "Caregiver Stress Reactions" subscale, or PAT total score) with outcomes being parent and child reports of 4 different QOL measures (Generic Total, Generic "Psychosocial" subscale, Generic "Physical Functioning" subscale, and Cancer Total).

Interestingly, neither PAT "Family Structure and Resources" nor PAT "Caregiver Stress Reactions" were significant contributors to any type of parent or child reported child QOL. This indicates that neither PAT subscale is an independent predictor of child QOL, as measured in the present study, at 6 months out from diagnosis.

However, PAT total score was predictive of parent proxy reports of the following measures of child QOL: Generic Total, Generic "Psychosocial" subscale, and Cancer Total. Interestingly, PAT was only significant for parent reports of child QOL, indicating that a child's report of their QOL is independent of psychosocial risk as indicated by the parent on the PAT (parent measure). This begs the question of whether a parent's psychosocial environment is coloring how they interpret their child's distress and resultant QOL. Furthermore, we consider whether the parent proxy QOL report, which apparently is affected by the parent-reported psychosocial environment, might be more a measure of the parent's state of distress which translates into false perceptions that if parent is experiencing psychosocial distress and poor QOL, the child must be experiencing poor QOL as well. This result from the present study suggests that the PAT, a parent reported measure, is a better indicator of

parent psychosocial state and perhaps than child QOL, perhaps impacting a parent's perception of their child's QOL.

Families who are found to be at high psychosocial risk by their elevated PAT scores are likely to benefit from additional psychosocial services both to improve parent functioning as well as to improve child and family functioning, as parent stress levels have been shown to impact family adjustment (Roddenberry & Renk, 2008; Vance et al., 2001). This specific result warrants question of whether parent-based interventions, as opposed to child-based interventions, might be more high impact, given the effect of a family's psychosocial risk (as measured by the PAT) on child QOL as reported by parent only.

Future studies might investigate the specific effect of parent mood on child QOL to uncover whether the effect of a family's psychosocial risk state on child QOL is impacted by parent feelings/emotions to a greater extent than family structure, family resources, and other concrete variables. The PAT assesses certain parent emotions as well as family structure/resources, but isolating "parent mood" would allow us to determine whether this component of a parent's state is driving their perception of their child's QOL.

Interestingly, male gender was associated with better QOL reports by both child and parent on 7/8 measures of child QOL, including Generic Total (child and parent reports), Generic "Psychosocial" subscale (parent report), Generic "Physical Functioning" subscale (child and parent reports), and Cancer Total (child and parent reports). There are several potential explanations for the reduced QOL in girls, as opposed to boys, in the current study. First, chemotherapy is a universal standard of treatment for pediatric cancers, and this modality of therapy has a physical side effect of hair loss, which is likely to disproportionately cause distress in young girls. Second, it is possible that girls, who are thought to be more emotional, may be more outward about expressing pain and physical/psychosocial suffering, as compared to their male counterparts (Pud, 2011). This tendency for girls to be more honest and less inhibited in conveying their true QOL might manifest as a reduced QOL by both child report as well as parent report, as parents whose children are more expressive might have increased insight into QOL. Regardless of underlying reasons why

female gender tends to be associated with poorer QOL at 6 months following diagnosis, it is of clinical importance for physicians and other members of the child's care team to realize that their female patients are at risk for lower QOL and might benefit from increased psychosocial services in treatment.

Interestingly, contrary to our hypothesis, intensity of treatment regimen, as measured by the ITR, was not an independent predictor of any type of child QOL reported by either child or parent. We anticipated that higher scores on the ITR, which indicate an increased burden of treatment, would have negatively affected a child's QOL, but this was not the case. Rather than interpreting this result as that child QOL is not impacted by intensity of treatment regimen, we suspect that our study did not have the variability in ITR scores to accurately parse out how this variable might affect QOL. In the present study, there was little variation in ITR scores across the sample of participants, so it is likely that we did not have enough of a range in treatment intensity to uncover how variability in this measure might affect QOL. Future research might investigate the relationship between ITR and QOL in a more heterogenous patient sample (with regards to spectrum of treatment) such that differences in QOL across a larger range of treatment intensities might be uncovered.

Concordance Between Child and Parent Proxy Reports

Concordance between parent and child proxy reports of child QOL is an area of research that is fairly well studied but has yet to yield conclusive, consistent results (Russell et al., 2006; Vance et al., 2001). In the present study, ICC's were used to assess concordance, and any value less than 0.4 was flagged as "low" parent-child concordance. In our patient sample, there was at least moderate concordance for three of four measures of child QOL at 6 months from diagnosis (Generic Total, Generic "Physical Functioning" subscale, and Cancer Total). The Generic "Psychosocial" subscale was the only QOL scale that demonstrated less than moderate concordance between child and parent proxy reports. This finding is consistent with the literature and with our hypothesis, as there is reason to believe that a child's internalizing QOL has the potential to be less transparent (and, consequently, more difficult for parents to interpret) than other, more objective

components of QOL, such as physical functioning (Russell et al., 2006). This low level of concordance between child and parent proxy reports of psychosocial functioning will be important for clinicians and psychosocial services providers to keep in mind as they identify children who are in need of services, particularly if the clinical situation and age/degree of sickness of the child mandates use of a parent proxy report and cannot utilize a child's own report.

We also examined parent-child concordance with respect to time since diagnosis, child gender, and child age. Concordance between child and parent proxy reports was similar across time points (initially, at diagnosis, as compared to 6 months following diagnosis), with the exception being that at diagnosis, there was moderate concordance between child and parent proxy reports of the child's psychosocial QOL. This concordance worsened to "fair" at 6 months following diagnosis. This is likely due to the fact that at initial diagnosis, a child has received no treatment and their QOL might be less disrupted and more transparent to their parent. In the present study, girls and boys had similar concordance levels, which is consistent with the literature and with our hypothesis (Buck et al., 2012; Feichtl et al., 2010; Pieper & Garvan, 2015; Tluczek et al., 2013). An interesting avenue of future research in the area of gender-related concordance would be to investigate whether the sex of the parent (and whether this is the same or different from the sex of the child) impacts concordance levels. Also interesting to study would be whether the parent providing the proxy QOL report is the most active caregiver during cancer treatment, and whether this affects parent-child agreement on QOL measures. Lastly, we divided our patient population into three age groups (age 5-7 years, age 8-12 years, and age 13-17 years) and examined concordance with respect to age groups. The literature suggests an inverse relationship between concordance and child age (Buck et al., 2012; Pieper & Garvan, 2015; Tluczek et al., 2013), which we did not find in the present study. In our sample, the lowest overall levels of concordance were found in the child age 8-12 group. However, our study is significantly limited by the small sample sizes when the patient population was subdivided by age, so this is an area of research worth investigating further.

With regards to directionality in cases of non-concordance, which we defined as any ICC less than "moderate" (<0.4), our study demonstrated that in all cases, with one exception (Generic "Psychosocial" subscale in children age 5-7), mean QOL as reported by child was greater than mean QOL reported by parent. This is consistent with the literature (Feichtl et al., 2010; Russell et al., 2006; Tluczek et al., 2013; Vance et al., 2001), stating that parents tend to underestimate child QOL. The one exception to the lower rating of child QOL by parents was in a sub group with a very small sample size (13 patients), so this inconsistency is likely attributable to the small sample size and cannot be interpreted in this study.

Furthermore, as discussed above, PAT scores predicted parent proxy reports of QOL ratings on three QOL measures (Generic Total, Generic "Psychosocial," and Cancer Total). Therefore, it is conceivable that a parent's state of psychosocial distress may be coloring their perception of a child's QOL, and that parents who carry high psychosocial risk may rate their child's QOL as lower because they assume their child is struggling as well. It will important for clinicians to discern whether parent proxy ratings of a child's QOL are biased by the parent's own psychosocial risk state, and whether parent interventions might help improve both the concordance between parent-child reports as well as child QOL itself.

Limitations of this study include a small sample size, particularly when investigating concordance levels between child and parent proxy QOL reports in subsets of our patient population (such as child age). Furthermore, there was limited variability in certain measures, such as ITR, which limited the power of our study to draw significant conclusions regarding how this variable might contribute to differences in child QOL. Lastly, the fact that the vast majority of measures utilized in the present study were self report warrants concern that subjects might have not been completely honest in their responses if they were operating under a social desirability bias.

In summary, though this study was limited by sample size, variability in certain measures (such as ITR), and the self-report nature of the study measures, we were able to draw meaningful results about factors contributing to child QOL in pediatric cancer patients as

well as the concordance between child and parent proxy QOL reports. PAT total score emerged as an important predictor of parent proxy reports of child QOL, which warrants consideration that a parent's psychosocial risk state might impact their perception of their child's QOL. This idea warrants consideration of parent interventions for families with high psychosocial risk, particularly because parent stress has been shown to adversely affect family and child adjustment in pediatric cancer cases (Abad, 2008; Kazak & Barakat, 1997; Litzelman et al., 2011; Meeske et al., 2007; Roddenberry & Renk, 2008; Vance et al., 2001). The fact that males experienced significantly higher QOL on many QOL subscales should attune physicians to the fact that females might require additional psychosocial services during treatment. With regards to concordance, the concordance levels in our sample were generally moderate or greater, with the exception of the Generic "Psychosocial" subscale in many cases, suggesting that clinicians should be wary of making conclusions about a child's psychosocial state based on parent proxy reports only. Given the importance of focusing on (and improving) child QOL in the treatment of pediatric cancer as well as other chronic pediatric illnesses, this study has wide implications.

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TABLES AND FIGURES

Table I: Demographic and Diagnostic Characteristics of Patient and Parent Population Sample

Variables	**Range**	**Mean (±SD)**	**Number (%)**
Child Age (Years)	2-20	10.02 ± 5.473	
Child Sex			
Male			47 (53.4)
Female			41 (46.6)
Malignancy			
Hematologic			52 (59.1)
Solid Tumor			28 (31.8)
Neurologic			7 (8.0)
Other			1 (1.1)
Parent			
Male			19 (21.6)
Female			69 (78.4)

Table 2: Descriptive information (means and standard deviations) for PAT, ITR, and QOL measures utilized in the present study (taken at 6 months out from diagnosis), as compared to averages in both healthy controls and a cancer population as reported by Varni et al. (2002).

Measure	**Mean (±SD) in Present Study**	**Mean (±SD) for Cancer Sample (Varni et al., 2002)**	**Corresponding Mean (±SD) for Healthy Sample (Varni et al., 2002)**
PAT Total Score	0.9412 (±0.66416)		
PAT "Family Structure and Resources" subscale	0.1494 (±.17793)		
PAT "Caregiver Stress Reactions" subscale	0.1891(±0.30677)		
ITR	2.76 (±0.695)		
QOL Measures			
Generic Total (child)	67.1356 (±18.94810)	72.20 (±16.38)	83.00 (±14.79)
Generic Total (proxy)	62.9042 (±19.56763)	69.70 (±19.17)	87.61 (±12.33)
Generic "Psychosocial" subscale (child)	72.7077 (±19.85457)	72.62 (±16.41)	82.38 (±15.51)
Generic "Psychosocial" subscale (proxy)	70.4820 (±18.20888)	70.31 (±17.96)	86.58 (±12.79)
Generic "Physical Functioning" subscale (child)	50.000 (±34.61735)	71.79 (±21.80)	84.41 (±17.26)
Generic "Physical	53.1548 (±33.77619)	68.75 (±24.98)	89.32 (±16.35)

Functioning" subscale (proxy)			
Cancer Total (child)	72.7816 (±17.65862)		
Cancer Total (proxy)	69.2659 (±14.61191)		

Table 3: Multivariate linear regression results for PAT total, child age, child gender, and ITR with outcome of child QOL. Only significant results ($p<0.05$) are displayed.

Outcome Variable (R^2)	**Significant Associations**	**p-value, β±SD, t**
Generic Total (child) (R^2=0.131)	Gender	p=0.024 β=(-)12.003±5.168 t=(-)2.322
Generic Total (proxy) (R^2=0.175)	PAT Total	p=0.031 β=(-)7.135±3.257 t=(-)2.191
	Gender	p=0.001 β=(-)13.383±4.216 t=(-)3.295
Generic "Psychosocial" subscale (child)	N/A	N/A
Generic "Psychosocial" subscale (proxy) (R^2=0.157)	PAT Total	p=0.004 β=(-)9.309±3.119 t=(-)2.984
	Gender	p=0.005 β=(-)11.495±4.013 t=(-)2.864
Generic "Physical Functioning" subscale (child) (R^2=0.081)	Gender	p=0.046 β=(-)19.828±9.695 t=(-)2.045
Generic "Physical Functioning" subscale (proxy) (R^2=0.126)	Gender	p=0.015 β=(-)18.714±7.548 t=(-)2.479)
Cancer Total (child) (R^2=0.118)	Gender	p=0.016 β=(-)11.531±4.629 t=(-)2.491
Cancer Total (proxy) (R^2=0.271)	PAT Total	p=0.001 β=(-)8.232±2.273 t=(-)3.622
	Age	p=0.003 β=(-).821±0.267 t=(-)3.073
	Gender	p<0.001 β=(-)12.143±2.879 t=(-)4.217

Table 4: Qualifying concordance based on ICC value, as per Landis & Koch (1977).

ICC Value	Strength of Agreement
<0.0	Poor
0.0-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Almost Perfect

Table 5: Quantifying concordance between child and parent proxy reports of child QOL at 6 months from initial diagnosis using single measure ICC's.

QOL Measure	Sample Size	ICC	95% CI	Agreement
Generic Total	55	.506	.279-.679	Moderate
Generic "Psychosocial" subscale	54	.290	.031-.514	Fair
Generic "Physical Functioning" subscale	54	.612	.412-.755	Substantial
Cancer Total	55	.637	.396-.785	Substantial

Table 6a: Quantifying concordance between child and parent proxy reports of child QOL using single measure ICC's, with regards to time since diagnosis. We compared ICC's within 4 weeks of initial diagnosis to ICC's at 6 months following diagnosis.

Permutation	QOL Measure	Sample Size	ICC	Agreement	95% CI
Within 4 Weeks of Diagnosis	Generic Total	56	.541	Moderate	.321-.705
	Generic "Psychosocial" subscale	55	.510	Moderate	.288-.680
	Generic "Physical Functioning" subscale	56	.628	Substantial	.433-.765
	Cancer Total	56	.429	Moderate	.185-.622
6 Months Following Diagnosis	Generic Total	55	.506	Moderate	.279-.679
	Generic "Psychosocial" subscale**	54	.290	Fair	.031-.514
	Generic "Physical Functioning" subscale	54	.612	Substantial	.412-.755
	Cancer Total	55	.637	Substantial	.396-.785

** Indicates an ICC less than 0.40 (which corresponds to less than "moderate" concordance between child and parent-proxy reports, with $p<0.05$

Table 6b: Quantifying concordance between child and parent proxy reports of child QOL using single measure ICC's, with regards to child gender (male or female). These ICC's represent concordance at 6 months following diagnosis.

Permutation	QOL Measure	Sample Size	ICC	Agreement	95% CI
Male	Generic Total	30	.499	Moderate	.175-.725
	Generic "Psychosocial" subscale**	29	.295	Fair	-.074-.593
	Generic "Physical Functioning" subscale	30	.610	Substantial	.326-.793
	Cancer Total	30	.555	Moderate	.250-.760
Female	Generic Total	25	.483	Moderate	.117-.734
	Generic "Psychosocial" subscale**	25	.208	Fair	-.198-.553
	Generic "Physical Functioning" subscale	24	.594	Moderate	.269-.799
	Cancer Total	25	.729	Substantial	.418-.878

** Indicates an ICC less than 0.40 (which corresponds to less than "moderate" concordance between child and parent-proxy reports, but ICC's were not significant (p>0.05)

Table 6c: Quantifying concordance between child and parent proxy reports of child QOL using single measure ICC's, with regards to child age (5-7 years, 8-12 years, 13-17 years). These ICC's represent concordance at 6 months following diagnosis.

Permutation	QOL Measure	Sample Size	ICC	Agreement	95% CI
Age 5-7 years	Generic Total	13	.651	Substantial	.162-.880
	Generic "Psychosocial" subscale**	13	.128	Slight	-.434-.618
	Generic "Physical Functioning" subscale	13	.724	Substantial	.335-.906
	Cancer Total	13	.792	Substantial	.441-.932
Age 8-12	Generic Total**	15	.201	Slight	-.184-.594
	Generic "Psychosocial" subscale	14	.434	Moderate	-.044-.868
	Generic "Physical Functioning" subscale	14	.469	Moderate	-.025-.789
	Cancer Total	15	.464	Moderate	-.044-.784
Age 13-17	Generic Total	27	.558	Moderate	.243-.769
	Generic "Psychosocial" subscale***	27	.369	Fair	.021-.645
	Generic "Physical Functioning" subscale	27	.611	Substantial	.304-.802
	Cancer Total	27	.597	Moderate	.238-.803

** Indicates an ICC less than 0.40 (which corresponds to less than "moderate" concordance between child and parent-proxy reports) but a p-value of >0.05

*** Indicates an ICC less than 0.40 (which corresponds to less than "moderate" concordance between child and parent-proxy reports) as well as a p-value of <0.05

Table 7: Means (±SD) for child and parent proxy QOL ratings in cases of low concordance (ICC<0.4).

QOL Measure	**Agreement**	**Child Mean (±SD)**	**Parent Proxy Mean (±SD)**
Generic "Psychosocial" subscale (N=55)	Fair (p<0.05)	74.7652 (±17.34555)	70.9524 (±16.59332)
Generic "Psychosocial" subscale (Males only, N=29)	Fair (P>0.05)	78.3066 (±18.71185)	74.0641 (±16.73167)
Generic "Psychosocial" subscale (Females only, N=25)	Fair (p>0.05)	70.6572 (±14.93972)	67.3428 (±16.00498)
Generic "Psychosocial" subscale (Child age 5-7 years, N=13)	Slight (p>0.05)	66.4838 (±25.20232)	73.2200 (±10.88477)
Generic Total (Child age 8-12 years, N=15)	Slight (p>0.05)	73.7767 (±15.53321)	62.3067 (±12.29643)
Generic "Psychosocial" subscale (Child age 13-17 years, N=27)	Fair (p<0.05)	76.5078 (±13.50191)	69.2037 (±19.84417)